National Asthma Council Australia

AUSTRALIAN ASTHMA HANDBOOK

VERSION 2.0

MANAGEMENT

Children

This PDF is a print-friendly reproduction of the content included in the *Management – Children* section of the *Australian Asthma Handbook* at **asthmahandbook.org.au/management/children**

Please note the content of this PDF reflects the *Australian Asthma Handbook* at publication of Version 2.0 (March 2019). For the most up-to-date content, please visit asthmahandbook.org.au

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ABBREVIATIONS

CFC	chlorofluorocarbon
COPD	chronic obstructive pulmonary disease
COX	cyclo-oxygenase
DXA	dual-energy X-ray absorptiometry
ED	emergency department
EIB	exercise-induced bronchoconstriction
FEV_1	forced expiratory volume over one second
FEV_6	forced expiratory volume over six seconds
FSANZ	Food Standards Australia and New Zealand
FVC	forced vital capacity
GORD	gastro-oesophageal reflux disease
HFA	formulated with hydrofluroalkane propellant
ICS	inhaled corticosteroid
ICU	intensive care unit
IgE	Immunoglobulin E
IL	interleukin
IU	international units
IV	intravenous
LABA	long-acting beta$_2$-adrenergic receptor agonist
LAMA	long-acting muscarinic antagonist
LTRA	leukotriene receptor antagonist
MBS	Medical Benefits Scheme
NHMRC	National Health and Medical Research Council
NIPPV	non-invasive positive pressure ventilation
NSAIDs	nonsteroidal anti-inflammatory drugs
OCS	oral corticosteroids
OSA	obstructive sleep apnoea
PaCO	carbon dioxide partial pressure on blood gas analysis
PaO	oxygen partial pressure on blood gas analysis
PBS	Pharmaceutical Benefits Scheme
PEF	peak expiratory flow
pMDI	pressurised metered-dose inhaler or 'puffer'
PPE	personal protective equipment
SABA	short-acting beta$_2$ -adrenergic receptor agonist
SAMA	short-acting muscarinic antagonist
SaO_2	oxygen saturation
SpO_2	peripheral capillary oxygen saturation measured by pulse oximetry
TGA	Therapeutic Goods Administration

RECOMMENDED CITATION

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DISCLAIMER

Managing asthma in children

Overview

Children aged 0–12 months

Wheezing infants aged less than 12 months old should not be treated for asthma. Wheezing in this age group is most commonly due to acute viral bronchiolitis or to small and/or floppy airways.

Advice should be obtained from a paediatric respiratory physician or paediatrician before administering short-acting beta$_2$ agonists, systemic corticosteroids or inhaled corticosteroids to an infant under 12 months.

Children with clinically significant wheezing that necessitates hospitalisation or occurs frequently (e.g. more than once per 6 weeks) should be referred to a paediatric respiratory physician or paediatrician.

▶ Go to: Paediatric Research in Emergency Departments International Collaborative (PREDICT) *Australasian bronchiolitis guideline*

Children aged 1–5 years

Many infants and preschoolers wheeze when they have viral respiratory infections, even if they do not have asthma.

As-needed salbutamol should be used to relieve symptoms during wheezing episodes in children with wheezing that has been shown to be salbutamol-responsive in a treatment trial.

A small proportion of infants and preschoolers may also need regular preventer treatment for preschool wheeze (e.g. those who have recurrent symptoms between viral respiratory infections.)

Table. Classification of preschool wheeze and indications for preventer treatment in children aged 1–5

Severity of flare-ups	**Frequency of symptoms**			
	Symptoms every 6 months or less	**Symptoms every 3–4 months**	**Symptoms every 4–6 weeks**	**Symptoms at least once per week**
Mild flare-ups *(managed with salbutamol in community)*	Not indicated	Not indicated	Consider	Indicated
Moderate–severe flare-ups *(require ED care/oral corticosteroids)*	Indicated	Indicated	Indicated	Indicated
Life-threatening flare-ups	Indicated	Indicated	Indicated	Indicated

Severity of flare-ups	Frequency of symptoms			
	Symptoms every 6 months or less	**Symptoms every 3–4 months**	**Symptoms every 4–6 weeks**	**Symptoms at least once per week**
(require hospitalisation or PICU)				

PICU: paediatric intensive care unit; ED: emergency department

Indicated: Prescribe preventer and monitor as a treatment trial. Discontinue if ineffective.

Not indicated: Preventer is unlikely to be beneficial

Consider prescribing preventer according to overall risk for severe flare-ups

Symptoms: wheeze, cough or breathlessness. May be triggered by viral infection, exercise or inhaled allergens

Flare-up: increase in symptoms from usual day-to-day symptoms (ranging from worsening asthma over a few days to an acute asthma episode)

Preventer options: an inhaled corticosteroid (low dose) or montelukast

[!] Advise parents/carers about potential adverse behavioural and/or neuropsychiatric effects of montelukast

Notes:

Preventer medication is unlikely to be beneficial in a child whose symptoms do not generally respond to salbutamol

In children taking preventer, symptoms should be managed with a short-acting inhaled beta$_2$ agonist reliever (e.g. when child shows difficulty breathing).

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Asset ID: 20

Figure. Stepped approach to adjusting asthma medication in children aged 1-5 years

Please view and print this figure separately: http://www.asthmahandbook.org.au/figure/show/18

Children aged 6 years and over

The diagnosis of asthma can be made with more certainty in school-aged children. In this age group, the presence of reversible expiratory airflow limitation on spirometry supports the diagnosis of asthma.

All school-aged children with asthma need a reliever to use when they have asthma symptoms.

Regular preventer treatment is indicated for those with frequent intermittent asthma (flare-ups every 6 weeks or more often) or persistent asthma symptoms (daytime asthma symptoms more than once per week or night-time symptoms more than twice per month) and those with severe flare-ups, irrespective of the frequency of flare-ups or symptoms between flare-ups.

Table. Classification of asthma and indications for initiating preventer treatment in children aged 6–11

	Average frequency of flare-ups and symptoms between flare-ups		
Severity of flare-ups	*Infrequent intermittent* **Flare-ups every 6 weeks or less and no symptoms between flare-ups**	*Frequent intermittent* **Flare-ups more than once every 6 weeks and no symptoms between flare-ups**	*Persistent* **Between flare-ups (any of):** • **Daytime symptoms‡ more than once per week** • **Night-time symptoms‡ more than**

			twice per month • **Symptoms restrict activity or sleep**
Mild flare-ups *(almost always managed with salbutamol in community)*	Not indicated	Consider	Indicated
Moderate–severe flare-ups *(>2 in past year requiring ED or oral corticosteroids)*	Consider	Indicated	Indicated
Life-threatening flare-ups *(require hospitalisation or PICU)*	Indicated	Indicated	Indicated

Preventer should be started as a treatment trial. Assess response after 4–6 weeks and review before prescribing long term.

ED: emergency department

Indicated: Prescribe preventer and monitor as a treatment trial. At follow-up, discontinue if ineffective

Not indicated: Preventer is unlikely to be beneficial

Consider prescribing preventer according to overall risk for severe flare-ups

‡ Symptoms between flare-ups. A flare-up is defined as a period of worsening asthma symptoms, from mild (e.g. symptoms that are just outside the normal range of variation for the child, documented when well) to severe (e.g. events that require urgent action by parents/carers and health professionals to prevent a serious outcome such as hospitalisation or death from asthma).

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Asset ID: 16

Figure. Stepped approach to adjusting asthma medication in children aged 6-11 years

Please view and print this figure separately: http://www.asthmahandbook.org.au/figure/show/120

General principles of asthma treatment in children

Aim for good control of asthma symptoms

Try to identify what triggers asthma symptoms (e.g. allergens).

Manage comorbid conditions that affect asthma (e.g. allergic rhinitis).

Show parents and children (if old enough) when and how to take reliever medicine.

Monitor regularly and adjust the treatment regimen to maintain good control of symptoms and prevent flare-ups, while minimising the dose of inhaled corticosteroids (if needed).

Provide parents/carers and children with information and skills to manage their asthma, including:

- a written asthma action plan to follow when symptoms worsen
- information about reducing exposure to triggers, where appropriate (e.g. all tobacco smoke, but allergens only when likely to be helpful

and cost-effective)
See: Asthma triggers
- training in correct use of medicines, including inhaler technique
- information and support to maximise adherence.
- advice about avoidance of tobacco smoke, healthy eating, physical activity, healthy weight and immunisation.

Table. Definition of levels of recent asthma symptom control in children (regardless of current treatment regimen)

Good control	Partial control	Poor control
All of: • Daytime symptoms† ≤2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • No limitation of activities‡ • No symptoms§ during night or when wakes up • Need for SABA reliever# ≤2 days per week	Any of: • Daytime symptoms† >2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • Any limitation of activities* • Any symptoms during night or when wakes up†† • Need for SABA reliever# >2 days per week	Either of: • Daytime symptoms† >2 days per week (lasting from minutes to hours or recurring, and partially or fully relieved by SABA reliever) • ≥3 features of partial control within the same week

SABA: short-acting beta$_2$ agonist

† e.g. wheezing or breathing problems

‡ child is fully active; runs and plays without symptoms

§ including no coughing during sleep

not including doses taken prophylactically before exercise. (Record this separately and take into account when assessing management.)

* e.g. wheeze or breathlessness during exercise, vigorous play or laughing

†† e.g. waking with symptoms of wheezing or breathing problems

Notes:

Recent asthma control is based on symptoms over the previous 4 weeks. Each child's risk factors for future asthma outcomes should also be assessed and taken into account in management.

Validated questionnaires can be used for assessing recent symptom control:
Test for Respiratory and Asthma Control in Kids (TRACK) for children < 5 years
Childhood Asthma Control Test (C-ACT) for children aged 4–11 years

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Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)	
	Low	High
Beclometasone dipropionate †	100–200	>200 (maximum 400)
Budesonide	200–400	>400 (maximum 800)

Inhaled corticosteroid	Daily dose (microg)	
	Low	High
Ciclesonide ‡	80–160	>160 (maximum 320)
Fluticasone propionate	100–200	>200 (maximum 500)

† Dose equivalents for *Qvar* (TGA-registered CFC-free formulation of beclometasone dipropionate)

‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

Source

van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma.* The Thoracic Society of Australia and New Zealand, 2010. Available from: http://www.thoracic.org.au/clinical-documents/area?command=record&id=14

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Figure. Stepped approach to adjusting asthma medication in children aged 1-5 years

Please view and print this figure separately: http://www.asthmahandbook.org.au/figure/show/18

Figure. Stepped approach to adjusting asthma medication in children aged 6-11 years

Please view and print this figure separately: http://www.asthmahandbook.org.au/figure/show/120

In this section

Management: ages 1–5

Managing wheezing and asthma in children aged 1–5 years, including use of relievers and preventers, reviewing and adjusting initial treatment, managing flare-ups and managing severe asthma

http://www.asthmahandbook.org.au/management/children/1-5-years

Management: age 6 and over

Managing asthma in children aged 6 years and over, including use of relievers and preventers, reviewing and adjusting initial treatment, managing flare-ups and managing severe asthma

http://www.asthmahandbook.org.au/management/children/6-years-and-over

Administering medicines

Administering inhaled medicines correctly in children, including the use of inhalers, spacers and masks

http://www.asthmahandbook.org.au/management/children/administering-medicines

Routine asthma reviews

Planning and conducting routine asthma review for children with asthma or preschool wheeze

http://www.asthmahandbook.org.au/management/children/routine-asthma-reviews

Triggers

Managing triggers in children with asthma or preschool wheeze

http://www.asthmahandbook.org.au/management/children/triggers

Education

Providing asthma management education for parents and older children

http://www.asthmahandbook.org.au/management/children/education

Figure. Stepped approach to adjusting asthma medication in children aged 1-5 years

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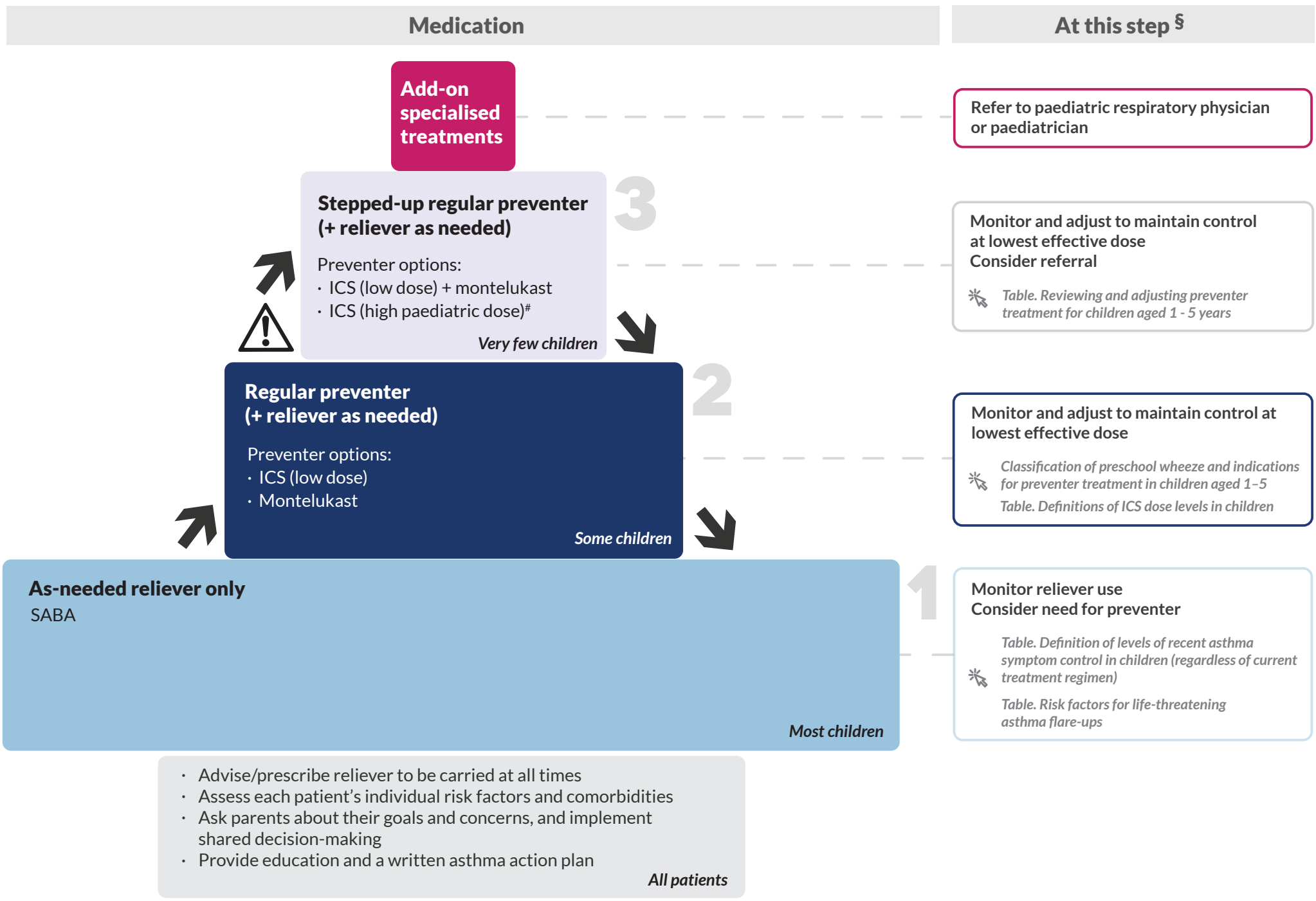

⚠	Before considering stepping up, check symptoms are due to asthma, inhaler technique is correct, and adherence is adequate
↗	Consider stepping up if good control is not achieved despite good adherence and correct inhaler technique.
↘	Consider stepping down when asthma is stable and well controlled for more than 6 months.

ICS: inhaled corticosteroid; SABA: short-acting $beta_2$ agonist; LABA: long-acting $beta_2$ agonist

§ At all steps: Review recent symptom control and risk regularly. Manage flare-ups with extra treatment when they occur. Manage exercise-related asthma symptoms as indicated.

Consultation with a specialist is recommended before prescribing high-dose inhaled corticosteroids in children aged 5 and under.

Figure. Stepped approach to adjusting asthma medication in children aged 6-11 years

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Medication	At this step§
Add-on specialised treatments	Refer to paediatric respiratory physician or paediatrician
Stepped-up regular preventer (+ reliever as needed) Preventer options: · ICS (high paediatric dose) · ICS/LABA combination (low dose) · ICS (low dose) + montelukast *Few children*	3 Monitor and adjust to maintain control at lowest effective dose Consider referral *Table. Reviewing and adjusting preventer treatment for children aged 6 years and over*
Regular preventer (+ reliever as needed) Preventer options: · ICS (low dose) · Montelukast *Some children*	2 Monitor and adjust to maintain control at lowest effective dose *Table. Initial preventer treatment for children 6 years and over* *Table. Definitions of ICS dose levels in children*
As-needed reliever only SABA *Many children*	1 Monitor reliever use Consider need for preventer *Table. Definition of levels of recent asthma symptom control in children (regardless of current treatment regimen)* *Table. Risk factors for life-threatening asthma flare-ups*
· Advise/prescribe reliever to be carried at all times · Assess each patient's individual risk factors and comorbidities · Ask parents (and children, when appropriate) about their goals and concerns, and implement shared decision-making · Provide education and a written asthma action plan ***All patients***	

⚠	Before considering stepping up, check symptoms are due to asthma, inhaler technique is correct, and adherence is adequate. Consider modifiable factors contributing to asthma symptoms (e.g. exposure to tobacco smoke or allergens, obesity or overweight).
↗	Consider stepping up if good control is not achieved despite good adherence and correct inhaler technique.
↘	Consider stepping down when asthma is stable and well controlled for more than 6 months.

ICS: inhaled corticosteroid; SABA: short-acting $beta_2$ agonist; LABA: long-acting $beta_2$ agonist

§ At all steps: Review recent symptom control and risk regularly. Manage flare-ups with extra treatment when they occur. Manage exercise-related asthma symptoms as indicated.

Managing wheezing and asthma in children aged 1–5 years

In this section

Reliever and preventer

Prescribing reliever and considering regular preventer treatment for children aged 1–5 years

http://www.asthmahandbook.org.au/management/children/1-5-years/reliever-and-preventer

Other treatments

The roles of other regular treatments in children aged 1–5 years

http://www.asthmahandbook.org.au/management/children/1-5-years/other-regular-treatments

Reviewing initial treatment

Reviewing initial treatment in children aged 1–5 years

http://www.asthmahandbook.org.au/management/children/1-5-years/reviewing-initial-treatment

Stepping down

Stepping down treatment in children aged 1–5 years

http://www.asthmahandbook.org.au/management/children/1-5-years/stepping-down

Flare-ups

Managing flare-ups in children aged 1–5 years

http://www.asthmahandbook.org.au/management/children/1-5-years/flare-ups

Severe asthma

Identifying and managing severe asthma in children aged 1–5 years

http://www.asthmahandbook.org.au/management/children/1-5-years/severe-asthma

Prescribing reliever and considering regular preventer treatment for children aged 1–5 years

Recommendations

For children with recurrent wheezing, when the diagnosis of asthma is uncertain, ask parents/carers about the frequency and severity of symptoms and what seems to trigger them.

Identify:

- **whether wheezing only occurs for a few days at a time when the child has a cold, or if the child coughs or wheezes at other times (e.g. when playing actively or laughing)**
- **whether there is increased work of breathing at these times (e.g. increased respiratory rate, tracheal tug, subcostal and intercostal recession, shortness of breath).**

Table. Classification of preschool wheeze and indications for preventer treatment in children aged 1–5

Severity of flare-ups	**Frequency of symptoms**			
	Symptoms every 6 months or less	**Symptoms every 3–4 months**	**Symptoms every 4–6 weeks**	**Symptoms at least once per week**
Mild flare-ups *(managed with salbutamol in community)*	**Not indicated**	**Not indicated**	**Consider**	**Indicated**
Moderate–severe flare-ups *(require ED care/oral corticosteroids)*	**Indicated**	**Indicated**	**Indicated**	**Indicated**
Life-threatening flare-ups *(require hospitalisation or PICU)*	**Indicated**	**Indicated**	**Indicated**	**Indicated**

PICU: paediatric intensive care unit; ED: emergency department

Indicated: Prescribe preventer and monitor as a treatment trial. Discontinue if ineffective.

Not indicated: Preventer is unlikely to be beneficial

Consider prescribing preventer according to overall risk for severe flare-ups

Symptoms: wheeze, cough or breathlessness. May be triggered by viral infection, exercise or inhaled allergens

Flare-up: increase in symptoms from usual day-to-day symptoms (ranging from worsening asthma over a few days to an acute asthma episode)

Preventer options: an inhaled corticosteroid (low dose) or montelukast

[!] Advise parents/carers about potential adverse behavioural and/or neuropsychiatric effects of montelukast

Notes:
Preventer medication is unlikely to be beneficial in a child whose symptoms do not generally respond to salbutamol

In children taking preventer, symptoms should be managed with a short-acting inhaled beta$_2$ agonist reliever (e.g. when child shows difficulty breathing).

Last reviewed version 2.0

Asset ID: 20

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- Brand et al. 2008[1]
- Brand et al. 2014[2]

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When the diagnosis of asthma is more certain, assess the frequency and severity of wheezing, other symptoms and flare-ups.

Table. Classification of preschool wheeze and indications for preventer treatment in children aged 1–5

Severity of flare-ups	**Frequency of symptoms**			
	Symptoms every 6 months or less	**Symptoms every 3–4 months**	**Symptoms every 4–6 weeks**	**Symptoms at least once per week**
Mild flare-ups (managed with salbutamol in community)	**Not indicated**	**Not indicated**	**Consider**	**Indicated**
Moderate–severe flare-ups (require ED care/oral corticosteroids)	**Indicated**	**Indicated**	**Indicated**	**Indicated**
Life-threatening flare-ups (require hospitalisation or	**Indicated**	**Indicated**	**Indicated**	**Indicated**

Severity of flare-ups	Frequency of symptoms			
	Symptoms every 6 months or less	Symptoms every 3–4 months	Symptoms every 4–6 weeks	Symptoms at least once per week
PICU)				

PICU: paediatric intensive care unit; ED: emergency department

Indicated: Prescribe preventer and monitor as a treatment trial. Discontinue if ineffective.

Not indicated: Preventer is unlikely to be beneficial

Consider prescribing preventer according to overall risk for severe flare-ups

Symptoms: wheeze, cough or breathlessness. May be triggered by viral infection, exercise or inhaled allergens

Flare-up: increase in symptoms from usual day-to-day symptoms (ranging from worsening asthma over a few days to an acute asthma episode)

Preventer options: an inhaled corticosteroid (low dose) or montelukast

[!] Advise parents/carers about potential adverse behavioural and/or neuropsychiatric effects of montelukast

Notes:

Preventer medication is unlikely to be beneficial in a child whose symptoms do not generally respond to salbutamol

In children taking preventer, symptoms should be managed with a short-acting inhaled beta$_2$ agonist reliever (e.g. when child shows difficulty breathing).

Last reviewed version 2.0

Asset ID: 20

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

If the diagnosis of asthma was made in the past or elsewhere, confirm the diagnosis, if possible.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

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Discuss the goals of asthma treatment with the child's parents/carers. Explain that the overall aims of treatment are to reduce the risk of flare-ups, make sure asthma does not interfere with play or preschool attendance, and minimise the side effects of treatment by using the lowest level of medication required to maintain good asthma control.

Ask parents about their own goals for the child's health and about their beliefs and concerns about medication.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

For all children with asthma or salbutamol-responsive preschool wheeze, prescribe a reliever suitable for the child's age: salbutamol 2–4 puffs (100 microg per puff) as needed via pressurised metered-dose inhaler plus spacer and face mask for children aged 1–2 years or pressurised metered-dose inhaler plus spacer for children aged 3–5 years (if able to cooperate).

Educate parents/carers how and when to give reliever, and advise them to carry reliever (and spacer, if needed) at all times to use when needed to manage symptoms.

- **Reliever should be used when wheezing episodes are associated with increased work of breathing. It should not be used for cough in the absence of other symptoms. In infants, it should not be used for noisy breathing when the child shows no increased work of breathing.**

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

Consider regular preventer treatment according to the child's age, frequency of symptoms, severity of flare-ups, and risk factors for severe flare-ups.

Consider regular preventer treatment for children with frequent symptoms (e.g. wheeze, cough or breathlessness at least once per week) or a history of severe flare-ups (e.g. requiring emergency department visits, intensive care or hospitalisation)

- **Regular preventer is not recommended for children younger than 12 months, except on the advice of a specialist.**

Note: This assessment should be based on overall pattern of symptoms including frequency of flare-ups and symptoms between flare-ups, not on symptoms seen during a flare-up.

Table. Classification of preschool wheeze and indications for preventer treatment in children aged 1–5

Severity of flare-ups	**Frequency of symptoms**			
	Symptoms every 6 months or less	**Symptoms every 3–4 months**	**Symptoms every 4–6 weeks**	**Symptoms at least once per week**
Mild flare-ups (managed with salbutamol in community)	**Not indicated**	**Not indicated**	**Consider**	**Indicated**
Moderate–severe flare-ups (require ED care/oral corticosteroids)	**Indicated**	**Indicated**	**Indicated**	**Indicated**
Life-threatening flare-ups (require hospitalisation or PICU)	**Indicated**	**Indicated**	**Indicated**	**Indicated**

PICU: paediatric intensive care unit; ED: emergency department

Indicated: Prescribe preventer and monitor as a treatment trial. Discontinue if ineffective.

Not indicated: Preventer is unlikely to be beneficial

Consider prescribing preventer according to overall risk for severe flare-ups

Symptoms: wheeze, cough or breathlessness. May be triggered by viral infection, exercise or inhaled allergens

Flare-up: increase in symptoms from usual day-to-day symptoms (ranging from worsening asthma over a few days to an acute asthma episode)

Preventer options: an inhaled corticosteroid (low dose) or montelukast

[!] Advise parents/carers about potential adverse behavioural and/or neuropsychiatric effects of montelukast

Notes:

Preventer medication is unlikely to be beneficial in a child whose symptoms do not generally respond to salbutamol

In children taking preventer, symptoms should be managed with a short-acting inhaled beta$_2$ agonist reliever (e.g. when child shows difficulty breathing).

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Table. Risk factors for life-threatening asthma flare-ups in children

Asthma-related factors

Poor asthma control

Admission to hospital in preceding 12 months

History of intubation for acute asthma

Over-use of short-acting beta$_2$ agonist reliever

Abnormal spirometry findings

Reversible expiratory airflow limitation on spirometry despite treatment

Poor adherence to preventer

Incorrect inhaler technique for preventer

Poor adherence to asthma action plan

Exposure to clinically relevant allergens

Exposure to tobacco smoke

Other clinical factors

Allergies to foods, insects, medicines

Obesity

Family-related factors

Frequent failure to attend consultations/lack of follow-up after an acute flare-up

Significant parental psychological or socioeconomic problems

Parent/carer unequipped to manage asthma emergency

Last reviewed version 2.0

Asset ID: 116

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s)

- van Asperen *et al.* 2010[3]
- Brand *et al.* 2014[2]

Last reviewed version 2.0

For children aged 12 months to less than 2 years, consider a treatment trial with a low dose of inhaled corticosteroids only if any of the following apply:

- **Symptoms (wheezing, cough, breathlessness) occur at least once per week and frequently disrupt child's sleeping or play.**
- **Flare-ups are generally severe enough to require ED or oral corticosteroids.**
- **The child has had a flare-up that required hospitalisation or ICU.**

Table. Classification of preschool wheeze and indications for preventer treatment in children aged 1–5

Severity of flare-ups	**Frequency of symptoms**			
	Symptoms every 6 months or less	**Symptoms every 3–4 months**	**Symptoms every 4–6 weeks**	**Symptoms at least once per week**
Mild flare-ups *(managed with salbutamol in community)*	**Not indicated**	**Not indicated**	**Consider**	**Indicated**
Moderate–severe flare-ups *(require ED care/oral corticosteroids)*	**Indicated**	**Indicated**	**Indicated**	**Indicated**
Life-threatening flare-ups *(require hospitalisation or PICU)*	**Indicated**	**Indicated**	**Indicated**	**Indicated**

PICU: paediatric intensive care unit; ED: emergency department

Indicated: Prescribe preventer and monitor as a treatment trial. Discontinue if ineffective.

Not indicated: Preventer is unlikely to be beneficial

Consider prescribing preventer according to overall risk for severe flare-ups

Symptoms: wheeze, cough or breathlessness. May be triggered by viral infection, exercise or inhaled allergens

Flare-up: increase in symptoms from usual day-to-day symptoms (ranging from worsening asthma over a few days to an acute asthma episode)

Preventer options: an inhaled corticosteroid (low dose) or montelukast

[!] Advise parents/carers about potential adverse behavioural and/or neuropsychiatric effects of montelukast

Notes:

Preventer medication is unlikely to be beneficial in a child whose symptoms do not generally respond to salbutamol

In children taking preventer, symptoms should be managed with a short-acting inhaled beta$_2$ agonist reliever (e.g. when child shows difficulty breathing).

Last reviewed version 2.0

Asset ID: 20

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

For children aged 2 years and older with frequent symptoms (e.g. wheeze, cough or breathlessness at least once per week) or a history of severe flare-ups (e.g. requiring emergency department visits or oral corticosteroids), consider a treatment trial of regular preventer with either of:

- **montelukast**
- **an inhaled corticosteroid (low dose).**

- **Advise parents/carers about potential adverse behavioural and/or neuropsychiatric effects of montelukast.**

▶ Go to: Therapeutic Goods Administration alert

Table. Classification of preschool wheeze and indications for preventer treatment in children aged 1–5

Severity of flare-ups	**Frequency of symptoms**			
	Symptoms every 6 months or less	**Symptoms every 3–4 months**	**Symptoms every 4–6 weeks**	**Symptoms at least once per week**
Mild flare-ups *(managed with salbutamol in community)*	**Not indicated**	**Not indicated**	**Consider**	**Indicated**
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PICU: paediatric intensive care unit; ED: emergency department

Indicated: Prescribe preventer and monitor as a treatment trial. Discontinue if ineffective.

Not indicated: Preventer is unlikely to be beneficial

Consider prescribing preventer according to overall risk for severe flare-ups

Symptoms: wheeze, cough or breathlessness. May be triggered by viral infection, exercise or inhaled allergens

Flare-up: increase in symptoms from usual day-to-day symptoms (ranging from worsening asthma over a few days to an acute asthma episode)

Preventer options: an inhaled corticosteroid (low dose) or montelukast

[!] Advise parents/carers about potential adverse behavioural and/or neuropsychiatric effects of montelukast

Notes:

Preventer medication is unlikely to be beneficial in a child whose symptoms do not generally respond to salbutamol

In children taking preventer, symptoms should be managed with a short-acting inhaled beta$_2$ agonist reliever (e.g. when child shows difficulty breathing).

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Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)	
	Low	High
Beclometasone dipropionate †	100–200	>200 (maximum 400)
Budesonide	200–400	>400 (maximum 800)
Ciclesonide ‡	80–160	>160 (maximum 320)
Fluticasone propionate	100–200	>200 (maximum 500)

† Dose equivalents for *Qvar* (TGA-registered CFC-free formulation of beclometasone dipropionate)

‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

Source

van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma*. **The Thoracic Society of Australia and New Zealand, 2010. Available from: http://www.thoracic.org.au/clinical-documents/area?command=record&id=14**

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Asset ID: 21

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Castro-Rodriguez *et al.* 2018[4]
- Fitzpatrick *et al.* 2016[5]
- Szefler *et al.* 2013[6]
- Bacharier *et al.* 2008[7]
- Kooi *et al.* 2008[8]
- Knorr *et al.* 2001[9]
- Brodlie *et al.* 2015[10]

Last reviewed version 2.0

An inhaled corticosteroid should be considered as the first choice preventer for those with symptoms that are frequent (e.g. daytime or night-time symptoms at least once per week), symptoms that restrict activity or sleep), or a history of severe flare-ups (e.g. requiring treatment in the emergency department or hospital admission).

An inhaled corticosteroid could also be preferable when either of the following are present:

- **atopy**
- **raised blood eosinophil count (if known; this test is not recommended routinely).**

When starting preventer for the first time for a child aged 2 years or over, the choice of agent can be guided by the following considerations.

Montelukast might be considered as alternative to an inhaled corticosteroid when any of the following apply:

- **The child is unable or refuses to use to pMDI + spacer/mask.**
- **The child has significant allergic rhinitis that requires treatment.**
- **Parents, despite education about risks and benefits, decline inhaled corticosteroids or are significantly concerned about their adverse effects (poor adherence is likely in this context).**

Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)	
	Low	High
Beclometasone dipropionate †	100–200	>200 (maximum 400)
Budesonide	200–400	>400 (maximum 800)
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Fluticasone propionate	100–200	>200 (maximum 500)

† Dose equivalents for *Qvar* **(TGA-registered CFC-free formulation of beclometasone dipropionate)**

‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

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- Fitzpatrick *et al.* 2016[5]
- Szefler *et al.* 2013[6]
- Bacharier *et al.* 2008[7]
- Kooi *et al.* 2008[8]
- Knorr *et al.* 2001[9]
- Brodlie *et al.* 2015[10]

Last reviewed version 2.0

For children aged 2 years and older with symptoms that are frequent (e.g. every day, or night-time symptoms at least once per week), symptoms that restrict activity or sleep), or a history of severe flare-ups (e.g. requiring treatment in the emergency department or hospital admission), consider an inhaled corticosteroid (low dose) as first-choice preventer.

Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)	
	Low	High

† Dose equivalents for *Qvar* (TGA-registered CFC-free formulation of beclometasone dipropionate)

‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

Source

van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma*. **The Thoracic Society of Australia and New Zealand, 2010. Available from:**
http://www.thoracic.org.au/clinical-documents/area?command=record&id=14

Last reviewed version 2.0

Asset ID: 21

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- van Asperen *et al.* 2010[3]
- Brand *et al.* 2014[2]

Last reviewed version 2.0

When prescribing montelukast, start as a treatment trial. Review effects at 4–6 weeks and discontinue if no response.

How this recommendation was developed

Evidence-based recommendation

Based on literature search and formulated by multidisciplinary working group

Key evidence considered:

- Fitzpatrick *et al.* 2016[5]
- Szefler *et al.* 2013[6]
- Bacharier *et al.* 2008[7]
- Kooi *et al.* 2008[8]
- Knorr *et al.* 2001[9]
- Brodlie *et al.* 2015[10]

Last reviewed version 2.0

When prescribing montelukast, warn parents/carers that behavioural and/or neuropsychiatric effects of montelukast are possible, but do not occur in the majority of children. Explain that if these adverse effects occur, they are typically seen within the first 2 weeks of starting regular treatment but resolve soon after discontinuing.

When dispensing montelukast in pharmacies, counsel parents/carers about behavioural and/or neuropsychiatric effects of montelukast and provide the consumer medicines information leaflet.

▶ Go to: TGA alert

How this recommendation was developed

Evidence-based recommendation

Based on literature search and formulated by multidisciplinary working group

Key evidence considered:

- Bernard *et al.* 2017[11]
- Aldea Perona *et al.* 2016[12]
- Wallerstedt *et al.* 2009[13]
- Philip *et al.* 2009[14]

- Philip *et al.* 2009[15]
- Ali *et al.* 2015[16]
- Therapeutic Goods Administration[17]
- Schumock *et al.* 2012[18]

Last reviewed version 2.0

When prescribing regular inhaled corticosteroids, begin with a low dose.

Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)	
	Low	High
Beclometasone dipropionate †	100–200	>200 (maximum 400)
Budesonide	200–400	>400 (maximum 800)
Ciclesonide ‡	80–160	>160 (maximum 320)
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Last reviewed version 2.0

Asset ID: 21

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- van Asperen *et al.* 2010[3]

Last reviewed version 2.0

More information

Short-acting beta-2 agonist relievers for children: 1–5 years

Infants under 12 months

In infants under 12 months, bronchiolitis is the most likely cause of acute respiratory distress. Bronchodilators are not recommended in children under 12 months old, consistent with current guidelines for the management of acute bronchiolitis.[19]

Children aged 1–5 years

Inhaled short-acting beta$_2$ agonists are effective bronchodilators in children aged 1–5 years.[1]

Short-acting beta$_2$ agonists may be less effective for wheezing in children under 2 years old than in older children.[20] However, many

clinical trials in infants have included those with bronchiolitis, so there is limited evidence for the effects of short-acting beta$_2$ agonists specifically in asthma.[20] Studies conducted in emergency departments have shown that short-acting beta$_2$ agonists are more effective than placebo in controlling acute wheeze in children under 2 years, but may not achieve clinically significant improvements.[20]

Inhaled short-acting beta$_2$ agonists are generally well tolerated in children aged 1–5 years.[1] Adverse effects can include muscle tremor, headache, palpitations and agitation. Muscle tremor and agitation are common with initial use of standard doses, but often settle over time. Serious adverse effects such as hypokalaemia have been reported at very high doses.[1]

Oral short-acting beta$_2$ agonists are associated with adverse effects[1] and should not be used for the treatment of asthma in any age group.

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Administration of inhaled medicines in children: 6 years and over

Parents, carers and children need training to use inhaler devices correctly, including inhaler technique, and care and cleaning of inhalers and spacers.

School-aged children (depending on the child's age, ability, and with individualised training) can learn to use a range of inhaler types, including manually actuated pressurised metered-dose inhalers with spacers, breath-actuated pressurised metered-dose inhalers (e.g. Autohaler), and dry-powder inhalers (e.g. Accuhaler, Turbuhaler).[21, 22, 23, 24, 25]

Table. Types of inhaler devices for delivering asthma and COPD medicines

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/75

A pressurised metered-dose inhaler and spacer is an appropriate first choice for most children.[23]

School-aged children are unlikely to use their inhaler device correctly without careful training and repeated checking.[26]

▶ Go to: National Asthma Council Australia's *How to use a puffer and spacer for kids* video
Go to: National Asthma Council Australia's information paper for health professionals on *Inhaler technique for people with asthma or COPD*

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Correct use of inhaler devices

Checking and correcting inhaler technique is essential to effective asthma management.

Most patients with asthma or COPD do not use their inhalers properly,[27, 28,29, 29, 30] and most have not had their technique checked or corrected by a health professional.

Incorrect inhaler technique when using maintenance treatments increases the risk of severe flare-ups and hospitalisation for people with asthma or COPD.[27, 28, 31, 32, 33, 34]

Poor asthma symptom control is often due to incorrect inhaler technique.[35, 36]

Incorrect inhaler technique when using inhaled corticosteroids increases the risk of local side effects like dysphonia and oral thrush.

The steps for using an inhaler device correctly differ between brands. Checklists of correct steps for each inhaler type and how-to videos are available from the National Asthma Council website.

▶ Go to: National Asthma Council Australia's *Using your inhaler* webpage for information, patient resources and videos on inhaler technique
Go to: National Asthma Council Australia's information paper for health professionals on *Inhaler technique for people with asthma or COPD*
Go to: NPS MedicineWise information on *Inhaler devices for respiratory medicines*

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Preparation of new spacers before first use

Spacers are made of plastic, antistatic polymer/polycarbonate polyurethane, or cardboard.

Plastic spacers (e.g. Breath-A-Tech, Volumatic)

Electrostatic surface charge on new spacers made of plastic (e.g. *Breath-A-Tech*, *Volumatic*) reduces the proportion of medicine available for delivery to the airway. This charge can be reduced by washing the plastic spacer in dishwashing liquid and allowing it to air dry or drip-dry without rinsing or wiping.[1]

Alternatively, priming the spacer by actuating the device several times into the spacer also overcomes the charge, but this wastes medicine. The optimal number of actuations for priming is not known and the findings of in vitro studies vary widely. One study (using older, CFC-based formulations of asthma medicines) reported that up to 40 actuations fired into a new plastic spacer overcame the effect of the electrostatic charge.[37] Others have concluded that the electrostatic charge on plastic spacers does not reduce in vivo efficacy of bronchodilator therapy in children with asthma.[38] The number of actuations necessary may be known when the results of recent studies become available.

When a new plastic spacer must be used immediately (e.g. for a person with asthma symptoms), patients, parents and carers should follow the manufacturer's priming instructions. In hospitals and emergency departments, a new spacer that has not been pre-treated by washing can be primed using multiple (at least 10) puffs of salbutamol. (This is an arbitrary number of actuations in the absence of evidence that would enable a precise guideline.)

Non-plastic spacers

Disposable cardboard spacers (e.g. DispozABLE, LiteAire) and polyurethane/antistatic polymer spacers (e.g. *Able A2A*, *AeroChamber Plus*, *La Petite E-Chamber*, *La Grande E-Chamber*) do not require preparation before first use.[1]

Note: The term 'priming' is also used for the preparation process that is necessary for new pressurised metered-dose inhalers that have not been used for more than a week. This involves first actuating the inhaler into the air (away from the patient). Users should follow the manufacturer's instructions for the particular brand of inhaler, which specify the number of actuations required.

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Classification of symptom patterns in children

The pattern and severity of symptoms in a child with asthma or preschool wheeze is a guide to initial treatment.

Table. Classification of preschool wheeze and indications for preventer treatment in children aged 1–5

Severity of flare-ups	**Frequency of symptoms**			
	Symptoms every 6 months or less	**Symptoms every 3–4 months**	**Symptoms every 4–6 weeks**	**Symptoms at least once per week**
Mild flare-ups *(managed with salbutamol in community)*	Not indicated	Not indicated	Consider	Indicated
Moderate–severe flare-ups *(require ED care/oral corticosteroids)*	Indicated	Indicated	Indicated	Indicated
Life-threatening flare-ups *(require hospitalisation or PICU)*	Indicated	Indicated	Indicated	Indicated

PICU: paediatric intensive care unit; ED: emergency department

Indicated: Prescribe preventer and monitor as a treatment trial. Discontinue if ineffective.

Not indicated: Preventer is unlikely to be beneficial

Consider prescribing preventer according to overall risk for severe flare-ups

Symptoms: wheeze, cough or breathlessness. May be triggered by viral infection, exercise or inhaled allergens

Flare-up: increase in symptoms from usual day-to-day symptoms (ranging from worsening asthma over a few days to an acute asthma episode)

Preventer options: an inhaled corticosteroid (low dose) or montelukast

[!] Advise parents/carers about potential adverse behavioural and/or neuropsychiatric effects of montelukast

Notes:

Preventer medication is unlikely to be beneficial in a child whose symptoms do not generally respond to salbutamol

In children taking preventer, symptoms should be managed with a short-acting inhaled beta$_2$ agonist reliever (e.g. when child shows difficulty breathing).

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Table. Definitions of asthma patterns in children aged 6 years and over not taking regular preventer

Category		Pattern and intensity of symptoms (when not taking regular treatment)
Infrequent intermittent asthma †		Symptom-free for at least 6 weeks at a time (flare-ups up to once every 6 weeks on average but no symptoms between flare-ups)
Frequent intermittent asthma		Flare-ups more than once every 6 weeks on average but no symptoms between flare-ups
Persistent asthma	*Mild*	FEV_1 ≥80% predicted and at least one of: • Daytime symptoms‡ more than once per week but not every day • Night-time symptoms‡ more than twice per month but not every week
	Moderate	Any of: • FEV_1 <80% predicted‡ • Daytime symptoms‡ daily • Night-time symptoms‡ more than once per week • Symptoms sometimes restrict activity or sleep
	Severe	Any of: • FEV_1 ≤60% predicted‡ • Daytime symptoms‡ continual • Night-time symptoms‡ frequent • Flare-ups frequent • Symptoms frequently restrict activity or sleep

† It may not be appropriate to make the diagnosis of asthma in children aged 6 or older who wheeze only during upper respiratory tract infections. These children can be considered to have episodic (viral) wheeze.

‡ Symptoms between flare-ups. A flare-up is defined as a period of worsening asthma symptoms, from mild (e.g. symptoms that are just outside the normal range of variation for the child, documented when well) to severe (e.g. events that require urgent action by parents and health professionals to prevent a serious outcome such as hospitalisation or death from asthma).

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Table. Classification of asthma and indications for initiating preventer treatment in children aged 6–11

Severity of flare-ups	**Average frequency of flare-ups and symptoms between flare-ups**		
	Infrequent intermittent **Flare-ups every 6 weeks or less and no symptoms between flare-ups**	*Frequent intermittent* **Flare-ups more than once every 6 weeks and no symptoms between flare-ups**	*Persistent* **Between flare-ups (any of):** • **Daytime symptoms‡ more than once per week** • **Night-time symptoms‡ more than twice per month** • **Symptoms restrict activity or sleep**
Mild flare-ups *(almost always managed with salbutamol in community)*	Not indicated	Consider	Indicated
Moderate–severe flare-ups *(>2 in past year requiring ED or oral corticosteroids)*	Consider	Indicated	Indicated
Life-threatening flare-ups *(require hospitalisation or PICU)*	Indicated	Indicated	Indicated

Preventer should be started as a treatment trial. Assess response after 4–6 weeks and review before prescribing long term.

ED: emergency department

Indicated: Prescribe preventer and monitor as a treatment trial. At follow-up, discontinue if ineffective

Not indicated: Preventer is unlikely to be beneficial

Consider prescribing preventer according to overall risk for severe flare-ups

‡ Symptoms between flare-ups. A flare-up is defined as a period of worsening asthma symptoms, from mild (e.g. symptoms that are just outside the normal range of variation for the child, documented when well) to severe (e.g. events that require urgent action by parents/carers and health professionals to prevent a serious outcome such as hospitalisation or death from asthma).

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For children already taking regular preventer treatment, adjustments to the treatment regimen are based on finding the lowest dose of medicines that will maintain good control of symptoms.

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Wheezing phenotypes in preschool children

Longitudinal population-based cohort studies[39, 40] of preschool children with wheezing have identified various long-term patterns (wheezing phenotypes).[1]

Table. Systems for retrospectively classifying the duration of childhood wheeze

Classification system/source	Phenotypes identified	Description
Tucson Children's Respiratory Study † ‡	*Transient wheeze*	Wheezing commences before the age of 3 years and disappear by age 6 years
	Persistent wheeze	Wheezing continues until up to or after age 6 years
	Late-onset wheeze	Wheezing starts after age 3 years.
Avon Longitudinal Study of Parents and Children §	*Transient early wheeze*	Wheezing mainly occurs before 18 months, then mainly disappears by age 3.5 years Not associated with hypersensitivity to airborne allergens
	Prolonged early wheeze	Wheezing occurs mainly between age 6 months and 4.5 years, then mainly disappears before child's 6th birthday Not associated with hypersensitivity to airborne allergens Associated with a higher risk of airway hyperresponsiveness and reduced lung function at age 8–9 years, compared with never/infrequent wheeze phenotype
	Intermediate-onset wheeze	Wheezing begins sometime after age 18 months and before 3.5 years. Strongly associated with atopy (especially house mite, cat allergen), higher risk of airway hyperresponsiveness and reduced lung function at age 8–9 years, compared with never/infrequent wheeze phenotype
	Late-onset wheeze	Wheezing mainly begins after age 3.5 years

Classification system/source	Phenotypes identified	Description
		Strongly associated with atopy (especially house mite, cat allergen, grass pollen)
	Persistent wheeze	Wheezing mainly begins after 6 months and continues through to primary school Strongly associated with atopy

Notes

Terms can only be identified after the child has stopped wheezing for several years and cannot be applied to a preschool child.

Transient wheeze, persistent wheeze and late-onset wheeze can be episodic or multiple-trigger wheeze.#

Sources

† Martinez FD, Wright AL, Taussig LM et al. Asthma and wheezing in the first six years of life. The Group Health Medical Associates. *N Engl J Med* 1995; 332: 133-8. Available from: http://www.nejm.org/doi/full/10.1056/NEJM199501193320301#t=article

‡ Morgan WJ, Stern DA, Sherrill DL et al. Outcome of asthma and wheezing in the first 6 years of life: follow-up through adolescence. *Am J Respir Crit Care Med* 2005; 172: 1253-8. Available from: http://ajrccm.atsjournals.org/content/172/10/1253.long

§ Henderson J, Granell R, Heron J et al. Associations of wheezing phenotypes in the first 6 years of life with atopy, lung function and airway responsiveness in mid-childhood. *Thorax* 2008; 63: 974-80. Available from: http://thorax.bmj.com/content/63/11/974.long

Brand PL, Baraldi E, Bisgaard H et al. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach [European Respiratory Society Task Force]. *Eur Respir J* 2008; 32: 1096-110. Available from: http://erj.ersjournals.com/content/32/4/1096.full

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Early childhood wheezing phenotypes cannot be recognised or applied clinically, because they are recognised retrospectively.[1] In an individual child with episodic wheeze, it is not possible to accurately predict epidemiological phenotype from clinical phenotype.[1]

Currently available tools for predicting whether a wheezing preschool child will have asthma at school age (e.g. the Asthma Predictive Index[41]) have limited clinical value.[42]

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Inhaled corticosteroids for children: efficacy

Role in treatment asthma in children

The effectiveness of ICS in children appears to depend on several factors including the child's age, which triggers are causing symptoms, wheezing phenotype, tobacco smoke exposure and genotype.[43] Overall, inhaled corticosteroids seem to be more effective in older children and those with more severe disease.[3]

Early introduction of inhaled corticosteroid for children with recurrent wheeze does not prevent airway remodelling, improve long-term lung function or prevent the onset of persistent asthma, according to current evidence from long-term randomised controlled clinical trials in preschool children and school-aged children with intermittent or mild persistent asthma.[3]

Current evidence does not support planned seasonal use of inhaled corticosteroids in children not taking preventer at other times.[44]

Children aged 1–5 years

Intermittent wheeze/asthma

In preschool children who only have wheezing episodes with viral respiratory infections, limited available evidence suggests that regular treatment with inhaled corticosteroids does not reduce the risk of hospitalisation, flare-ups that require oral corticosteroid use, or reduce the frequency and duration of acute episodes.[43, 45] Inhaled corticosteroid treatment does not reduce these children's risk of developing persistent wheeze by age 6 years.[1]

Persistent wheeze/asthma

In preschool children who have episodes of wheezing from time to time, but also cough and wheezes at other times when they do not have a viral cold (e.g. when cries, plays or laughs), regular inhaled corticosteroids are moderately effective in controlling symptoms, though less effective than in older children.[1] When wheeze improves markedly during a short treatment trial (e.g. 3 months), it is not possible to tell whether improvement was due to the treatment or spontaneous resolution of symptoms.[1] However, this can be clarified by stopping inhaled corticosteroid treatment, monitoring symptoms, and re-starting.

In infants and preschoolers with persistent wheezing or asthma of at least 6 months' duration, regular treatment with inhaled corticosteroids improves wheezing, asthma symptoms and lung function, and reduces flare-ups.[3, 46]

Children aged 6 years and over

Most clinical trials of regular inhaled corticosteroid treatment in children have been conducted among children with asthma symptoms every week or more often ('persistent asthma').[3]

Beclometasone dipropionate, budesonide, ciclesonide and fluticasone propionate have all been shown to be effective in children. There have been relatively fewer studies of ciclesonide in children,[3] but, overall, randomised clinical trials show that it is equally effective as budesonide or fluticasone propionate in improving asthma symptoms and reducing flare-ups.[47] In some studies, ciclesonide was associated with less adrenal suppression or height than comparator inhaled corticosteroids.[47]

In a study of school-aged children with more than 2 days per week with symptoms, night waking more than twice per month due to asthma symptoms, or needing regular preventer, regular low-dose daily inhaled corticosteroid treatment reduced the rate of flare-ups that require treatment with oral corticosteroids, compared with no regular preventer treatment and as-needed short-acting beta$_2$agonist for wheezing episodes.[48]

In a study of children aged 4–11 years with asthma diagnosed within the previous 2 years and symptoms more than weekly in the previous 3 months, regular preventer was associated with a reduction in serious flare-ups, school absence due to asthma, an increase in symptom-free days, and improved lung function, compared with placebo.[49, 50]

The Thoracic Society of Australia and New Zealand's current position statement on the use of inhaled corticosteroids in children[3] recommends regular treatment with inhaled corticosteroid:

- as a first-choice preventer for children with asthma symptoms at least daily or night-time symptoms at least twice per week between flare-ups
- as an alternative to cromones (nedocromil or sodium cromoglycate) or montelukast in children with any daytime or night-time symptoms between flare-ups, or those with flare-ups every 6 weeks or more.

Doses

In the majority of children, asthma control can be achieved with any of the following initial doses:[3]

- budesonide up to 400 microg/day
- beclometasone (*Qvar*) up to 200 microg/day
- ciclesonide up to 160 microg/day
- fluticasone propionate up to 200 microg/day.

If these doses do not achieve control of symptoms, possible explanations include alternative diagnoses, adherence, incorrect inhaler technique, psychosocial factors and exposure to tobacco smoke or other triggers such as allergens.[3]

Dose–response studies of inhaled corticosteroids show that the maximal efficacy is generally achieved at a dose equivalent to approximately 200 microg/day fluticasone propionate,[3] while the risk of adrenal suppression increases exponentially at doses above 500 microg/day.[3] Therefore (based on theoretical equivalents between different agents), upper limits of daily doses for children are:

- budesonide 800 microg/day
- beclometasone dipropionate [*Qvar*] 400 microg/day
- ciclesonide 320 microg/day
- fluticasone propionate 500 microg/day.

Higher doses are unlikely to be more effective, and are likely to cause systemic effects.[3]

Most studies of inhaled corticosteroids in children have used twice-daily dosing.[3] Fluticasone propionate is only approved for twice-daily dosing, but the other inhaled corticosteroids are approved for once daily dosing. Ciclesonide is effective when given once daily.[3]

Note: Do not use beclometasone dose recommendations from outdated or overseas guidelines based on older formulations containing CFC propellant – doses are different.

Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)

	Low	High
Beclometasone dipropionate †	100–200	>200 (maximum 400)
Budesonide	200–400	>400 (maximum 800)
Ciclesonide ‡	80–160	>160 (maximum 320)
Fluticasone propionate	100–200	>200 (maximum 500)

† Dose equivalents for *Qvar* (TGA-registered CFC-free formulation of beclometasone dipropionate)

‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

Source

van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma.* The Thoracic Society of Australia and New Zealand, 2010. Available from: http://www.thoracic.org.au/clinical-documents/area?command=record&id=14

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Inhaled corticosteroids for children: adverse effects

Local adverse effects

Hoarseness and pharyngeal candidiasis are not commonly reported among preschool children or school-aged children talking inhaled corticosteroids. [1, 3, 51]

Topical effects can be reduced by use of spacer devices (which reduce oropharyngeal deposition), and by mouth-rinsing and spitting after use.[3] Immediate quick mouth-rinsing removes more residual medicine in the mouth than delayed rinsing.[52]

There is limited evidence that inhaled asthma medication can affect dental health.[3, 53] Mouth rinsing might reduce this risk.

Systemic adverse effects

Systemic effects of inhaled corticosteroids in children depend on the dose, but clinically significant adverse effects are uncommon.[3]

The use of spacers and mouth rinsing will not reduce systemic effects, but the use of a spacer may increase efficacy so that a lower dose is required.

Growth

Short-term suppression of linear growth has been demonstrated in children taking inhaled corticosteroids.[54,55] The effect seems to be maximal during the first year of therapy and only one study has reported an effect in subsequent years of treatment.[55] A Cochrane systematic review concluded that regular use of inhaled corticosteroid at low or medium daily doses is associated with a mean reduction of 0.48 cm per year in linear growth velocity and 0.61 cm less gain in height during 1 year of treatment in children with mild to moderate persistent asthma.[55]

One study of patients who participated in a clinical trial of inhaled corticosteroids as children, reported a reduction in adult height of approximately 1 cm,[54, 56, 57, 58] whereas several studies have reported that children taking inhaled corticosteroids attained normal adult height.[59, 60, 61]

The effect is dose-dependent[57,58] and may be more likely in children who begin inhaled corticosteroid treatment before age 10.[56]

Other factors affect growth in children with asthma. Uncontrolled asthma itself reduces growth and final adult height.[60] One study found that inhaled corticosteroid equivalent to budesonide 400 microg/day affected growth less than low socioeconomic status.[61]

Bone density

Inhaled corticosteroids have not been associated with effects on bone density or fractures in children. [3] However, data from a recent study in Australia suggested asthma itself is associated with increased incidence of fractures in children, independent of medication.[62]

Given that the total dose of corticosteroids (both inhaled corticosteroids and oral corticosteroids) influences bone health, the aim of

asthma management is to maintain symptom control using the lowest inhaled corticosteroid dose required, and to avoid repeated courses of oral corticosteroids.

Adrenal suppression

Biochemical testing in a research setting suggests that hypothalamic–pituitary–adrenal axis suppression may occur in up to two-thirds of children treated with inhaled corticosteroids, and may occur at even low doses.[63] The risk is higher among children receiving concomitant intranasal steroids and those with lower body mass index,[63] and is influenced by genetics.[64]

Clinical adrenal insufficiency in children taking inhaled corticosteroids is rare but has been reported, [65, 66, 67] including cases in Australia.[67] Most cases have involved children given more than 500 microg per day fluticasone propionate.[65]

Adrenal suppression is associated with hypoglycaemia, hypotension, weakness, failure to grow, and is potentially fatal. Hypothalamic–pituitary–adrenal axis suppression may not be detected until adrenal crisis is precipitated by physical stress.[68]

Written information (e.g. a steroid alert card) can be prepared for children receiving long-term high-dose inhaled corticosteroids. Parents/carers can be instructed to present the card if the child ever needs to go to the emergency department (for any reason) or be admitted to hospital. A steroid alert card should state that child has asthma and the inhaled corticosteroid dose. A medical alert bracelet could also be considered.

There are no nationally accepted protocols for routine assessment of adrenal function in primary care because it has not yet been possible to identify precisely which children should be tested, to interpret test results reliably, to identify the appropriate interval for retesting, and because a clinical benefit has not been clearly demonstrated.

Regular monitoring of height might help detect adrenal suppression, based on the findings of a study in which a reduction in linear growth velocity occurred before adrenal suppression.[69]

Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)	
	Low	High
Beclometasone dipropionate †	100–200	>200 (maximum 400)
Budesonide	200–400	>400 (maximum 800)
Ciclesonide ‡	80–160	>160 (maximum 320)
Fluticasone propionate	100–200	>200 (maximum 500)

† Dose equivalents for *Qvar* (TGA-registered CFC-free formulation of beclometasone dipropionate)

‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

Source

van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma.* The Thoracic Society of Australia and New Zealand, 2010. Available from: http://www.thoracic.org.au/clinical-documents/area?command=record&id=14

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▶ Go to: The Thoracic Society of Australia and New Zealand's *Position Statement: The role of corticosteroids in the management of childhood asthma*

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Montelukast for children: efficacy

- Montelukast use has been associated with behavioural and/or neuropsychiatric adverse effects, including suicidality.

▶ Go to: TGA alert

Overview

Montelukast is a leukotriene receptor antagonist preventer. It is registered by the TGA for the treatment of asthma in children aged 2 years and older, and for the symptomatic treatment of allergic rhinitis.[70]

Montelukast can be used as an alternative to inhaled corticosteroids or as an add-on treatment in a child already taking regular inhaled corticosteroids.

However, it is not effective for all children. Overall, only approximately 20–30% of children will respond to montelukast treatment. The effect is thought to depend mainly on the child's genotype.[71, 72, 73] Clinically, it is not possible to predict accurately which children will benefit most from montelukast treatment.

Montelukast as first-line preventer in children aged 2–5 years

Viral-induced wheezing

Overall, regular maintenance montelukast treatment does not reduce the risk of wheezing episodes requiring oral corticosteroid treatment among preschool children who only have wheezing episodes when they have viral upper respiratory tract infections.[10]

However, montelukast may be effective for some children. Some randomised controlled trials have reported a reduction the risk of flare-ups in preschool children with intermittent asthma/wheeze,[74, 75] while others have not.[76]

Persistent asthma or wheezing

A systematic review comparing montelukast with inhaled corticosteroids in preschoolers with asthma or recurrent wheezing requiring daily preventer treatment[4] reported that inhaled corticosteroids appeared to achieve better symptom control and reduce flare-ups (including severe flare-ups requiring treatment with systemic corticosteroids). However, results were inconsistent and meta-analysis was not possible due to heterogeneity of outcomes measured in available clinical trials.[4]

Some preschool children with persistent asthma/wheeze respond to montelukast. A crossover study in preschool children with persistent asthma/wheeze reported that some children showed their best response to montelukast, while most responded better to regular inhaled corticosteroids.[5] Predictors of a better response to inhaled corticosteroids than montelukast were aeroallergen hypersensitivity and blood eosinophilia (eosinophil counts ≥ 300/μL).[5] However, routine blood eosinophil count is not feasible or recommended for this purpose.

Montelukast as first-line preventer children aged 6 years and over

In school-aged children with persistent asthma, inhaled corticosteroids are more effective overall than montelukast in improving lung function and controlling asthma symptoms.[77, 78]

However, symptoms will respond to a treatment trial of montelukast in approximately one-quarter to one-third of children,[77, 79,80] and some may benefit more than from an inhaled corticosteroid.[77] More severe asthma and markers of allergic inflammation may predict a better response to inhaled corticosteroids.[77]

Montelukast as add-on treatment

A systematic review of studies in children over 6 years and adolescents with mild-to-moderate persistent asthma found that the addition of montelukast to inhaled corticosteroids did reduce flare-ups requiring oral corticosteroids or hospital admissions for asthma, compared with the same or an increased dose.[78]

In a study comparing step-up treatments in children with asthma symptoms uncontrolled by low-dose inhaled corticosteroids, the addition of a long-acting beta$_2$ agonist was effective in more children than either montelukast or increasing the dose of inhaled corticosteroid for controlling asthma symptoms and preventing flare-ups requiring systemic corticosteroids.[81] However, some studies in school-aged children with persistent asthma already taking regular inhaled corticosteroids have reported that add-on montelukast reduced the risk of flare-ups[81, 82] and exercise-induced asthma symptoms.[82] Not all children will respond.

In a small study in children with persistent asthma already taking regular inhaled corticosteroids who were homozygous for the Arg16 genotype, montelukast was more effective as an add-on therapy than long-acting beta$_2$ agonist in reducing symptoms, reliever use and days absent from school due to asthma, depending on the child's beta receptor genotype.[73] However, children were given inhaled corticosteroid and long-acting beta$_2$ agonists in separate inhalers, which is which is known to be associated with increased risks.

However, genotyping it is not currently feasible in clinical practice. In practice, a treatment trial of 4–6 weeks can determine which preventer is suitable for controlling a child's asthma symptoms,[77] but longer treatment may be required to evaluate effect on flare-ups, because flare-ups may be independent of symptom control.

Exercise-induced symptoms

In school-aged children who experience exercise-induced symptoms despite taking regular inhaled corticosteroids, the addition of montelukast is effective in controlling symptoms, but not all children experience a response.[83, 84]

See: *Investigation and management of exercise-induced bronchoconstriction*

Short-term use in the management of flare-ups

Some, but not all studies suggest that a short course of montelukast, introduced at the first signs of an upper respiratory tract infection, may be effective in controlling flare-ups. An Australian study reported that this strategy could achieve a small reduction in symptoms, school absence and medical consultations in preschool and school-aged children with episodic wheeze.[85]

However, the evidence is inconsistent, with some studies showing no benefit.[76,86, 87, 88, 7] The findings of one study suggested that whether or not intermittent montelukast is effective in wheezing children aged 5 years and under depends on genotype.[72]

Montelukast is not TGA-approved or PBS-subsidised for intermittent use.

Note: PBS status as at March 2019: Montelukast is not subsidised by the PBS for adolescents 15 years and over.

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Montelukast for children: behavioural and/or neuropsychiatric adverse effects

Montelukast is generally very well tolerated. Behavioural and psychiatric adverse effects were rare in clinical trials.[89, 90] However, post-marketing surveillance reports have identified behavioural and/or neuropsychiatric adverse effects associated with montelukast use in some children.[13]

Behavioural treatment-associated effects are difficult to assess in young children. No factors have been identified to predict which children are at risk.

Reported adverse events include nightmares, sleep disturbance, anxiety, irritability, aggression and depression.[13, 91, 11, 12]

Suicidal ideation has been reported in adolescents and adults taking montelukast.[12] A nested case-control study concluded that children with asthma aged 5–18 years taking leukotriene receptor antagonists were not at increased risk of suicide attempts.[93]

Reported adverse effects are usually mild.[11] The majority occur within 7–14 days of starting montelukast,[13, 11] but some may appear after several months.[12]

Behavioural and/or neuropsychiatric adverse effects typically disappear within 4 days of stopping montelukast treatment.[11] There is no evidence of long term effects.

The TGA recommends that clinicians treating children with montelukast should educate caregivers about these potential adverse effects and should consider providing them with the CMI. Advise them to seek medical advice if they have any concerns.

▶ Go to: TGA's 2018 safety review of montelukast

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'Wheeze-detecting' devices

Some hand-held devices and smart phone applications are marketed for detecting and measuring wheeze by audio recording and analysis.

There is not enough evidence to recommend these devices and apps for use in monitoring asthma symptoms or asthma control in adults or children, or in distinguishing wheeze from other airway sounds in children.

- Reliance on these devices could result in over- or under-treatment.

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References

1. Brand PL, Baraldi E, Bisgaard H, *et al*. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. *Eur Respir J*. 2008; 32: 1096-1110. Available from: http://erj.ersjournals.com/content/32/4/1096.full
2. Brand PL, Caudri D, Eber E et al. Classification and pharmacological treatment of preschool wheezing: changes since 2008. *Eur Respir J*. 2014; 43: 1172-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24525447
3. van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma*. The Thoracic Society of Australia and New Zealand, 2010. Available from: https://www.thoracic.org.au/journal-publishing/command/download_file/id/25/filename/The_role_of_corticosteroids_in_the_management_of_childhood_asthma_-_2010.pdf
4. Castro-Rodriguez JA, Rodriguez-Martinez CE, Ducharme FM. Daily inhaled corticosteroids or montelukast for preschoolers with asthma or recurrent wheezing: A systematic review. *Pediatr Pulmonol*. 2018; Epub ahead of print 6 November. Available from: https://www.ncbi.nlm.nih.gov/pubmed/30394700
5. Fitzpatrick AM, Jackson DJ, Mauger DT et al. Individualized therapy for persistent asthma in young children. *J Allergy Clin Immunol*. 2016; 138: 1608-18.e12. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27777180

6. Szefler, S. J., Carlsson, L. G., Uryniak, T., Baker, J. W.. Budesonide inhalation suspension versus montelukast in children aged 2 to 4 years with mild persistent asthma. *J Allergy Clin Immunol Pract*. 2013; 1: 58-64. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24229823
7. Bacharier LB, Phillips BR, Zeiger RS, *et al*. Episodic use of an inhaled corticosteroid or leukotriene receptor antagonist in preschool children with moderate-to-severe intermittent wheezing. *J Allergy Clin Immunol*. 2008; 122: 1127-1135. Available from: https://www.ncbi.nlm.nih.gov/pubmed/18973936
8. Kooi, EM, Schokker, S, Marike Boezen, H, *et al*. Fluticasone or montelukast for preschool children with asthma-like symptoms: randomized controlled trial. *Pulm Pharmacol Ther*. 2008; 21: 798-804. Available from: https://www.ncbi.nlm.nih.gov/pubmed/18647656
9. Knorr, B, Franchi, LM, Bisgaard, H, *et al*. Montelukast, a leukotriene receptor antagonist, for the treatment of persistent asthma in children aged 2 to 5 years. *Pedriatrics*. 2001; 108: E48. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11533366
10. Brodlie M, Gupta A, Rodriguez-Martinez CE, *et al*. Leukotriene receptor antagonists as maintenance and intermittent therapy for episodic viral wheeze in children. *Cochrane Database Syst Rev*. 2015; Issue 10: CD008202. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26482324
11. Benard, B., Bastien, V., Vinet, B., *et al*. Neuropsychiatric adverse drug reactions in children initiated on montelukast in real-life practice. *Eur Respir J*. 2017; 50: . Available from: https://www.ncbi.nlm.nih.gov/pubmed/28818882
12. Aldea Perona, A., Garcia-Saiz, M., Sanz Alvarez, E.. Psychiatric disorders and montelukast in children: a disproportionality analysis of the VigiBase®. *Drug Saf*. 2016; 39: 69-78. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26620206
13. Wallerstedt, S. M., Brunlof, G., Sundstrom, A., Eriksson, A. L.. Montelukast and psychiatric disorders in children. *Pharmacoepidemiol Drug Saf*. 2009; 18: 858-64. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19551697
14. Philip, G, Hustad, C, Noonan, G, *et al*. Reports of suicidality in clinical trials of montelukast. *J Allergy Clin Immunol*. 2009; 124: 691-696. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19815114
15. Philip, G., Hustad, C. M., Malice, M. P., *et al*. Analysis of behavior-related adverse experiences in clinical trials of montelukast. *J Allergy Clin Immunol*. 2009; 124: 699-706. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19815116
16. Ali, M. M., O'Brien, C. E., Cleves, M. A., Martin, B. C.. Exploring the possible association between montelukast and neuropsychiatric events among children with asthma: a matched nested case-control study. *Pharmacoepidemiol Drug Saf*. 2015; 24: 435-45. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25683909
17. Therapeutic Goods Administration,. Montelukast – neuropsychiatric risks. *Aust Prescr*. 2013; 36: 168-171. Available from: https://www.nps.org.au/australian-prescriber/articles/medicines-safety-update-2-58#article
18. Schumock, G T, Stayner, L T, Valuck, R J, *et al*. Risk of suicide attempt in asthmatic children and young adults prescribed leukotriene-modifying agents: a nested case-control study. *J Allergy Clin Immunol*. 2012; 130: 368-375. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22698520
19. Paediatric Research in Emergency Departments International Collaborative. *Australasian bronchiolitis guideline*. PREDICT; 2016. Available from: http://www.predict.org.au/publications/2016-pubs/
20. Chavasse RJ, Bara A, McKean MC. Short acting beta2-agonists for recurrent wheeze in children under two years of age. *Cochrane Database Syst Rev*. 2002; Issue 2: CD002873. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002873/full
21. Gillette, C., Rockich-Winston, N., Kuhn, J. A., *et al*. Inhaler technique in children with asthma: a systematic review. *Acad Pediatr*. 2016; 16: 605-15. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27130811
22. Capanoglu, M., Dibek Misirlioglu, E., Toyran, M., *et al*. Evaluation of inhaler technique, adherence to therapy and their effect on disease control among children with asthma using metered dose or dry powder inhalers. *J Asthma*. 2015; 52: 838-45. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26037396
23. Ram, F S F, Brocklebank, D D M, White, J, *et al*. Pressurised metered dose inhalers versus all other hand-held inhaler devices to deliver beta-2 agonist bronchodilators for non-acute asthma. *Cochrane Database Syst Rev*. 2002; Issue 2: .
24. Nikander, K, Turpeinen, M, Pelkonen, A S, *et al*. True adherence with the Turbuhaler in young children with asthma. *Arch Dis Child*. 2011; 96: 168-173.
25. Pedersen, S., Mortensen, S.. Use of different inhalation devices in children. *Lung*. 1990; 168 Suppl: 653-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/2117175
26. Sleath, B, Ayala, G X, Gillette, C, *et al*. Provider demonstration and assessment of child device technique during pediatric asthma visits. *Pediatrics*. 2011; 127: 642-648.
27. The Inhaler Error Steering Committee,, Price, D., Bosnic-Anticevich, S., *et al*. Inhaler competence in asthma: common errors, barriers to use and recommended solutions. *Respir Med*. 2013; 107: 37-46. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23098685
28. Bjermer, L.. The importance of continuity in inhaler device choice for asthma and chronic obstructive pulmonary disease. *Respiration; international review of thoracic diseases*. 2014; 88: 346-52. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25195762
29. Basheti, I A, Armour, C L, Bosnic-Anticevich, S Z, Reddel, H K. Evaluation of a novel educational strategy, including inhaler-based reminder labels, to improve asthma inhaler technique. *Patient Educ Couns*. 2008; 72: 26-33. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18314294
30. Bosnic-Anticevich, S. Z., Sinha, H., So, S., Reddel, H. K.. Metered-dose inhaler technique: the effect of two educational interventions delivered in community pharmacy over time. *The Journal of asthma : official journal of the Association for the Care of Asthma*. 2010; 47: 251-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20394511
31. Melani AS, Bonavia M, Cilenti V, *et al*. Inhaler mishandling remains common in real life and is associated with reduced disease control. *Respir Med*. 2011; 105: 930-8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21367593
32. Levy ML, Dekhuijzen PN, Barnes PJ, *et al*. Inhaler technique: facts and fantasies. A view from the Aerosol Drug Management

Improvement Team (ADMIT). *NPJ Prim Care Respir Med*. 2016; 26: 16017. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27098045
33. Haughney, J., Price, D., Barnes, N. C., *et al*. Choosing inhaler devices for people with asthma: current knowledge and outstanding research needs. *Respiratory medicine*. 2010; 104: 1237-45. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20472415
34. Giraud, V., Roche, N.. Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability. *The European respiratory journal*. 2002; 19: 246-51. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11866004
35. Harnett, C. M., Hunt, E. B., Bowen, B. R., *et al*. A study to assess inhaler technique and its potential impact on asthma control in patients attending an asthma clinic. *J Asthma*. 2014; 51: 440-5.
36. Hardwell, A., Barber, V., Hargadon, T., *et al*. Technique training does not improve the ability of most patients to use pressurised metered-dose inhalers (pMDIs). *Prim Care Respir J*. 2011; 20: 92-6. Available from: http://www.nature.com/articles/pcrj201088
37. Berg E. In vitro properties of pressurized metered dose inhalers with and without spacer devices. *J Aerosol Med*. 1995; 8 Suppl 3: S3-10; discussion S11. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10157897
38. Dompeling E, Oudesluys-Murphy AM, Janssens HM, *et al*. Randomised controlled study of clinical efficacy of spacer therapy in asthma with regard to electrostatic charge. *Arch Dis Child*. 2001; 84: 178-182. Available from: http://adc.bmj.com/content/84/2/178.full
39. Martinez FD, Wright AL, Taussig LM, *et al*. Asthma and wheezing in the first six years of life. *N Engl J Med*. 1995; 332: 133-138. Available from: http://www.nejm.org/doi/full/10.1056/NEJM199501193320301#t=article
40. Henderson J, Granell R, Heron J, *et al*. Associations of wheezing phenotypes in the first 6 years of life with atopy, lung function and airway responsiveness in mid-childhood. *Thorax*. 2008; 63: 974-980. Available from: http://thorax.bmj.com/content/63/11/974.long
41. Castro-Rodriguez JA. The Asthma Predictive Index: a very useful tool for predicting asthma in young children. *J Allergy Clin Immunol*. 2010; 126: 212-216. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20624655
42. Savenije OE, Kerkhof M, Koppelman GH, Postma DS. Predicting who will have asthma at school age among preschool children. *J Allergy Clin Immunol*. 2012; 130: 325-331. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22704537
43. Ducharme FM, Krajinovic M. Steroid responsiveness and wheezing phenotypes. *Paediatr Respir Rev*. 2011; 12: 170-176. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21722845
44. Chong J, Haran C, Chauhan BF, Asher I. Intermittent inhaled corticosteroid therapy versus placebo for persistent asthma in children and adults. *Cochrane Database Syst Rev*. 2015; : Cd011032. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26197430
45. McKean MC, Ducharme F. Inhaled steroids for episodic viral wheeze of childhood. *Cochrane Database Syst Rev*. 2000; 2: CD001107. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001107/full
46. Castro-Rodriguez JA, Rodrigo GJ. Efficacy of inhaled corticosteroids in infants and preschoolers with recurrent wheezing and asthma: A systematic review with meta-analysis. *Pediatrics*. 2009; 123: e519-e525. Available from: http://pediatrics.aappublications.org/content/123/3/e519.full
47. Kramer S, Rottier BL, Scholten RJ, Boluyt N. Ciclesonide versus other inhaled corticosteroids for chronic asthma in children. *Cochrane Database Syst Rev*. 2013; Issue 2: CD010352. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010352/full
48. Martinez FD, Chinchilli VM, Morgan WJ, *et al*. Use of beclomethasone dipropionate as rescue treatment for children with mild persistent asthma (TREXA): a randomised, double-blind, placebo-controlled trial. *Lancet*. 2011; 377: 650-7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21324520
49. Weiss K, Buxton M, Andersson FL et al. Cost-effectiveness of early intervention with once-daily budesonide in children with mild persistent asthma: results from the START study. *Pediatr Allergy Immunol* 2006; 17 Suppl 17: 21-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/16573705
50. Chen YZ, Busse WW, Pedersen S et al. Early intervention of recent onset mild persistent asthma in children aged under 11 yrs: the Steroid Treatment As Regular Therapy in early asthma (START) trial. *Pediatr Allergy Immunol* 2006; 17 Suppl 17: 7-13. Available from: https://www.ncbi.nlm.nih.gov/pubmed/16573703
51. Cazeiro C, Silva C, Mayer S et al. Inhaled corticosteroids and respiratory infections in children with asthma: a meta-analysis. *Pediatrics*. 2017; 139. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28235797
52. Yokoyama H, Yamamura Y, Ozeki T, *et al*. Effects of mouth washing procedures on removal of budesonide inhaled by using Turbuhaler. *Yakugaku Zasshi*. 2007; 127: 1245-1249. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17666876
53. Godara N, Godara R, Khullar M. Impact of inhalation therapy on oral health. *Lung India*. 2011; 28: 272-5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/22084541
54. Loke YK, Blanco P, Thavarajah M, Wilson AM. Impact of inhaled corticosteroids on growth in children with asthma: systematic review and meta-analysis. *PloS One*. 2015; 10: e0133428. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26191797
55. Zhang L, Prietsch SO, Ducharme FM. Inhaled corticosteroids in children with persistent asthma: effects on growth. *Cochrane Database Syst Rev*. 2014: Cd009471. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25030198
56. Kelly HW, Sternberg AL, Lescher R, *et al*. Effect of inhaled glucocorticoids in childhood on adult height. *N Engl J Med*. 2012; 367: 904-12. Available from: http://www.nejm.org/doi/full/10.1056/NEJMoa1203229
57. Pruteanu AI, Chauhan BF, Zhang L et al. Inhaled corticosteroids in children with persistent asthma: dose-response effects on growth. *Cochrane Database Syst Rev*. 2014: Cd009878. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25030199
58. De Leonibus C, Attanasi M, Roze Z et al. Influence of inhaled corticosteroids on pubertal growth and final height in asthmatic children. *Pediatr Allergy Immunol*. 2016; 27: 499-506. Available from:https://www.ncbi.nlm.nih.gov/pubmed/26919136
59. Pauwels RA, Pedersen S, Busse WW, *et al*. Early intervention with budesonide in mild persistent asthma: a randomised, double-blind trial. *Lancet*. 2003; 361: 1071-1076. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12672309

60. Pedersen S. Do inhaled corticosteroids inhibit growth in children? *Am J Respir Crit Care Med*. 2001; 164: 521-35. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11520710
61. Agertoft L, Pedersen S. Effect of long-term treatment with inhaled budesonide on adult height in children with asthma. *N Engl J Med*. 2000; 343: 1064-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11027740
62. Degabriele EL, Holloway KL, Pasco JA et al. Associations between asthma status and radiologically confirmed fracture in children: A data-linkage study. *J Paediatr Child Health*. 2018; 54(8): 855-860. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29614205
63. Zöllner EW, Lombard CJ, Galal U, *et al*. Hypothalamic-adrenal-pituitary axis suppression in asthmatic school children. *Pediatrics*. 2012; 130: e1512-19. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23147980
64. Hawcutt DB, Francis B, Carr DF et al. Susceptibility to corticosteroid-induced adrenal suppression: a genome-wide association study. *Lancet Respir Med*. 2018; 6:442-450. Available from: https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(18)30058-4/fulltext
65. Ahmet A, Kim H, Spier S. Adrenal suppression: A practical guide to the screening and management of this under-recognized complication of inhaled corticosteroid therapy. *Allergy Asthma Clin Immunol*. 2011; 7: 13. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3177893/
66. Priftis, K N, Papadimitriou, A, Anthracopoulos, M B, Fretzayas, A, Chrousos, G P. Endocrine-immune interactions in adrenal function of asthmatic children on inhaled corticosteroids. *Neuroimmunomodulation* 2008; 16: 333-339.
67. Macdessi JS, Randell TL, Donaghue KC, *et al*. Adrenal crises in children treated with high-dose inhaled corticosteroids for asthma. *Med J Aust*. 2003; 178: 214-6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12603184
68. Rao Bondugulapati LN, Rees DA. Inhaled corticosteroids and HPA axis suppression: how important is it and how should it be managed? *Clin Endocrinol (Oxf)*. 2016; 85: 165-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27038017
69. Liddell BS, Oberlin JM, Hsu DP. Inhaled corticosteroid related adrenal suppression detected by poor growth and reversed with ciclesonide. *J Asthma*. 2017; 54: 99-104. Available from:https://www.ncbi.nlm.nih.gov/pubmed/27284755
70. Merck, Sharp and Dohme Australia Pty Ltd. *Product Information: Singulair (montelukast sodium) Tablets*. Therapeutic Goods Administration, Canberra, 2013. Available from: https://www.ebs.tga.gov.au/
71. Bush A. Montelukast in paediatric asthma: where we are now and what still needs to be done? *Paediatr Respir Rev*. 2015; 16: 97-100. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25499571
72. Nwokoro C, Pandya H, Turner S, *et al*. Intermittent montelukast in children aged 10 months to 5 years with wheeze (WAIT trial): a multicentre, randomised, placebo-controlled trial. *Lancet Respir Med*. 2014; 2: 796-803. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25212745
73. Lipworth BJ, Basu K, Donald HP, *et al*. Tailored second-line therapy in asthmatic children with the Arg(16) genotype. *Clin Sci (Lond)*. 2013; 124: 521-528. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23126384
74. Bisgaard H, Zielen S, Garcia-Garcia ML, *et al*. Montelukast reduces asthma exacerbations in 2- to 5-year-old children with intermittent asthma. *Am J Respir Crit Care Med*. 2005; 171: 315-322. Available from: http://ajrccm.atsjournals.org/content/171/4/315.long
75. Nagao M, Ikeda M, Fukuda N, *et al*. Early control treatment with montelukast in preschool children with asthma: a randomized controlled trial. *Allergol Int*. 2018; 67: 72-78. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28526210
76. Valovirta, E., Boza, M. L., Robertson, C. F., *et al*. Intermittent or daily montelukast versus placebo for episodic asthma in children. *Ann Allergy Asthma Immunol*. 2011; 106: 518-26. Available from: https://www.ncbi.nlm.nih.gov/pubmed/21624752
77. Jartti T. Inhaled corticosteroids or montelukast as the preferred primary long-term treatment for pediatric asthma? *Eur J Pediatr*. 2008; 167: 731-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/18214538
78. Chauhan BF, Ben Salah R, Ducharme FM. Addition of anti-leukotriene agents to inhaled corticosteroids in children with persistent asthma. *Cochrane Database Syst Rev*. 2013; Issue 10: CD009585. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24089325
79. Maspero, J, Guerra, F, Cuevas, F, *et al*. Efficacy and tolerability of salmeterol/fluticasone propionate versus montelukast in childhood asthma: a prospective, randomized, double-blind, double-dummy, parallel-group study. *Clin Ther*. 2008; 30: 1492-1504.
80. Pedersen S, Maspero J, Gul N, Sharma R. Components of asthma control and treatment response of individual control criteria in children: analysis of the PEACE study. *Pediatr Pulmonol*. 2011; 46: 1182-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/21751432
81. Malka J, Mauger DT, Covar R, *et al*. Eczema and race as combined determinants for differential response to step-up asthma therapy. *J Allergy Clin Immunol*. 2014; 134: 483-5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24835502
82. Stelmach I, Ozarek-Hanc A, Zaczeniuk M et al. Do children with stable asthma benefit from addition of montelukast to inhaled corticosteroids: randomized, placebo controlled trial. *Pulm Pharmacol Ther*. 2015; 31: 42-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25640020
83. Grzelewski, T, Stelmach, I. Exercise-induced bronchoconstriction in asthmatic children: a comparative systematic review of the available treatment options. *Drugs*. 2009; 69: 1533-1553. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19678711
84. Fogel RB, Rosario N, Aristizabal G, *et al*. Effect of montelukast or salmeterol added to inhaled fluticasone on exercise-induced bronchoconstriction in children. *Ann Allergy Asthma Immunol*. 2010; 104: 511-517. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20568384
85. Robertson CF, Price D, Henry R, *et al*. Short-course montelukast for intermittent asthma in children: a randomized controlled trial. *Am J Respir Crit Care Med*. 2007; 175: 323-329. Available from: http://ajrccm.atsjournals.org/content/175/4/323.long
86. Watts, K, Chavasse, R J P G. Leukotriene receptor antagonists in addition to usual care for acute asthma in adults and children. *Cochrane Database Syst Rev*. 2012; Issue 5: . Available from: http://cochranelibrary-wiley.com/doi/10.1002/14651858.CD006100.pub2/full
87. Capsomidis, A., Tighe, M.. Archimedes. Question 2. Is oral montelukast beneficial in treating acute asthma exacerbations in

children?. *Arch Dis Child*. 2010; 95: 948-50. Available from: http://adc.bmj.com/content/95/11/948.long
88. Schuh, S, Willan, AR, Stephens, D, *et al*. Can montelukast shorten prednisolone therapy in children with mild to moderate acute asthma? A randomized controlled trial. *J Pediatr*. 2009; 155: 795-800. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19656525
89. Philip G, Hustad C, Noonan G, *et al*. Reports of suicidality in clinical trials of montelukast. *J Allergy Clin Immunol*. 2009; 124: 691-6.e6. Available from: http://www.jacionline.org/article/S0091-6749(09)01247-0/fulltext
90. Philip G, Hustad CM, Malice MP, *et al*. Analysis of behavior-related adverse experiences in clinical trials of montelukast. *J Allergy Clin Immunol*. 2009; 124: 699-706.e8. Available from: http://www.jacionline.org/article/S0091-6749(09)01248-2/fulltext
91. Haarman M, van Hunsel F, de Vries T. Adverse drug reactions of montelukast in children and adults. *Pharmacol Res Perspect* 2017; 5: e00341. Available from: http://onlinelibrary.wiley.com/doi/10.1002/prp2.341/full
92. Robertson, CF, Price, D, Henry, R, *et al*. Short-course montelukast for intermittent asthma in children: a randomized controlled trial. *Am J Respir Crit Care Med*. 2007; 175: 323-329. Available from: https://www.ncbi.nlm.nih.gov/pubmed/17110643
93. Schumock GT, Stayner LT, Valuck RJ, *et al*. Risk of suicide attempt in asthmatic children and young adults prescribed leukotriene-modifying agents: a nested case-control study. *J Allergy Clin Immunol*. 2012; 130: 368-75. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22698520

Other regular treatments in children aged 1–5 years

Recommendations

Cromones can be considered for children who are unable to tolerate montelukast or where a nonsteroidal treatment option is preferred.

For children aged 1-2 years, sodium cromoglycate can be considered.

For children 2 years and older, sodium cromoglycate or nedocromil can be considered.

Note: Cromone inhaler device mouthpieces require meticulous daily washing to avoid blocking.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

Inhaled corticosteroid/long-acting beta$_2$ agonist combinations are not recommended for children aged 5 years and under, unless on the advice of a paediatric physician or paediatrician.

Note: The combination of fluticasone propionate and salmeterol xinafoate in a single inhaler is approved by TGA for use in children aged 4 years and over. Other inhaled corticosteroid/long-acting beta$_2$ agonist combinations are not recommended for children younger than 12 years.

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- van Asperen *et al.* 2010[1]

Last reviewed version 2.0

Regular treatment with a theophyllines (aminophylline or theophylline) is not recommended for children aged 5 years and under.

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- Brand *et al.* 2008[2]

Last reviewed version 2.0

Ipratropium is not recommended for the regular management of asthma in children aged 5 years and under.

Note: Ipratropium is used in the management of acute asthma.

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- Brand *et al.* 2008[2]

Last reviewed version 2.0

More information

Cromones for children

0-5 years

Few clinical trials have assessed the use of inhaled sodium cromoglycate in preschool children and none have assessed nedocromil.[2] Overall, sodium cromoglycate has not been shown to be effective in preschool children with multiple-trigger wheeze.[2, 3]

However, cromones are well tolerated and registered for use in infants. Therefore, a treatment trial can be considered before considering other preventers, particularly for children less than 2 years old.

6 years and over

Cromones are rarely prescribed in school-aged children.

Inhaled sodium cromoglycate might be effective in school-aged children, but interpretations of available evidence are inconsistent.[1] Sodium cromoglycate is less effective than inhaled corticosteroid in achieving asthma control and improving lung function in children with persistent asthma.[4]

Nedocromil sodium appears to be have some benefit in children with persistent asthma, but its relative effectiveness compared with inhaled corticosteroids is not clear.[5] Long-term (4–6 years) treatment with budesonide achieved better asthma control than long-term nedocromil in children with mild-to-moderate asthma aged 5–12 in a randomised placebo-controlled clinical trial.[6]

Practical issues

Cromones (sodium cromoglycate and nedocromil) may not be practical for most patients, because they require three–four times daily dosing until control is gained, and inhaler devices for cromones tend to block easily unless the mouthpiece is washed every day and dried for 24 hours before re-use.[1]

Nedocromil can cause an unusual or unpleasant taste[7] and is not tolerated by some children.

Last reviewed version 2.0

Inhaled corticosteroid/long-acting beta-2 agonist combinations for children aged 4–11 years

The combination of salmeterol plus fluticasone propionate in a single inhaler is TGA-registered for use in children 4 years and older.

Efficacy

A very large (n=6208) randomised controlled trial in children aged 4–11 years reported that, unlike in adults, the combination of inhaled corticosteroid and long-acting beta$_2$ agonist was not associated with a significant reduction in severe flare-ups, compared with inhaled corticosteroid alone.[8] Combination treatment was not associated with an increase in in symptom-free days or a reduction in reliever use, compared with inhaled corticosteroid alone.[8]

Safety

Clinical response to long-acting beta$_2$ agonists partly depends on genetics. A beta$_2$receptor genotype (Arg16 polymorphism in the beta$_2$ receptor gene) pre-disposes children with asthma to down-regulation of the beta$_2$ receptor and increased susceptibility to flare-ups during regular treatment with regular long-acting beta$_2$agonists.[9, 10] However, routine genetic testing to tailor asthma therapy is not yet available in clinical practice.

Earlier systematic reviews and meta-analyses led to concern about the possibility that the use of long-acting beta-agonists (even in combination with inhaled corticosteroids) might even increase the risk of flare-ups that require treatment with oral steroids or hospital admission, or of severe flare-ups.[1,11, 12] A meta-analysis commissioned by the US Food and Drug Administration found that the use of long-acting beta$_2$ agonists was associated with increased risk of severe asthma-associated adverse events (both overall and among the subset of people using concomitant inhaled corticosteroid and long-acting beta$_2$ agonist), and that this risk was greatest in children aged 4–11 years.[12] However, the increased risk was only seen in studies where inhaled corticosteroid was not provided, or where inhaled corticosteroid and long-acting beta$_2$ agonist were not combined in a single inhaler (i.e. where there was the possibility of selective non-adherence to the inhaled corticosteroid).

The PBAC Post-market review of medicines used to treat asthma in children[13] concluded that there was insufficient evidence to ascertain whether tolerance to long-acting beta$_2$ agonist could explain why it is less effective than montelukast and inhaled corticosteroids in managing exercise-induced asthma symptoms.[13]

A very large randomised controlled trial of children aged 4–11 years, stratified by asthma symptom control and pre-study treatment, found no increased risk of serious adverse outcomes with combination fluticasone propionate and salmeterol in a single inhaler, compared with fluticasone propionate alone.[8] Subsequent to the publication of this and similar studies in adults,[14] regulators in the USA and Australia removed previous 'black box' warnings from combination inhaled corticosteroid–long-acting beta$_2$ agonist products for asthma.[15]

PBS status as at March 2019: All formulations that contain a combination of inhaled corticosteroid plus long-acting beta$_2$ agonist are listed as 'Authority required - streamlined'. Patient using these combinations for asthma must have previously had frequent episodes of asthma while receiving treatment with oral corticosteroids or optimal doses of inhaled corticosteroids.

Last reviewed version 2.0

References

1. van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma*. The Thoracic Society of Australia and New Zealand, 2010. Available from: https://www.thoracic.org.au/journal-publishing/command/download_file/id/25/filename/The_role_of_corticosteroids_in_the_management_of_childhood_asthma_-_2010.pdf
2. Brand PL, Baraldi E, Bisgaard H, *et al*. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. *Eur Respir J*. 2008; 32: 1096-1110. Available from: http://erj.ersjournals.com/content/32/4/1096.full
3. van der Wouden JC, Uijen JH, Bernsen RM, *et al*. Inhaled sodium cromoglycate for asthma in children. *Cochrane Database Syst Rev*. 2008; Issue 4: CD002173. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002173.pub2/full
4. Guevara JP, Ducharme F M, Keren R, *et al*. Inhaled corticosteroids versus sodium cromoglycate in children and adults with asthma. *Cochrane Database Syst Rev*. 2006; Issue 2: CD003558. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003558.pub2/full
5. Sridhar AV, McKean M. Nedocromil sodium for chronic asthma in children. *Cochrane Database Syst Rev*. 2006; Issue 3: CD004108. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004108.pub2/full
6. The Childhood Asthma Management Program Research Group. Long-term effects of budesonide or nedocromil in children with asthma. The Childhood Asthma Management Program Research Group. *N Engl J Med*. 2000; 343: 1054-63. Available from: http://www.nejm.org/doi/full/10.1056/NEJM200010123431501#t=article
7. Sanofi-Aventis Australia Pty Ltd. *Product information: Tilade CFC-free (nedocromil sodium)*. Therapeutic Goods Administration, Canberra, 2008. Available from: https://www.ebs.tga.gov.au/
8. Stempel, D. A., Szefler, S. J., Pedersen, S., *et al*. Safety of adding salmeterol to fluticasone propionate in children with asthma. *N Engl J Med*. 2016; 375: 840-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27579634
9. Lipworth BJ, Basu K, Donald HP, *et al*. Tailored second-line therapy in asthmatic children with the Arg(16) genotype. *Clin Sci (Lond)*. 2013; 124: 521-528. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23126384
10. Finkelstein Y, Bournissen FG, Hutson JR, Shannon M. Polymorphism of the ADRB2 gene and response to inhaled beta- agonists in children with asthma: a meta-analysis. *J Asthma* 2009; 46: 900-5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19905915
11. van Asperen PP. Long-acting beta agonists for childhood asthma. *Aust Prescr*. 2012; 35: 111-3. Available from: https://www.nps.org.au/australian-prescriber/articles/long-acting-beta2-agonists-for-childhood-asthma
12. McMahon AW, Levenson MS, McEvoy BW, *et al*. Age and risks of FDA-approved long-acting β2-adrenergic receptor agonists. *Pediatrics*. 2011; 128: e1147-1154. Available from: http://pediatrics.aappublications.org/content/128/5/e1147.long
13. Pharmaceutical Benefits Scheme,. *Post-market review. PBS medicines used to treat asthma in children. Report to PBAC. Final Report*. 2017.
14. Busse WW, Bateman ED, Caplan AL et al. Combined analysis of asthma safety trials of long-acting beta2-agonists. *N Engl J Med* 2018; 378: 2497-505. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29949492
15. Seymour SM, Lim R, Xia C et al. Inhaled corticosteroids and LABAs - removal of the FDA's boxed warning. *N Engl J Med* 2018; 378: 2461-3. Available from: https://www.nejm.org/doi/10.1056/NEJMp1716858

Reviewing initial treatment in children aged 1–5 years

Recommendations

When prescribing any preventer medicine for a child, consider each adjustment to the regimen as a treatment trial: monitor response continually, review within 4–6 weeks (or earlier as needed in response to parents' concerns), and adjust treatment according to response.

Table. Reviewing and adjusting preventer treatment for children aged 1–5 years

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/25

Figure. Stepped approach to adjusting asthma medication in children aged 1-5 years

Please view and print this figure separately: http://www.asthmahandbook.org.au/figure/show/18

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

If symptoms are not controlled during treatment with a preventer (despite good adherence and correct inhaler technique), consider whether they may be due to comorbidity or an alternative diagnosis such as rhinosinusitis or suppurative lung disease.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

If treatment-related behavioural and/or neuropsychiatric symptoms are suspected in a child taking montelukast, discontinue treatment and advise parents/carers to monitor and treat asthma symptoms with reliever while off preventer treatment.

If unsure whether a change in behaviour could be due to medication or normal for age, consider stopping for a short time (e.g. 1 week or more) and re-starting to monitor effects.

▶ **Go to: TGA alert**

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

If parents/carers report behavioural changes possibly related to treatment in a child taking regular inhaled corticosteroids, consider reducing the dose, changing to a different corticosteroid and monitoring effect, or trialling a different preventer.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

If cough is the predominant symptom, carefully reassess the diagnosis before changing treatment. Do not use inhaled corticosteroids specifically for cough. Refer to national guidelines for diagnosis and management of cough.

▶ **Go to:** *Australian Cough Guidelines*

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- Gibson *et al.* 2010[1]
- van Asperen *et al.* 2010[2]

Last reviewed version 2.0

More information

Classification of recent asthma symptom control in children

Ongoing review of asthma involves both assessing recent asthma symptom control and assessing risks for poor asthma outcomes such as flare-ups and adverse effects of medicines.

Recent asthma symptom control is assessed according to the frequency of asthma symptoms over the previous 4 weeks.

Table. Definition of levels of recent asthma symptom control in children (regardless of current treatment regimen)

Good control	Partial control	Poor control
All of: • Daytime symptoms† ≤2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • No limitation of activities‡ • No symptoms§ during night or when wakes up • Need for SABA reliever# ≤2 days per week	Any of: • Daytime symptoms† >2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • Any limitation of activities* • Any symptoms during night or when wakes up†† • Need for SABA reliever# >2 days per week	Either of: • Daytime symptoms† >2 days per week (lasting from minutes to hours or recurring, and partially or fully relieved by SABA reliever) • ≥3 features of partial control within the same week

SABA: short-acting $beta_2$ agonist

† e.g. wheezing or breathing problems

‡ child is fully active; runs and plays without symptoms

§ including no coughing during sleep

not including doses taken prophylactically before exercise. (Record this separately and take into account when assessing management.)

* e.g. wheeze or breathlessness during exercise, vigorous play or laughing

†† e.g. waking with symptoms of wheezing or breathing problems

Notes:

Recent asthma control is based on symptoms over the previous 4 weeks. Each child's risk factors for future asthma outcomes should also be assessed and taken into account in management.

Validated questionnaires can be used for assessing recent symptom control:
Test for Respiratory and Asthma Control in Kids (TRACK) for children < 5 years
Childhood Asthma Control Test (C-ACT) for children aged 4–11 years

Last reviewed version 2.0

Asset ID: 23

Table. Risk factors for life-threatening asthma flare-ups in children

Asthma-related factors

Poor asthma control

Admission to hospital in preceding 12 months

History of intubation for acute asthma

Over-use of short-acting beta$_2$ agonist reliever

Abnormal spirometry findings

Reversible expiratory airflow limitation on spirometry despite treatment

Poor adherence to preventer

Incorrect inhaler technique for preventer

Poor adherence to asthma action plan

Exposure to clinically relevant allergens

Exposure to tobacco smoke

Other clinical factors

Allergies to foods, insects, medicines

Obesity

Family-related factors

Frequent failure to attend consultations/lack of follow-up after an acute flare-up

Significant parental psychological or socioeconomic problems

Parent/carer unequipped to manage asthma emergency

Last reviewed version 2.0

Asset ID: 116

Last reviewed version 2.0

Montelukast for children: behavioural and/or neuropsychiatric adverse effects

Montelukast is generally very well tolerated. Behavioural and psychiatric adverse effects were rare in clinical trials.[3, 4] However, post-marketing surveillance reports have identified behavioural and/or neuropsychiatric adverse effects associated with montelukast use in some children.[5]

Behavioural treatment-associated effects are difficult to assess in young children. No factors have been identified to predict which children are at risk.

Reported adverse events include nightmares, sleep disturbance, anxiety, irritability, aggression and depression.[5, 6, 8, 9]

Suicidal ideation has been reported in adolescents and adults taking montelukast.[9] A nested case-control study concluded that children with asthma aged 5–18 years taking leukotriene receptor antagonists were not at increased risk of suicide attempts.[10]

Reported adverse effects are usually mild.[8] The majority occur within 7–14 days of starting montelukast,[5, 8] but some may appear after several months.[9]

Behavioural and/or neuropsychiatric adverse effects typically disappear within 4 days of stopping montelukast treatment.[8] There is no evidence of long term effects.

The TGA recommends that clinicians treating children with montelukast should educate caregivers about these potential adverse

effects and should consider providing them with the CMI. Advise them to seek medical advice if they have any concerns.

▶ Go to: TGA's 2018 safety review of montelukast

Last reviewed version 2.0

Inhaled corticosteroids for children: adverse effects

Local adverse effects

Hoarseness and pharyngeal candidiasis are not commonly reported among preschool children or school-aged children talking inhaled corticosteroids. [11, 2, 12]

Topical effects can be reduced by use of spacer devices (which reduce oropharyngeal deposition), and by mouth-rinsing and spitting after use.[2] Immediate quick mouth-rinsing removes more residual medicine in the mouth than delayed rinsing.[13]

There is limited evidence that inhaled asthma medication can affect dental health.[2, 14] Mouth rinsing might reduce this risk.

Systemic adverse effects

Systemic effects of inhaled corticosteroids in children depend on the dose, but clinically significant adverse effects are uncommon.[2]

The use of spacers and mouth rinsing will not reduce systemic effects, but the use of a spacer may increase efficacy so that a lower dose is required.

Growth

Short-term suppression of linear growth has been demonstrated in children taking inhaled corticosteroids.[15,16] The effect seems to be maximal during the first year of therapy and only one study has reported an effect in subsequent years of treatment.[16] A Cochrane systematic review concluded that regular use of inhaled corticosteroid at low or medium daily doses is associated with a mean reduction of 0.48 cm per year in linear growth velocity and 0.61 cm less gain in height during 1 year of treatment in children with mild to moderate persistent asthma.[16]

One study of patients who participated in a clinical trial of inhaled corticosteroids as children, reported a reduction in adult height of approximately 1 cm,[15, 17, 18, 19] whereas several studies have reported that children taking inhaled corticosteroids attained normal adult height.[20, 21, 22]

The effect is dose-dependent[18,19] and may be more likely in children who begin inhaled corticosteroid treatment before age 10.[17]

Other factors affect growth in children with asthma. Uncontrolled asthma itself reduces growth and final adult height.[21] One study found that inhaled corticosteroid equivalent to budesonide 400 microg/day affected growth less than low socioeconomic status.[22]

Bone density

Inhaled corticosteroids have not been associated with effects on bone density or fractures in children. [2] However, data from a recent study in Australia suggested asthma itself is associated with increased incidence of fractures in children, independent of medication.[23]

Given that the total dose of corticosteroids (both inhaled corticosteroids and oral corticosteroids) influences bone health, the aim of asthma management is to maintain symptom control using the lowest inhaled corticosteroid dose required, and to avoid repeated courses of oral corticosteroids.

Adrenal suppression

Biochemical testing in a research setting suggests that hypothalamic–pituitary–adrenal axis suppression may occur in up to two-thirds of children treated with inhaled corticosteroids, and may occur at even low doses.[24] The risk is higher among children receiving concomitant intranasal steroids and those with lower body mass index,[24] and is influenced by genetics.[25]

Clinical adrenal insufficiency in children taking inhaled corticosteroids is rare but has been reported, [26, 27, 28] including cases in Australia.[28] Most cases have involved children given more than 500 microg per day fluticasone propionate.[26]

Adrenal suppression is associated with hypoglycaemia, hypotension, weakness, failure to grow, and is potentially fatal. Hypothalamic–pituitary–adrenal axis suppression may not be detected until adrenal crisis is precipitated by physical stress.[29]

Written information (e.g. a steroid alert card) can be prepared for children receiving long-term high-dose inhaled corticosteroids. Parents/carers can be instructed to present the card if the child ever needs to go to the emergency department (for any reason) or be admitted to hospital. A steroid alert card should state that child has asthma and the inhaled corticosteroid dose. A medical alert bracelet could also be considered.

There are no nationally accepted protocols for routine assessment of adrenal function in primary care because it has not yet been possible to identify precisely which children should be tested, to interpret test results reliably, to identify the appropriate interval for retesting, and because a clinical benefit has not been clearly demonstrated.

Regular monitoring of height might help detect adrenal suppression, based on the findings of a study in which a reduction in linear

growth velocity occurred before adrenal suppression.[30]

Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)	
	Low	High
Beclometasone dipropionate †	100–200	>200 (maximum 400)
Budesonide	200–400	>400 (maximum 800)
Ciclesonide ‡	80–160	>160 (maximum 320)
Fluticasone propionate	100–200	>200 (maximum 500)

† Dose equivalents for *Qvar* (TGA-registered CFC-free formulation of beclometasone dipropionate)

‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

Source

van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma.* The Thoracic Society of Australia and New Zealand, 2010. Available from: http://www.thoracic.org.au/clinical-documents/area?command=record&id=14

Last reviewed version 2.0

Asset ID: 21

▶ Go to: The Thoracic Society of Australia and New Zealand's *Position Statement: The role of corticosteroids in the management of childhood asthma*

Last reviewed version 2.0

Administration of inhaled medicines in children: 1-5 years

To use inhaler devices correctly, parents and children need training in inhaler technique and in the care and cleaning of inhalers and spacers.

Children need careful supervision when taking their inhaled medicines (e.g. at preschool), especially when using a reliever for acute asthma symptoms.

Types of inhalers suitable for preschool children

Preschool children cannot use pressurised metered-dose inhalers properly unless a spacer is attached (with mask when necessary), because it is difficult for them to coordinate inspiratory effort with actuating the device.[11] Note that breath-actuated pressurised metered-dose inhalers cannot be used with a spacer.

Dry-powder inhalers are usually ineffective for preschool children because they cannot generate sufficient inspiratory air flow.[11]

Drug delivery is very variable in young children with any type of inhaler, including pressurised metered dose inhalers and spacers.[31] Filter studies have shown high day-to-day variability in delivered doses in preschool children.[11] This variation might explain fluctuations in effectiveness, even if the child's parents have been trained to use the device correctly.

Table. Types of inhaler devices for delivering asthma and COPD medicines

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/75

Pressurised metered-dose inhalers plus spacers for relievers

During acute wheezing episodes, delivery of short-acting beta2 agonist to airways is more effective with a pressurised metered-dose inhaler plus spacer than with a nebuliser.[11] In older children, salbutamol has also been associated with a greater increase in heart rate when delivered by nebuliser than when delivered by pressurised metered-dose inhaler plus spacer.[32]

When administering salbutamol to relieve asthma symptoms in a preschool child, the standard recommendation is to shake the

inhaler, actuate one puff at a time into the spacer and have the child take 4–6 breaths in and out of the spacer (tidal breathing).[33] Fewer breaths may suffice; in children with asthma aged 2–7 years (not tested during an acute asthma episode), the number of tidal breaths needed to inhale salbutamol adequately from a spacer has been estimated at 2 breaths for small-volume spacers, 2 breaths for a spacer made from a 500-mL modified soft drink bottle, and 3 breaths for a large (Volumatic) spacer.[34]

Face masks for infants

When using a spacer with face mask (e.g. for an infant too young or uncooperative to be able to use a mouthpiece), effective delivery of medicine to the airways depends on a tight seal around the face.

When masks are used for inhaled corticosteroids, there is a risk of exposure to eyes and skin if the seal over the mouth and nose is not adequate. Parents should be advised to wash the child's face after administering inhaled corticosteroids by mask.

Babies are unlikely to inhale enough medicine while crying.[32] The use of a spacer and face mask for a crying infant may require patience and skill: the child can be comforted (e.g. held by a parent, in own pram, or sitting on the floor) while the mask is kept on, and the actuation carefully timed just before the next intake of breath. Most infants will tolerate the spacer and mask eventually. The child may be more likely to accept the spacer and mask if allowed to handle them first (and at other times), if the devices are personalised (e.g. with stickers), or if the mask has a scent associated with the mother (e.g. lip gloss). The use of a spacer with a coloured valve allows parents to see the valve move as the child breathes in and out.

▶ Go to: National Asthma Council Australia's information paper for health professionals on *Inhaler technique for people with asthma or COPD*

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Correct use of inhaler devices

Checking and correcting inhaler technique is essential to effective asthma management.

Most patients with asthma or COPD do not use their inhalers properly,[35, 36,37, 37, 38] and most have not had their technique checked or corrected by a health professional.

Incorrect inhaler technique when using maintenance treatments increases the risk of severe flare-ups and hospitalisation for people with asthma or COPD.[35, 36, 39, 40, 41, 42]

Poor asthma symptom control is often due to incorrect inhaler technique.[43, 44]

Incorrect inhaler technique when using inhaled corticosteroids increases the risk of local side effects like dysphonia and oral thrush.

The steps for using an inhaler device correctly differ between brands. Checklists of correct steps for each inhaler type and how-to videos are available from the National Asthma Council website.

▶ Go to: National Asthma Council Australia's *Using your inhaler* webpage for information, patient resources and videos on inhaler technique
Go to: National Asthma Council Australia's information paper for health professionals on *Inhaler technique for people with asthma or COPD*
Go to: NPS MedicineWise information on *Inhaler devices for respiratory medicines*

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Step-up options in children with asthma that is not controlled by low-dose inhaled corticosteroids

In children whose asthma is inadequately controlled by low-dose inhaled corticosteroids alone (and adherence is good, inhaler technique is correct and diagnosis has been confirmed), treatment options include:

- increasing the inhaled corticosteroid dose
- adding montelukast
- switching to inhaled corticosteroid/long-acting beta$_2$ agonist combination.

Table. Step-up options for children when good asthma control is not achieved with low-dose ICS

Option	TGA-registered indications for add-on therapy	PBS considerations
High-dose ICS	N/A	Subsidised

Option	TGA-registered indications for add-on therapy	PBS considerations
ICS plus montelukast	2 years and over	2–5 years: not subsidised* 6–14 years: not subsidised unless for exercise-induced bronchoconstriction despite ICS treatment† 15 years and over: not subsidised‡
ICS/long-acting beta$_2$ agonist combination	4 years and over for fluticasone propionate/ salmeterol xinafoate 12 years and over for budesonide/formoterol fumarate dihydrate	Subsidised

- Advise parents about potential adverse psychiatric effects of montelukast

* Montelukast is not subsidised for use in combination with other preventers or for children who require inhaled corticosteroids.

† Montelukast is subsidised for prevention of exercise-induced asthma if asthma is otherwise well controlled while taking optimal-dose inhaled corticosteroids – it is not otherwise subsidised in combination with inhaled corticosteroids (or inhaled corticosteroid/long-acting beta$_2$ agonist combinations).

‡ Montelukast is not subsidised for people aged over 15 years.

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In the majority of children with persistent asthma that requires preventive treatment, control can be achieved with one of these options.[2]

Few studies have been conducted in preschool-aged children. The preferred step-up option for children aged 6–12 years is controversial and guidelines differ in their recommendations.[45]

Increasing inhaled corticosteroid dose versus adding a long-acting beta$_2$ agonist

In school-aged children with persistent asthma taking regular inhaled corticosteroid, the addition of a long-acting beta$_2$ agonist does not reduce the rate of asthma flare-ups requiring systemic steroids compared with the same or higher doses of inhaled corticosteroid.[46, 47] However, the long-acting beta$_2$ agonist–inhaled corticosteroid was superior for improving lung function.[46] Growth is reduced in children treated with higher-dose inhaled corticosteroid, compared with those taking same dose plus a long-acting beta$_2$ agonist.[46]

Adolescents may benefit more from combination inhaled corticosteroid/long-acting beta$_2$ agonist treatment than children under 12 years. In adolescents with persistent asthma that is not controlled by a low dose of inhaled corticosteroids, the combination of a long-acting beta$_2$ agonist and an inhaled corticosteroid is modestly more effective in reducing the risk of flare-ups requiring oral corticosteroids than a higher dose of inhaled corticosteroids.[48]

Adding montelukast versus adding a long-acting beta-2 agonist or increasing inhaled corticosteroid dose

Children aged 1–5 years

In one study in children aged 5 years or less with persistent asthma/wheeze requiring preventer treatment, raised blood eosinophil levels and atopy predicted better short-term response to high-dose inhaled corticosteroid than to montelukast.[49] However, routine eosinophil counts are currently not recommended to guide treatment in children.

In children aged 1–5 years with asthma/wheeze that is not adequately controlled by low-dose inhaled corticosteroid alone, adding montelukast is preferable to increasing the dose of inhaled corticosteroids when the safety profiles of these options are compared.[50] Long-acting beta$_2$ agonists are not recommended for this age group.

- Montelukast use has been associated with behavioural and/or neuropsychiatric adverse effects.

▶ Go to: TGA alert

Note: Montelukast is TGA-approved for children aged 2 years and over.

Children aged 6 years and over

Among children 6 years and over with asthma that is not controlled by low-dose inhaled corticosteroids, the optimal regimen varies between individuals.[51] In one study of children selected for high adherence with maintenance treatment, short-term responses varied between individuals: in some children the best response was achieved by adding a long-acting beta$_2$ agonist, in others by adding montelukast, and in others by increasing the dose of inhaled corticosteroid.[51]

Note: The use of inhaled corticosteroids and long-acting beta$_2$ agonists in separate inhalers is not recommended for either children or adults because of the potential for increased risk due to selective non-adherence to the inhaled corticosteroid.[52]

Overall, the addition of montelukast to an inhaled corticosteroid does not reduce the need for rescue oral corticosteroids or hospital admission, compared with the same or an increased dose of inhaled corticosteroids, in children aged 6 years and over or adolescents with mild-to-moderate asthma.[53]

For children aged 6–14 years with persistent asthma and exercise-induced bronchoconstriction, adding montelukast is more effective in protecting against exercise-induced bronchoconstriction than switching to a combination of inhaled corticosteroid and a long-acting beta$_2$ agonist.[54] The use of montelukast also avoids beta-receptor tolerance associated with long-acting beta$_2$ agonists, so a short-acting beta$_2$ agonist taken after exercise produces a greater bronchodilator response than it does in children taking regular long-acting beta$_2$ agonist.[54]

A treatment trial of montelukast for 4–6 weeks is the best option when effects on exercise-induced symptoms and safety are also considered.[50]

- Montelukast use has been associated with behavioural and/or neuropsychiatric adverse effects.

▶ Go to: TGA alert

See: *Investigation and management of exercise-induced bronchoconstriction*

Genetic influence on effect of long-acting beta$_2$ agonists

Clinical response to long-acting beta$_2$ agonists partly depends on genetics. A beta$_2$receptor genotype (Arg16 polymorphism in the beta$_2$ receptor gene) pre-disposes children with asthma to down-regulation of the beta$_2$ receptor and increased susceptibility to flare-ups during regular treatment with regular long-acting beta$_2$agonists.[55] However, routine genetic testing to tailor asthma therapy is not yet available in clinical practice.

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Montelukast for children: efficacy

- Montelukast use has been associated with behavioural and/or neuropsychiatric adverse effects, including suicidality.

▶ Go to: TGA alert

Overview

Montelukast is a leukotriene receptor antagonist preventer. It is registered by the TGA for the treatment of asthma in children aged 2 years and older, and for the symptomatic treatment of allergic rhinitis.[56]

Montelukast can be used as an alternative to inhaled corticosteroids or as an add-on treatment in a child already taking regular inhaled corticosteroids.

However, it is not effective for all children. Overall, only approximately 20–30% of children will respond to montelukast treatment. The effect is thought to depend mainly on the child's genotype.[57, 58, 55] Clinically, it is not possible to predict accurately which children will benefit most from montelukast treatment.

Montelukast as first-line preventer in children aged 2–5 years

Viral-induced wheezing

Overall, regular maintenance montelukast treatment does not reduce the risk of wheezing episodes requiring oral corticosteroid treatment among preschool children who only have wheezing episodes when they have viral upper respiratory tract infections.[59]

However, montelukast may be effective for some children. Some randomised controlled trials have reported a reduction the risk of flare-ups in preschool children with intermittent asthma/wheeze,[60, 61] while others have not.[62]

Persistent asthma or wheezing

A systematic review comparing montelukast with inhaled corticosteroids in preschoolers with asthma or recurrent wheezing requiring

daily preventer treatment[63] reported that inhaled corticosteroids appeared to achieve better symptom control and reduce flare-ups (including severe flare-ups requiring treatment with systemic corticosteroids). However, results were inconsistent and meta-analysis was not possible due to heterogeneity of outcomes measured in available clinical trials.[63]

Some preschool children with persistent asthma/wheeze respond to montelukast. A crossover study in preschool children with persistent asthma/wheeze reported that some children showed their best response to montelukast, while most responded better to regular inhaled corticosteroids.[49] Predictors of a better response to inhaled corticosteroids than montelukast were aeroallergen hypersensitivity and blood eosinophilia (eosinophil counts ≥ 300/μL).[49] However, routine blood eosinophil count is not feasible or recommended for this purpose.

Montelukast as first-line preventer children aged 6 years and over

In school-aged children with persistent asthma, inhaled corticosteroids are more effective overall than montelukast in improving lung function and controlling asthma symptoms.[64, 53]

However, symptoms will respond to a treatment trial of montelukast in approximately one-quarter to one-third of children,[64, 65,66] and some may benefit more than from an inhaled corticosteroid.[64] More severe asthma and markers of allergic inflammation may predict a better response to inhaled corticosteroids.[64]

Montelukast as add-on treatment

A systematic review of studies in children over 6 years and adolescents with mild-to-moderate persistent asthma found that the addition of montelukast to inhaled corticosteroids did reduce flare-ups requiring oral corticosteroids or hospital admissions for asthma, compared with the same or an increased dose.[53]

In a study comparing step-up treatments in children with asthma symptoms uncontrolled by low-dose inhaled corticosteroids, the addition of a long-acting beta$_2$ agonist was effective in more children than either montelukast or increasing the dose of inhaled corticosteroid for controlling asthma symptoms and preventing flare-ups requiring systemic corticosteroids.[67] However, some studies in school-aged children with persistent asthma already taking regular inhaled corticosteroids have reported that add-on montelukast reduced the risk of flare-ups[67, 68] and exercise-induced asthma symptoms.[68] Not all children will respond.

In a small study in children with persistent asthma already taking regular inhaled corticosteroids who were homozygous for the Arg16 genotype, montelukast was more effective as an add-on therapy than long-acting beta$_2$ agonist in reducing symptoms, reliever use and days absent from school due to asthma, depending on the child's beta receptor genotype.[55] However, children were given inhaled corticosteroid and long-acting beta$_2$ agonists in separate inhalers, which is which is known to be associated with increased risks.

However, genotyping it is not currently feasible in clinical practice. In practice, a treatment trial of 4–6 weeks can determine which preventer is suitable for controlling a child's asthma symptoms,[64] but longer treatment may be required to evaluate effect on flare-ups, because flare-ups may be independent of symptom control.

Exercise-induced symptoms

In school-aged children who experience exercise-induced symptoms despite taking regular inhaled corticosteroids, the addition of montelukast is effective in controlling symptoms, but not all children experience a response.[69, 70]

See: *Investigation and management of exercise-induced bronchoconstriction*

Short-term use in the management of flare-ups

Some, but not all studies suggest that a short course of montelukast, introduced at the first signs of an upper respiratory tract infection, may be effective in controlling flare-ups. An Australian study reported that this strategy could achieve a small reduction in symptoms, school absence and medical consultations in preschool and school-aged children with episodic wheeze.[71]

However, the evidence is inconsistent, with some studies showing no benefit.[62,72, 73, 74, 75] The findings of one study suggested that whether or not intermittent montelukast is effective in wheezing children aged 5 years and under depends on genotype.[58]

Montelukast is not TGA-approved or PBS-subsidised for intermittent use.

Note: PBS status as at March 2019: Montelukast is not subsidised by the PBS for adolescents 15 years and over.

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Approaches to assessment and monitoring of asthma control in children

Assessment of asthma control in children is based mainly on:

- recent asthma symptom control (assessed by the frequency and severity of symptoms between flare-ups
- the degree to which asthma symptoms affect daily activities such as interference with physical activity or missed school days)
- the frequency of flare-ups
- spirometry in children who are able to perform the test reliably.

Standardised questionnaires

Questionnaire-based instruments have been validated for assessing asthma control in children:

- *Test for Respiratory and Asthma Control in Kids (TRACK)* for children less than 5 years old – consists of five questions about frequency of respiratory symptoms (wheeze, cough, shortness of breath), activity limitation, and night-time awakenings in the past 4 weeks, rescue medication use in the past 3 months, and oral corticosteroid use in the previous year.[76, 77] A lower score indicates worse asthma control.

  Childhood Asthma Control Test (C-ACT) for children aged 4–11 years – consists of seven items: three for the parent/carer (about the child's symptoms over the previous 4 weeks) and four for the child.[78, 79] A lower score indicates worse asthma control. **Note:** C-ACT is intended for US use.

Lung function tests

Frequent spirometry to guide asthma treatment in children has not been shown to achieve superior outcomes to symptom-based treatment.[80] Current evidence does not support use of home spirometers to guide asthma treatment in children.[81] However, low FEV_1 predicts clinically significant flare-ups, so spirometry should be performed at asthma reviews for children who are old enough to do the test.

The quality and utility of spirometry depends on the skill, clinical expertise and experience of the person doing and interpreting spirometry.

The results of one study in children aged 6–16 years with moderate atopic asthma suggest that asthma treatment guided by airway hyperresponsiveness (measured by bronchial provocation testing) may have a benefit over symptom-guided treatment in improving lung, but this effect was lost after 3–7 years of usual care.[82, 83] Repeated bronchial provocation testing is not feasible in clinical practice.

Measures of airway inflammation

Measures of airway inflammation (e.g. sputum eosinophil count, exhaled nitric oxide measurement) are not recommended in primary care to guide treatment decisions, but are increasingly used in specialist clinics.

Asthma treatment guided by sputum eosinophil count has been shown to reduce the frequency of flare-ups in adults with asthma, but there is insufficient evidence to ascertain its value for children.[84]

Exhaled nitric oxide measurement may be useful in guiding asthma management in some children. In children not taking inhaled corticosteroid, a high nitric oxide level probably predicts a good short-term response to inhaled corticosteroid treatment,[85] but it does not distinguish between asthma and eosinophilic bronchitis and is often high in children with atopy. There is insufficient evidence to ascertain whether a low exhaled nitric oxide level predicts successful withdrawal from inhaled corticosteroids without asthma relapse,[85] or safety of treating asthma without inhaled corticosteroids.

A Cochrane review[86] found that exhaled nitric oxide-guided management was significantly better than other approaches to adjusting medicines for reducing the number of children with flare-ups and the number of children who needed oral corticosteroids, but did not reduce the frequency of flare-ups or the rate of flare-ups requiring hospitalisation, improve lung function or symptoms scores, or reduce inhaled corticosteroid doses. The authors concluded that it could not be recommended for all children but may be beneficial for a subset not yet defined.[86]

Towards personalised asthma care

Emerging understanding of asthma phenotypes and of genetic factors that predict therapeutic response to preventer options is leading to the possibility of personalised, genomics-based treatment for asthma in children.[87] In the near future, individual tailored therapy is may replace the standardised step model based on population data.

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Common reasons for poor response to preventer treatment

Apparent lack of response to asthma treatment is commonly due to one or more of the following:[88]

- poor adherence (which may be due to lack of perceived need for the medication, concern about potential or actual side-effects, cost of medicines, a busy lifestyle, misunderstanding of the purpose and effects of asthma medicines, or inability to follow the medical instructions)
- poor inhaler technique
- mishandling devices (e.g. failure to clean spacer, allowing mouthpiece of dry-powder inhalers to become blocked)
- incorrect dose or frequency
- empty inhaler
- expired medicines
- continued exposure to smoke or allergen triggers.

Failure to identify these causes before adjusting medicines could result in over-medication with preventers.

▶ See: *Management challenges*

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Managing cough in children

When cough is the predominant symptom in a young child, careful assessment is needed to avoid making an incorrect diagnosis of asthma, or instigating inappropriate treatment.[1] Cough alone (recurrent non-specific cough) is most likely due to recurrent viral bronchitis, which is unresponsive to both bronchodilators and preventive therapy including inhaled corticosteroids. Recurrent non-specific cough usually resolves by age 6 or 7 years and leaves no residual pulmonary pathology.

If cough is a problem for a child with known asthma, it should be managed according to national *Cough in Children and Adults: Diagnosis and Assessment (CICADA)* guidelines.[1]

- There are significant concerns about use of cough medicines in children.

▶ Go to: *Australian Cough Guidelines*
Go to: *Therapeutic Goods Administration (TGA) recommendations on the use of cough and cold medicines in children*

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References

1. Gibson PG, Chang AB, Glasgow NJ, *et al*. CICADA: cough in children and adults: diagnosis and assessment. Australian cough guidelines summary statement. *Med J Aust*. 2010; 192: 265-271. Available from: https://www.mja.com.au/journal/2010/192/5/cicada-cough-children-and-adults-diagnosis-and-assessment-australian-cough
2. van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma*. The Thoracic Society of Australia and New Zealand, 2010. Available from: https://www.thoracic.org.au/journal-publishing/command/download_file/id/25/filename/The_role_of_corticosteroids_in_the_management_of_childhood_asthma_-_2010.pdf
3. Philip G, Hustad C, Noonan G, *et al*. Reports of suicidality in clinical trials of montelukast. *J Allergy Clin Immunol*. 2009; 124: 691-6.e6. Available from: http://www.jacionline.org/article/S0091-6749(09)01247-0/fulltext
4. Philip G, Hustad CM, Malice MP, *et al*. Analysis of behavior-related adverse experiences in clinical trials of montelukast. *J Allergy Clin Immunol*. 2009; 124: 699-706.e8. Available from: http://www.jacionline.org/article/S0091-6749(09)01248-2/fulltext
5. Wallerstedt, S. M., Brunlof, G., Sundstrom, A., Eriksson, A. L.. Montelukast and psychiatric disorders in children. *Pharmacoepidemiol Drug Saf*. 2009; 18: 858-64. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19551697
6. Haarman M, van Hunsel F, de Vries T. Adverse drug reactions of montelukast in children and adults. *Pharmacol Res Perspect* 2017; 5: e00341. Available from: http://onlinelibrary.wiley.com/doi/10.1002/prp2.341/full
7. Robertson, CF, Price, D, Henry, R, *et al*. Short-course montelukast for intermittent asthma in children: a randomized controlled trial. *Am J Respir Crit Care Med*. 2007; 175: 323-329. Available from: https://www.ncbi.nlm.nih.gov/pubmed/17110643
8. Benard, B., Bastien, V., Vinet, B., *et al*. Neuropsychiatric adverse drug reactions in children initiated on montelukast in real-life practice. *Eur Respir J*. 2017; 50: . Available from: https://www.ncbi.nlm.nih.gov/pubmed/28818882
9. Aldea Perona, A., Garcia-Saiz, M., Sanz Alvarez, E.. Psychiatric disorders and montelukast in children: a disproportionality analysis of the VigiBase®. *Drug Saf*. 2016; 39: 69-78. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26620206
10. Schumock GT, Stayner LT, Valuck RJ, *et al*. Risk of suicide attempt in asthmatic children and young adults prescribed leukotriene-modifying agents: a nested case-control study. *J Allergy Clin Immunol*. 2012; 130: 368-75. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22698520
11. Brand PL, Baraldi E, Bisgaard H, *et al*. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. *Eur Respir J*. 2008; 32: 1096-1110. Available from: http://erj.ersjournals.com/content/32/4/1096.full
12. Cazeiro C, Silva C, Mayer S et al. Inhaled corticosteroids and respiratory infections in children with asthma: a meta-analysis. *Pediatrics*. 2017; 139. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28235797
13. Yokoyama H, Yamamura Y, Ozeki T, *et al*. Effects of mouth washing procedures on removal of budesonide inhaled by using Turbuhaler. *Yakugaku Zasshi*. 2007; 127: 1245-1249. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17666876
14. Godara N, Godara R, Khullar M. Impact of inhalation therapy on oral health. *Lung India*. 2011; 28: 272-5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/22084541
15. Loke YK, Blanco P, Thavarajah M, Wilson AM. Impact of inhaled corticosteroids on growth in children with asthma: systematic review and meta-analysis. *PloS One*. 2015; 10: e0133428. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26191797
16. Zhang L, Prietsch SO, Ducharme FM. Inhaled corticosteroids in children with persistent asthma: effects on growth. *Cochrane Database Syst Rev*. 2014: Cd009471. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25030198
17. Kelly HW, Sternberg AL, Lescher R, *et al*. Effect of inhaled glucocorticoids in childhood on adult height. *N Engl J Med*. 2012; 367: 904-12. Available from: http://www.nejm.org/doi/full/10.1056/NEJMoa1203229
18. Pruteanu AI, Chauhan BF, Zhang L et al. Inhaled corticosteroids in children with persistent asthma: dose-response effects on growth. *Cochrane Database Syst Rev*. 2014: Cd009878. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25030199
19. De Leonibus C, Attanasi M, Roze Z et al. Influence of inhaled corticosteroids on pubertal growth and final height in asthmatic

children. *Pediatr Allergy Immunol*. 2016; 27: 499-506. Available from:https://www.ncbi.nlm.nih.gov/pubmed/26919136
20. Pauwels RA, Pedersen S, Busse WW, *et al*. Early intervention with budesonide in mild persistent asthma: a randomised, double-blind trial. *Lancet*. 2003; 361: 1071-1076. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12672309
21. Pedersen S. Do inhaled corticosteroids inhibit growth in children? *Am J Respir Crit Care Med*. 2001; 164: 521-35. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11520710
22. Agertoft L, Pedersen S. Effect of long-term treatment with inhaled budesonide on adult height in children with asthma. *N Engl J Med*. 2000; 343: 1064-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11027740
23. Degabriele EL, Holloway KL, Pasco JA et al. Associations between asthma status and radiologically confirmed fracture in children: A data-linkage study. *J Paediatr Child Health*. 2018; 54(8): 855-860. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29614205
24. Zöllner EW, Lombard CJ, Galal U, *et al*. Hypothalamic-adrenal-pituitary axis suppression in asthmatic school children. *Pediatrics*. 2012; 130: e1512-19. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23147980
25. Hawcutt DB, Francis B, Carr DF et al. Susceptibility to corticosteroid-induced adrenal suppression: a genome-wide association study. *Lancet Respir Med*. 2018; 6:442-450. Available from: https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(18)30058-4/fulltext
26. Ahmet A, Kim H, Spier S. Adrenal suppression: A practical guide to the screening and management of this under-recognized complication of inhaled corticosteroid therapy. *Allergy Asthma Clin Immunol*. 2011; 7: 13. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3177893/
27. Priftis, K N, Papadimitriou, A, Anthracopoulos, M B, Fretzayas, A, Chrousos, G P. Endocrine-immune interactions in adrenal function of asthmatic children on inhaled corticosteroids. *Neuroimmunomodulation* 2008; 16: 333-339.
28. Macdessi JS, Randell TL, Donaghue KC, *et al*. Adrenal crises in children treated with high-dose inhaled corticosteroids for asthma. *Med J Aust*. 2003; 178: 214-6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12603184
29. Rao Bondugulapati LN, Rees DA. Inhaled corticosteroids and HPA axis suppression: how important is it and how should it be managed? *Clin Endocrinol (Oxf)*. 2016; 85: 165-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27038017
30. Liddell BS, Oberlin JM, Hsu DP. Inhaled corticosteroid related adrenal suppression detected by poor growth and reversed with ciclesonide. *J Asthma*. 2017; 54: 99-104. Available from:https://www.ncbi.nlm.nih.gov/pubmed/27284755
31. Schultz A, Sly PD, Zhang G, *et al*. Incentive device improves spacer technique but not clinical outcome in preschool children with asthma. *J Paediatr Child Health*. 2012; 48: 52-6. Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1440-1754.2011.02190.x/full
32. Schuh, S., Johnson, D. W., Stephens, D., *et al*. Comparison of albuterol delivered by a metered dose inhaler with spacer versus a nebulizer in children with mild acute asthma. *The Journal of pediatrics*. 1999; 135: 22-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/10393599
33. National Asthma Council Australia. *Kids' First Aid for Asthma*. National Asthma Council Australia, Melbourne, 2011. Available from: http://www.nationalasthma.org.au/first-aid
34. Schultz A, Le Souëf TJ, Venter A, *et al*. Aerosol inhalation from spacers and valved holding chambers requires few tidal breaths for children. *Pediatrics*. 2010; 126: e1493-8. Available from: http://pediatrics.aappublications.org/content/126/6/e1493.long
35. The Inhaler Error Steering Committee,, Price, D., Bosnic-Anticevich, S., *et al*. Inhaler competence in asthma: common errors, barriers to use and recommended solutions. *Respir Med*. 2013; 107: 37-46. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23098685
36. Bjermer, L.. The importance of continuity in inhaler device choice for asthma and chronic obstructive pulmonary disease. *Respiration; international review of thoracic diseases*. 2014; 88: 346-52. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25195762
37. Basheti, I A, Armour, C L, Bosnic-Anticevich, S Z, Reddel, H K. Evaluation of a novel educational strategy, including inhaler-based reminder labels, to improve asthma inhaler technique. *Patient Educ Couns*. 2008; 72: 26-33. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18314294
38. Bosnic-Anticevich, S. Z., Sinha, H., So, S., Reddel, H. K.. Metered-dose inhaler technique: the effect of two educational interventions delivered in community pharmacy over time. *The Journal of asthma : official journal of the Association for the Care of Asthma*. 2010; 47: 251-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20394511
39. Melani AS, Bonavia M, Cilenti V, *et al*. Inhaler mishandling remains common in real life and is associated with reduced disease control. *Respir Med*. 2011; 105: 930-8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21367593
40. Levy ML, Dekhuijzen PN, Barnes PJ, *et al*. Inhaler technique: facts and fantasies. A view from the Aerosol Drug Management Improvement Team (ADMIT). *NPJ Prim Care Respir Med*. 2016; 26: 16017. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27098045
41. Haughney, J., Price, D., Barnes, N. C., *et al*. Choosing inhaler devices for people with asthma: current knowledge and outstanding research needs. *Respiratory medicine*. 2010; 104: 1237-45. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20472415
42. Giraud, V., Roche, N.. Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability. *The European respiratory journal*. 2002; 19: 246-51. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11866004
43. Harnett, C. M., Hunt, E. B., Bowen, B. R., *et al*. A study to assess inhaler technique and its potential impact on asthma control in patients attending an asthma clinic. *J Asthma*. 2014; 51: 440-5.
44. Hardwell, A., Barber, V., Hargadon, T., *et al*. Technique training does not improve the ability of most patients to use pressurised metered-dose inhalers (pMDIs). *Prim Care Respir J*. 2011; 20: 92-6. Available from: http://www.nature.com/articles/pcrj201088
45. Papi, A., Brightling, C., Pedersen, S. E., Reddel, H. K.. Asthma. *Lancet*. 2018; 391: 783-800. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29273246
46. Chauhan BF, Chartrand C, Ni Chroinin M et al. Addition of long-acting beta2-agonists to inhaled corticosteroids for chronic asthma

in children. *Cochrane Database Syst Rev* 2015; Volume 11: CD007949. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26594816
47. Castro-Rodriguez, J. A., Rodrigo, G. J., Rodriguez-Martinez, C. E.. Principal findings of systematic reviews for chronic treatment in childhood asthma. *J Asthma*. 2015; 52: 1038-45. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26303207
48. Ducharme FM, Ni Chroinin M, Greenstone I, Lasserson TJ. Addition of long-acting beta2-agonists to inhaled corticosteroids versus same dose inhaled corticosteroids for chronic asthma in adults and children. *Cochrane Database Syst Rev*. 2010; Issue 5: CD005535. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005535.pub2/full
49. Fitzpatrick AM, Jackson DJ, Mauger DT et al. Individualized therapy for persistent asthma in young children. *J Allergy Clin Immunol*. 2016; 138: 1608-18.e12. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27777180
50. van Asperen PP. Long-acting beta agonists for childhood asthma. *Aust Prescr*. 2012; 35: 111-3. Available from: https://www.nps.org.au/australian-prescriber/articles/long-acting-beta2-agonists-for-childhood-asthma
51. Lemanske RF, Mauger DT, Sorkness CA, *et al*. Step-up therapy for children with uncontrolled asthma receiving inhaled corticosteroids. *N Engl J Med*. 2010; 362: 975-985. Available from: http://www.nejm.org/doi/full/10.1056/NEJMoa1001278#t=article
52. McMahon AW, Levenson MS, McEvoy BW, *et al*. Age and risks of FDA-approved long-acting β2-adrenergic receptor agonists. *Pediatrics*. 2011; 128: e1147-1154. Available from: http://pediatrics.aappublications.org/content/128/5/e1147.long
53. Chauhan BF, Ben Salah R, Ducharme FM. Addition of anti-leukotriene agents to inhaled corticosteroids in children with persistent asthma. *Cochrane Database Syst Rev*. 2013; Issue 10: CD009585. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24089325
54. Fogel RB, Rosario N, Aristizabal G et al. Effect of montelukast or salmeterol added to inhaled fluticasone on exercise-induced bronchoconstriction in children. *Ann Allergy Asthma Immunol* 2010; 104: 511-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20568384
55. Lipworth BJ, Basu K, Donald HP, *et al*. Tailored second-line therapy in asthmatic children with the Arg(16) genotype. *Clin Sci (Lond)*. 2013; 124: 521-528. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23126384
56. Merck, Sharp and Dohme Australia Pty Ltd. *Product Information: Singulair (montelukast sodium) Tablets*. Therapeutic Goods Administration, Canberra, 2013. Available from: https://www.ebs.tga.gov.au/
57. Bush A. Montelukast in paediatric asthma: where we are now and what still needs to be done? *Paediatr Respir Rev*. 2015; 16: 97-100. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25499571
58. Nwokoro C, Pandya H, Turner S, *et al*. Intermittent montelukast in children aged 10 months to 5 years with wheeze (WAIT trial): a multicentre, randomised, placebo-controlled trial. *Lancet Respir Med*. 2014; 2: 796-803. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25212745
59. Brodlie M, Gupta A, Rodriguez-Martinez CE, *et al*. Leukotriene receptor antagonists as maintenance and intermittent therapy for episodic viral wheeze in children. *Cochrane Database Syst Rev*. 2015; Issue 10: CD008202. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26482324
60. Bisgaard H, Zielen S, Garcia-Garcia ML, *et al*. Montelukast reduces asthma exacerbations in 2- to 5-year-old children with intermittent asthma. *Am J Respir Crit Care Med*. 2005; 171: 315-322. Available from: http://ajrccm.atsjournals.org/content/171/4/315.long
61. Nagao M, Ikeda M, Fukuda N, *et al*. Early control treatment with montelukast in preschool children with asthma: a randomized controlled trial. *Allergol Int*. 2018; 67: 72-78. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28526210
62. Valovirta, E., Boza, M. L., Robertson, C. F., *et al*. Intermittent or daily montelukast versus placebo for episodic asthma in children. *Ann Allergy Asthma Immunol*. 2011; 106: 518-26. Available from: https://www.ncbi.nlm.nih.gov/pubmed/21624752
63. Castro-Rodriguez JA, Rodriguez-Martinez CE, Ducharme FM. Daily inhaled corticosteroids or montelukast for preschoolers with asthma or recurrent wheezing: A systematic review. *Pediatr Pulmonol*. 2018; Epub ahead of print 6 November. Available from: https://www.ncbi.nlm.nih.gov/pubmed/30394700
64. Jartti T. Inhaled corticosteroids or montelukast as the preferred primary long-term treatment for pediatric asthma? *Eur J Pediatr*. 2008; 167: 731-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/18214538
65. Maspero, J, Guerra, F, Cuevas, F, *et al*. Efficacy and tolerability of salmeterol/fluticasone propionate versus montelukast in childhood asthma: a prospective, randomized, double-blind, double-dummy, parallel-group study. *Clin Ther*. 2008; 30: 1492-1504.
66. Pedersen S, Maspero J, Gul N, Sharma R. Components of asthma control and treatment response of individual control criteria in children: analysis of the PEACE study. *Pediatr Pulmonol*. 2011; 46: 1182-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/21751432
67. Malka J, Mauger DT, Covar R, *et al*. Eczema and race as combined determinants for differential response to step-up asthma therapy. *J Allergy Clin Immunol*. 2014; 134: 483-5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24835502
68. Stelmach I, Ozarek-Hanc A, Zaczeniuk M et al. Do children with stable asthma benefit from addition of montelukast to inhaled corticosteroids: randomized, placebo controlled trial. *Pulm Pharmacol Ther*. 2015; 31: 42-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25640020
69. Grzelewski, T, Stelmach, I. Exercise-induced bronchoconstriction in asthmatic children: a comparative systematic review of the available treatment options. *Drugs*. 2009; 69: 1533-1553. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19678711
70. Fogel RB, Rosario N, Aristizabal G, *et al*. Effect of montelukast or salmeterol added to inhaled fluticasone on exercise-induced bronchoconstriction in children. *Ann Allergy Asthma Immunol*. 2010; 104: 511-517. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20568384
71. Robertson CF, Price D, Henry R, *et al*. Short-course montelukast for intermittent asthma in children: a randomized controlled trial. *Am J Respir Crit Care Med*. 2007; 175: 323-329. Available from: http://ajrccm.atsjournals.org/content/175/4/323.long
72. Watts, K, Chavasse, R J P G. Leukotriene receptor antagonists in addition to usual care for acute asthma in adults and children. *Cochrane Database Syst Rev*. 2012; Issue 5: . Available from: http://cochranelibrary-wiley.com/doi/10.1002

/14651858.CD006100.pub2/full
73. Capsomidis, A., Tighe, M.. Archimedes. Question 2. Is oral montelukast beneficial in treating acute asthma exacerbations in children?. *Arch Dis Child*. 2010; 95: 948-50. Available from: http://adc.bmj.com/content/95/11/948.long
74. Schuh, S, Willan, AR, Stephens, D, *et al*. Can montelukast shorten prednisolone therapy in children with mild to moderate acute asthma? A randomized controlled trial. *J Pediatr*. 2009; 155: 795-800. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19656525
75. Bacharier LB, Phillips BR, Zeiger RS, *et al*. Episodic use of an inhaled corticosteroid or leukotriene receptor antagonist in preschool children with moderate-to-severe intermittent wheezing. *J Allergy Clin Immunol*. 2008; 122: 1127-1135. Available from: https://www.ncbi.nlm.nih.gov/pubmed/18973936
76. Murphy KR, Zeiger RS, Kosinski M, *et al*. Test for respiratory and asthma control in kids (TRACK): a caregiver-completed questionnaire for preschool-aged children. *J Allergy Clin Immunol*. 2009; 123: 833-9. Available from: http://www.jacionline.org/article/S0091-6749(09)00212-7/fulltext
77. Zeiger RS, Mellon M, Chipps B, *et al*. Test for Respiratory and Asthma Control in Kids (TRACK): clinically meaningful changes in score. *J Allergy Clin Immunol*. 2011; 128: 983-8. Available from: http://www.jacionline.org/article/S0091-6749(11)01287-5/fulltext
78. Liu AH, Zeiger R, Sorkness C, *et al*. Development and cross-sectional validation of the Childhood Asthma Control Test. *J Allergy Clin Immunol*. 2007; 119: 817-25. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17353040
79. Liu AH, Zeiger RS, Sorkness CA, *et al*. The Childhood Asthma Control Test: retrospective determination and clinical validation of a cut point to identify children with very poorly controlled asthma. *J Allergy Clin Immunol*. 2010; 126: 267-73, 273.e1. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20624640
80. Abramson MJ, Schattner RL, Holton C et al. Spirometry and regular follow-up do not improve quality of life in children or adolescents with asthma: Cluster randomized controlled trials. *Pediatr Pulmonol* 2015; 50: 947-54. (Available from: https://www.ncbi.nlm.nih.gov/pubmed/25200397
81. Deschildre A, Beghin L, Salleron J, *et al*. Home telemonitoring (forced expiratory volume in 1 s) in children with severe asthma does not reduce exacerbations. *Eur Respir J*. 2012; 39: 290-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/21852334
82. Nuijsink M, Hop WC, Sterk PJ et al. Long-term asthma treatment guided by airway hyperresponsiveness in children: a randomised controlled trial. *Eur Respir J* 2007; 30: 457-66. (Available from: https://www.ncbi.nlm.nih.gov/pubmed/17537770
83. Nuijsink M, Vaessen-Verberne AA, Hop WC et al. Long-term follow-up after two years of asthma treatment guided by airway responsiveness in children. *Respir Med* 2013; 107: 981-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23672993
84. Petsky HL, Li A, Chang AB. Tailored interventions based on sputum eosinophils versus clinical symptoms for asthma in children and adults. *Cochrane Database Syst Rev* 2017; 8: Cd005603. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28837221
85. Lehtimaki L, Csonka P, Makinen E et al. Predictive value of exhaled nitric oxide in the management of asthma: a systematic review. *Eur Respir J* 2016; 48: 706-14. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27492830
86. Petsky HL, Kew KM, Chang AB. Exhaled nitric oxide levels to guide treatment for children with asthma. *Cochrane Database Syst*. Rev 2016; Issue 11: CD011439. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27825189/
87. Turner S, Francis B, Vijverberg S et al. Childhood asthma exacerbations and the Arg16 beta2-receptor polymorphism: A meta-analysis stratified by treatment. *J Allergy Clin Immunol* 2016; 138: 107-13.e5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26774659
88. Bush A, Saglani S. Management of severe asthma in children. *Lancet*. 2010; 376: 814-25. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20816548

Stepping down treatment in children aged 1–5 years

Recommendations

If symptoms have been well controlled for at least 6 months in a child taking regular inhaled corticosteroid treatment, consider reducing the dose.

Monitor symptom control within 4–6 weeks after stepping down.

Do not attempt to step down treatment at the start of the preschool year or during the child's peak asthma season (if there is a predictable seasonal pattern).

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- Brand *et al.* 2008[1]
- van Asperen *et al.* 2010[2]

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If symptoms have been well controlled for at least 6 months in a child taking regular treatment with a fixed-dose combination of inhaled corticosteroid–long-acting beta$_2$ agonist, consider switching to inhaled corticosteroid only.

Monitor symptom control within 4–6 weeks after stepping down.

Do not attempt to step down treatment at the start of the preschool year or during the child's peak asthma season (if there is a predictable seasonal pattern). Take into account previous treatment response, the result of any previous attempts to step down, and changes in the child's environment that could affect exposure to triggers.

- **Combination inhaled corticosteroid plus long-acting beta$_2$ agonist is not recommended for children younger than 6 years.**

How this recommendation was developed

Consensus recommendation following inconclusive literature search

Based on clinical experience and expert opinion after literature review yielded insufficient evidence for an evidence-based recommendation

Key evidence considered:

- Kew *et al.* 2015[3]
- Rank *et al.* 2015[4]

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If symptoms are well controlled for at least 6 months on the lowest available inhaled corticosteroid dose, consider stopping treatment and monitor for symptoms and flare-ups.

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- van Asperen *et al.* 2010[2]
- Brand *et al.* 2008[1]

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More information

Stepping down preventer treatment in children

Stepping down can be considered when asthma has been well controlled for 6 months (depending on severity of previous symptoms). This will help identify the minimal dose or regimen needed to maintain control and may minimise the risk of treatment-related adverse effects and help identify the minimal dose or regimen needed to maintain control.

Children who have stable asthma are at increased risk of a flare-up when stepping down treatment, so close monitoring is needed. Stepping down should not be attempted at the beginning of the school year.[5]

Stepping down from regular inhaled corticosteroid

For children already taking the lowest available dose, options are stop preventer treatment entirely, or switch to montelukast. Few studies have compared different options for stepping down.

Children may be at higher risk of a flare-up or loss of asthma control after stopping low-dose inhaled corticosteroid treatment.[6, 7, 8]

Stepping down from regular inhaled corticosteroid plus long-acting beta-2 agonist

Options for stepping down from regular treatment with a combination inhaled corticosteroid and long-acting beta$_2$ agonist are to reduce the inhaled corticosteroid dose or switch to inhaled corticosteroid only (i.e. discontinue the long-acting beta$_2$ agonist).

There is insufficient evidence from randomised trials on which to base recommendations on whether and how to discontinue long-acting beta$_2$ agonist treatment in children once good asthma control has been achieved with the combination of inhaled corticosteroid and long-acting beta$_2$ agonist.[9]

In a study of children aged 4–11 years whose asthma was well controlled while using a combination of inhaled corticosteroid and long-acting beta$_2$-agonist, stepping down to inhaled corticosteroid monotherapy was associated with a higher rate of flare-ups than continuing on combination therapy.[10]

In a study of children aged 5–15 years with well-controlled asthma, halving the inhaled corticosteroid component and discontinuing the long-acting beta$_2$ agonist had equivalent outcomes for asthma symptoms and lung function.[11]

In a study of children with asthma well controlled on twice-daily fluticasone propionate, switching to montelukast was associated with a higher rate of treatment failure and poorer asthma control than halving the fluticasone dose and adding salmeterol.[12]

Stepping down from montelukast

In children taking montelukast, treatment can be stopped abruptly.

Asthma control should be monitored and the child's written asthma action plan updated to ensure parents/carers know how to manage symptoms.

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Inhaled corticosteroids for children: adverse effects

Local adverse effects

Hoarseness and pharyngeal candidiasis are not commonly reported among preschool children or school-aged children talking inhaled corticosteroids. [1, 2, 13]

Topical effects can be reduced by use of spacer devices (which reduce oropharyngeal deposition), and by mouth-rinsing and spitting after use.[2] Immediate quick mouth-rinsing removes more residual medicine in the mouth than delayed rinsing.[14]

There is limited evidence that inhaled asthma medication can affect dental health.[2, 15] Mouth rinsing might reduce this risk.

Systemic adverse effects

Systemic effects of inhaled corticosteroids in children depend on the dose, but clinically significant adverse effects are uncommon.[2]

The use of spacers and mouth rinsing will not reduce systemic effects, but the use of a spacer may increase efficacy so that a lower dose is required.

Growth

Short-term suppression of linear growth has been demonstrated in children taking inhaled corticosteroids.[16,17] The effect seems to be

maximal during the first year of therapy and only one study has reported an effect in subsequent years of treatment.[17] A Cochrane systematic review concluded that regular use of inhaled corticosteroid at low or medium daily doses is associated with a mean reduction of 0.48 cm per year in linear growth velocity and 0.61 cm less gain in height during 1 year of treatment in children with mild to moderate persistent asthma.[17]

One study of patients who participated in a clinical trial of inhaled corticosteroids as children, reported a reduction in adult height of approximately 1 cm,[16, 18, 19, 20] whereas several studies have reported that children taking inhaled corticosteroids attained normal adult height.[21, 22, 23]

The effect is dose-dependent[19,20] and may be more likely in children who begin inhaled corticosteroid treatment before age 10.[18]

Other factors affect growth in children with asthma. Uncontrolled asthma itself reduces growth and final adult height.[22] One study found that inhaled corticosteroid equivalent to budesonide 400 microg/day affected growth less than low socioeconomic status.[23]

Bone density

Inhaled corticosteroids have not been associated with effects on bone density or fractures in children. [2] However, data from a recent study in Australia suggested asthma itself is associated with increased incidence of fractures in children, independent of medication.[24]

Given that the total dose of corticosteroids (both inhaled corticosteroids and oral corticosteroids) influences bone health, the aim of asthma management is to maintain symptom control using the lowest inhaled corticosteroid dose required, and to avoid repeated courses of oral corticosteroids.

Adrenal suppression

Biochemical testing in a research setting suggests that hypothalamic–pituitary–adrenal axis suppression may occur in up to two-thirds of children treated with inhaled corticosteroids, and may occur at even low doses.[25] The risk is higher among children receiving concomitant intranasal steroids and those with lower body mass index,[25] and is influenced by genetics.[26]

Clinical adrenal insufficiency in children taking inhaled corticosteroids is rare but has been reported, [27, 28, 29] including cases in Australia.[29] Most cases have involved children given more than 500 microg per day fluticasone propionate.[27]

Adrenal suppression is associated with hypoglycaemia, hypotension, weakness, failure to grow, and is potentially fatal. Hypothalamic–pituitary–adrenal axis suppression may not be detected until adrenal crisis is precipitated by physical stress.[30]

Written information (e.g. a steroid alert card) can be prepared for children receiving long-term high-dose inhaled corticosteroids. Parents/carers can be instructed to present the card if the child ever needs to go to the emergency department (for any reason) or be admitted to hospital. A steroid alert card should state that child has asthma and the inhaled corticosteroid dose. A medical alert bracelet could also be considered.

There are no nationally accepted protocols for routine assessment of adrenal function in primary care because it has not yet been possible to identify precisely which children should be tested, to interpret test results reliably, to identify the appropriate interval for retesting, and because a clinical benefit has not been clearly demonstrated.

Regular monitoring of height might help detect adrenal suppression, based on the findings of a study in which a reduction in linear growth velocity occurred before adrenal suppression.[31]

Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)	
	Low	**High**
Beclometasone dipropionate †	100–200	>200 (maximum 400)
Budesonide	200–400	>400 (maximum 800)
Ciclesonide ‡	80–160	>160 (maximum 320)
Fluticasone propionate	100–200	>200 (maximum 500)

† Dose equivalents for *Qvar* (TGA-registered CFC-free formulation of beclometasone dipropionate)

‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

Source

van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma.* The Thoracic Society of Australia and New Zealand, 2010. Available from: http://www.thoracic.org.au/clinical-documents/area?command=record&id=14

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▶ Go to: The Thoracic Society of Australia and New Zealand's *Position Statement: The role of corticosteroids in the management of childhood asthma*

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Classification of recent asthma symptom control in children

Ongoing review of asthma involves both assessing recent asthma symptom control and assessing risks for poor asthma outcomes such as flare-ups and adverse effects of medicines.

Recent asthma symptom control is assessed according to the frequency of asthma symptoms over the previous 4 weeks.

Table. Definition of levels of recent asthma symptom control in children (regardless of current treatment regimen)

Good control	Partial control	Poor control
All of: • Daytime symptoms† ≤2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • No limitation of activities‡ • No symptoms§ during night or when wakes up • Need for SABA reliever# ≤2 days per week	Any of: • Daytime symptoms† >2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • Any limitation of activities* • Any symptoms during night or when wakes up†† • Need for SABA reliever# >2 days per week	Either of: • Daytime symptoms† >2 days per week (lasting from minutes to hours or recurring, and partially or fully relieved by SABA reliever) • ≥3 features of partial control within the same week

SABA: short-acting $beta_2$ agonist

† e.g. wheezing or breathing problems

‡ child is fully active; runs and plays without symptoms

§ including no coughing during sleep

not including doses taken prophylactically before exercise. (Record this separately and take into account when assessing management.)

* e.g. wheeze or breathlessness during exercise, vigorous play or laughing

†† e.g. waking with symptoms of wheezing or breathing problems

Notes:

Recent asthma control is based on symptoms over the previous 4 weeks. Each child's risk factors for future asthma outcomes should also be assessed and taken into account in management.

Validated questionnaires can be used for assessing recent symptom control:
Test for Respiratory and Asthma Control in Kids (TRACK) for children < 5 years
Childhood Asthma Control Test (C-ACT) for children aged 4–11 years

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Table. Risk factors for life-threatening asthma flare-ups in children

Asthma-related factors

Poor asthma control

Admission to hospital in preceding 12 months

History of intubation for acute asthma

Over-use of short-acting beta$_2$ agonist reliever

Abnormal spirometry findings

Reversible expiratory airflow limitation on spirometry despite treatment

Poor adherence to preventer

Incorrect inhaler technique for preventer

Poor adherence to asthma action plan

Exposure to clinically relevant allergens

Exposure to tobacco smoke

Other clinical factors

Allergies to foods, insects, medicines

Obesity

Family-related factors

Frequent failure to attend consultations/lack of follow-up after an acute flare-up

Significant parental psychological or socioeconomic problems

Parent/carer unequipped to manage asthma emergency

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Approaches to assessment and monitoring of asthma control in children

Assessment of asthma control in children is based mainly on:

- recent asthma symptom control (assessed by the frequency and severity of symptoms between flare-ups
- the degree to which asthma symptoms affect daily activities such as interference with physical activity or missed school days)
- the frequency of flare-ups
- spirometry in children who are able to perform the test reliably.

Standardised questionnaires

Questionnaire-based instruments have been validated for assessing asthma control in children:

▶ *Test for Respiratory and Asthma Control in Kids (TRACK)* for children less than 5 years old – consists of five questions about frequency of respiratory symptoms (wheeze, cough, shortness of breath), activity limitation, and night-time awakenings in the past 4 weeks, rescue medication use in the past 3 months, and oral corticosteroid use in the previous year.[32, 33] A lower score indicates worse asthma control.

Childhood Asthma Control Test (C-ACT) for children aged 4–11 years – consists of seven items: three for the parent/carer (about the child's symptoms over the previous 4 weeks) and four for the child.[34, 35] A lower score indicates worse asthma control. **Note:** C-ACT is intended for US use.

Lung function tests

Frequent spirometry to guide asthma treatment in children has not been shown to achieve superior outcomes to symptom-based treatment.[36] Current evidence does not support use of home spirometers to guide asthma treatment in children.[37] However, low FEV_1 predicts clinically significant flare-ups, so spirometry should be performed at asthma reviews for children who are old enough to do the test.

The quality and utility of spirometry depends on the skill, clinical expertise and experience of the person doing and interpreting spirometry.

The results of one study in children aged 6–16 years with moderate atopic asthma suggest that asthma treatment guided by airway hyperresponsiveness (measured by bronchial provocation testing) may have a benefit over symptom-guided treatment in improving lung, but this effect was lost after 3–7 years of usual care.[38, 39] Repeated bronchial provocation testing is not feasible in clinical practice.

Measures of airway inflammation

Measures of airway inflammation (e.g. sputum eosinophil count, exhaled nitric oxide measurement) are not recommended in primary care to guide treatment decisions, but are increasingly used in specialist clinics.

Asthma treatment guided by sputum eosinophil count has been shown to reduce the frequency of flare-ups in adults with asthma, but there is insufficient evidence to ascertain its value for children.[40]

Exhaled nitric oxide measurement may be useful in guiding asthma management in some children. In children not taking inhaled corticosteroid, a high nitric oxide level probably predicts a good short-term response to inhaled corticosteroid treatment,[41] but it does not distinguish between asthma and eosinophilic bronchitis and is often high in children with atopy. There is insufficient evidence to ascertain whether a low exhaled nitric oxide level predicts successful withdrawal from inhaled corticosteroids without asthma relapse,[41] or safety of treating asthma without inhaled corticosteroids.

A Cochrane review[42] found that exhaled nitric oxide-guided management was significantly better than other approaches to adjusting medicines for reducing the number of children with flare-ups and the number of children who needed oral corticosteroids, but did not reduce the frequency of flare-ups or the rate of flare-ups requiring hospitalisation, improve lung function or symptoms scores, or reduce inhaled corticosteroid doses. The authors concluded that it could not be recommended for all children but may be beneficial for a subset not yet defined.[42]

Towards personalised asthma care

Emerging understanding of asthma phenotypes and of genetic factors that predict therapeutic response to preventer options is leading to the possibility of personalised, genomics-based treatment for asthma in children.[43] In the near future, individual tailored therapy is may replace the standardised step model based on population data.

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'Wheeze-detecting' devices

Some hand-held devices and smart phone applications are marketed for detecting and measuring wheeze by audio recording and analysis.

There is not enough evidence to recommend these devices and apps for use in monitoring asthma symptoms or asthma control in adults or children, or in distinguishing wheeze from other airway sounds in children.

- Reliance on these devices could result in over- or under-treatment.

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References

1. Brand PL, Baraldi E, Bisgaard H, *et al*. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. *Eur Respir J*. 2008; 32: 1096-1110. Available from: http://erj.ersjournals.com/content/32/4/1096.full
2. van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma*. The Thoracic Society of Australia and New Zealand, 2010. Available from: https://www.thoracic.org.au/journal-publishing/command/download_file/id/25/filename/The_role_of_corticosteroids_in_the_management_of_childhood_asthma_-_2010.pdf
3. Kew KM, Beggs S, Ahmad S. Stopping long-acting beta2-agonists (LABA) for children with asthma well controlled on LABA and inhaled corticosteroids. *Cochrane Database Syst Rev*. 2015; Issue 5: CD011316. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25997166
4. Rank, M. A., Johnson, R., Branda, M., *et al*. Long-term outcomes after stepping down asthma controller medications: a claims-based, time-to-event analysis. *Chest*. 2015; 148: 630-639. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4556120/
5. Rank, M. A., Branda, M. E., McWilliams, D. B., *et al*. Outcomes of stepping down asthma medications in a guideline-based pediatric asthma management program. *Ann Allergy Asthma Immunol*. 2013; 110: 354-358.e2. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23622006
6. Kwong KY, Morphew T, Huynh P et al. Loss of asthma control in inner city children with asthma after withdraw of asthma controller medication. *J Asthma* 2009; 46: 1001-5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19995137
7. Rank MA, Hagan JB, Park MA, *et al*. The risk of asthma exacerbation after stopping low-dose inhaled corticosteroids: a systematic review and meta-analysis of randomized controlled trials. *J Allergy Clin Immunol*. 2013; 131: 724-9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23321206
8. Ciolkowski, J., Mazurek, H., Stasiowska, B.. Evaluation of step-down therapy from an inhaled steroid to montelukast in childhood

asthma. *Allergol Immunopathol (Madr)*. 2014; 42: 282-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23684855
9. Kew, K. M., Beggs, S., Ahmad, S.. Stopping long-acting beta2-agonists (LABA) for children with asthma well controlled on LABA and inhaled corticosteroids. *Cochrane Database Syst Rev*. 2015; Issue 5: CD011316. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25997166 Full text at: http://cochranelibrary-wiley.com/doi/10.1002/14651858.CD011316.pub2/full
10. Stempel, D. A., Szefler, S. J., Pedersen, S., *et al*. Safety of adding salmeterol to fluticasone propionate in children with asthma. *N Engl J Med*. 2016; 375: 840-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27579634
11. Akashi K, Mezawa H, Tabata Y, *et al*. Optimal step-down approach for pediatric asthma controlled by salmeterol/fluticasone: A randomized, controlled trial (OSCAR study). *Allergol Int*. 2016; 65: 306-11. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27155753
12. Peters SP, Anthonisen N, Castro M, *et al*. Randomized comparison of strategies for reducing treatment in mild persistent asthma. *N Engl J Med*. 2007; 356: 2027-39. Available from: https://www.ncbi.nlm.nih.gov/pubmed/17507702
13. Cazeiro C, Silva C, Mayer S et al. Inhaled corticosteroids and respiratory infections in children with asthma: a meta-analysis. *Pediatrics*. 2017; 139. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28235797
14. Yokoyama H, Yamamura Y, Ozeki T, *et al*. Effects of mouth washing procedures on removal of budesonide inhaled by using Turbuhaler. *Yakugaku Zasshi*. 2007; 127: 1245-1249. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17666876
15. Godara N, Godara R, Khullar M. Impact of inhalation therapy on oral health. *Lung India*. 2011; 28: 272-5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/22084541
16. Loke YK, Blanco P, Thavarajah M, Wilson AM. Impact of inhaled corticosteroids on growth in children with asthma: systematic review and meta-analysis. *PloS One*. 2015; 10: e0133428. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26191797
17. Zhang L, Prietsch SO, Ducharme FM. Inhaled corticosteroids in children with persistent asthma: effects on growth. *Cochrane Database Syst Rev*. 2014: Cd009471. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25030198
18. Kelly HW, Sternberg AL, Lescher R, *et al*. Effect of inhaled glucocorticoids in childhood on adult height. *N Engl J Med*. 2012; 367: 904-12. Available from: http://www.nejm.org/doi/full/10.1056/NEJMoa1203229
19. Pruteanu AI, Chauhan BF, Zhang L et al. Inhaled corticosteroids in children with persistent asthma: dose-response effects on growth. *Cochrane Database Syst Rev*. 2014: Cd009878. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25030199
20. De Leonibus C, Attanasi M, Roze Z et al. Influence of inhaled corticosteroids on pubertal growth and final height in asthmatic children. *Pediatr Allergy Immunol*. 2016; 27: 499-506. Available from:https://www.ncbi.nlm.nih.gov/pubmed/26919136
21. Pauwels RA, Pedersen S, Busse WW, *et al*. Early intervention with budesonide in mild persistent asthma: a randomised, double-blind trial. *Lancet*. 2003; 361: 1071-1076. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12672309
22. Pedersen S. Do inhaled corticosteroids inhibit growth in children? *Am J Respir Crit Care Med*. 2001; 164: 521-35. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11520710
23. Agertoft L, Pedersen S. Effect of long-term treatment with inhaled budesonide on adult height in children with asthma. *N Engl J Med*. 2000; 343: 1064-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11027740
24. Degabriele EL, Holloway KL, Pasco JA et al. Associations between asthma status and radiologically confirmed fracture in children: A data-linkage study. *J Paediatr Child Health*. 2018; 54(8): 855-860. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29614205
25. Zöllner EW, Lombard CJ, Galal U, *et al*. Hypothalamic-adrenal-pituitary axis suppression in asthmatic school children. *Pediatrics*. 2012; 130: e1512-19. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23147980
26. Hawcutt DB, Francis B, Carr DF et al. Susceptibility to corticosteroid-induced adrenal suppression: a genome-wide association study. *Lancet Respir Med*. 2018; 6:442-450. Available from: https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(18)30058-4/fulltext
27. Ahmet A, Kim H, Spier S. Adrenal suppression: A practical guide to the screening and management of this under-recognized complication of inhaled corticosteroid therapy. *Allergy Asthma Clin Immunol*. 2011; 7: 13. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3177893/
28. Priftis, K N, Papadimitriou, A, Anthracopoulos, M B, Fretzayas, A, Chrousos, G P. Endocrine-immune interactions in adrenal function of asthmatic children on inhaled corticosteroids. *Neuroimmunomodulation* 2008; 16: 333-339.
29. Macdessi JS, Randell TL, Donaghue KC, *et al*. Adrenal crises in children treated with high-dose inhaled corticosteroids for asthma. *Med J Aust*. 2003; 178: 214-6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12603184
30. Rao Bondugulapati LN, Rees DA. Inhaled corticosteroids and HPA axis suppression: how important is it and how should it be managed? *Clin Endocrinol (Oxf)*. 2016; 85: 165-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27038017
31. Liddell BS, Oberlin JM, Hsu DP. Inhaled corticosteroid related adrenal suppression detected by poor growth and reversed with ciclesonide. *J Asthma*. 2017; 54: 99-104. Available from:https://www.ncbi.nlm.nih.gov/pubmed/27284755
32. Murphy KR, Zeiger RS, Kosinski M, *et al*. Test for respiratory and asthma control in kids (TRACK): a caregiver-completed questionnaire for preschool-aged children. *J Allergy Clin Immunol*. 2009; 123: 833-9. Available from: http://www.jacionline.org/article/S0091-6749(09)00212-7/fulltext
33. Zeiger RS, Mellon M, Chipps B, *et al*. Test for Respiratory and Asthma Control in Kids (TRACK): clinically meaningful changes in score. *J Allergy Clin Immunol*. 2011; 128: 983-8. Available from: http://www.jacionline.org/article/S0091-6749(11)01287-5/fulltext
34. Liu AH, Zeiger R, Sorkness C, *et al*. Development and cross-sectional validation of the Childhood Asthma Control Test. *J Allergy Clin Immunol*. 2007; 119: 817-25. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17353040
35. Liu AH, Zeiger RS, Sorkness CA, *et al*. The Childhood Asthma Control Test: retrospective determination and clinical validation of a cut point to identify children with very poorly controlled asthma. *J Allergy Clin Immunol*. 2010; 126: 267-73, 273.e1. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20624640

36. Abramson MJ, Schattner RL, Holton C et al. Spirometry and regular follow-up do not improve quality of life in children or adolescents with asthma: Cluster randomized controlled trials. *Pediatr Pulmonol* 2015; 50: 947-54. (Available from: https://www.ncbi.nlm.nih.gov/pubmed/25200397
37. Deschildre A, Beghin L, Salleron J, *et al*. Home telemonitoring (forced expiratory volume in 1 s) in children with severe asthma does not reduce exacerbations. *Eur Respir J*. 2012; 39: 290-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/21852334
38. Nuijsink M, Hop WC, Sterk PJ et al. Long-term asthma treatment guided by airway hyperresponsiveness in children: a randomised controlled trial. *Eur Respir J* 2007; 30: 457-66. (Available from: https://www.ncbi.nlm.nih.gov/pubmed/17537770
39. Nuijsink M, Vaessen-Verberne AA, Hop WC et al. Long-term follow-up after two years of asthma treatment guided by airway responsiveness in children. *Respir Med* 2013; 107: 981-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23672993
40. Petsky HL, Li A, Chang AB. Tailored interventions based on sputum eosinophils versus clinical symptoms for asthma in children and adults. *Cochrane Database Syst Rev* 2017; 8: Cd005603. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28837221
41. Lehtimaki L, Csonka P, Makinen E et al. Predictive value of exhaled nitric oxide in the management of asthma: a systematic review. *Eur Respir J* 2016; 48: 706-14. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27492830
42. Petsky HL, Kew KM, Chang AB. Exhaled nitric oxide levels to guide treatment for children with asthma. *Cochrane Database Syst*. Rev 2016; Issue 11: CD011439. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27825189/
43. Turner S, Francis B, Vijverberg S et al. Childhood asthma exacerbations and the Arg16 beta2-receptor polymorphism: A meta-analysis stratified by treatment. *J Allergy Clin Immunol* 2016; 138: 107-13.e5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26774659

Managing flare-ups in children aged 1–5 years

Recommendations

Manage wheezing with an inhaled short-acting beta$_2$ agonist bronchodilator (reliever) as needed for relief of symptoms, according to age and clinical significance. Educate parents/carers how and when to give reliever.

Note: The recommended dose for non-emergency bronchodilator in children aged 1–5 years is salbutamol 2–4 puffs (100 microg per puff) as needed, 1 puff at a time, via pressurised metered-dose inhaler plus spacer and face mask for infants aged 1–2 years or pressurised metered-dose inhaler plus spacer for children aged 3–5 years (if able to cooperate). Repeat as needed.

- **Do not prescribe oral salbutamol. Inhalation is the recommended route for delivering relievers for all children and adults.**

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

For children with acute asthma/wheezing that is associated with increased work of breathing and is severe enough to require hospital admission, consider a course of oral corticosteroids, e.g. 1 mg/kg prednisolone (maximum 50 mg) each morning for 3 days.

How this recommendation was developed

Consensus recommendation following inconclusive literature search

Based on clinical experience and expert opinion after literature review yielded insufficient evidence for an evidence-based recommendation

Key evidence considered:

- Foster et al. 2018[1]
- Castro-Rodriguez et al. 2016[2]
- van Asperen et al. 2010[3]
- Panickar et al. 2009[4]
- Chang et al. 2008[5]
- Smith et al. 2003[6]
- Rowe et al. 2001[7]

Last reviewed version 2.0

For wheezing children younger than 6 years, do not instruct parents/carers to start a course of oral corticosteroids at their own discretion and do not prescribe or recommend oral corticosteroids to be started at home as part of the child's written asthma action plan.

Instruct parents/carers to seek medical advice each time.

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- van Asperen et al. 2010[3]
- Brand et al. 2014[8]

Last reviewed version 2.0

If oral corticosteroids are needed to manage severe acute flare-ups, reassess regular medicine regimen (including adherence and inhaler technique) and consider specialist referral.

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- van Asperen et al. 2010[3]

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Do not prescribe long-term oral corticosteroids without specialist assessment by a paediatric respiratory physician.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

Advise parents/carers that children taking a preventer medicine should continue taking it during wheezing episodes.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

In children not taking regular preventer treatment, do not initiate inhaled corticosteroid treatment to manage worsening asthma symptoms or wheeze or during an acute flare-up, and do not recommend intermittent use of inhaled corticosteroids as part of a written asthma action plan.

How this recommendation was developed

Consensus recommendation following inconclusive literature search

Based on clinical experience and expert opinion after literature review yielded insufficient evidence for an evidence-based recommendation

Key evidence considered:

- Kew et al. 2016[9]
- Chong et al. 2015[10]
- Yousef et al. 2012[11]

Last reviewed version 2.0

For a child taking low-dose inhaled corticosteroid regularly, do not prescribe high-dose inhaled corticosteroids to manage worsening asthma symptoms or wheeze, and do not recommend that parents/carers give children high doses of inhaled corticosteroid treatment during wheezing episodes (e.g. as part of a written asthma action plan).

Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)

	Low	High
Beclometasone dipropionate †	**100–200**	**>200 (maximum 400)**
Budesonide	**200–400**	**>400 (maximum 800)**
Ciclesonide ‡	**80–160**	**>160 (maximum 320)**
Fluticasone propionate	**100–200**	**>200 (maximum 500)**

† Dose equivalents for *Qvar* **(TGA-registered CFC-free formulation of beclometasone dipropionate)**

‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

Source

van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma***. The Thoracic Society of Australia and New Zealand, 2010. Available from: http://www.thoracic.org.au/clinical-documents/area?command=record&id=14**

Last reviewed version 2.0

Asset ID: 21

How this recommendation was developed

Consensus recommendation following inconclusive literature search

Based on clinical experience and expert opinion after literature review yielded insufficient evidence for an evidence-based recommendation

Key evidence considered:

- Kew et al. 2016[9]
- Chong et al. 2015[10]
- Yousef et al. 2012[11]

Last reviewed version 2.0

For children with intermittent asthma symptoms and no interval symptoms for whom regular preventer is not indicated, a short course of montelukast at the onset of worsening asthma or wheezing can be considered (e.g. continue for 7 days or until symptoms have resolved for 48 hours). Advise parents/carers that montelukast does not work for all children.

How this recommendation was developed

Consensus recommendation following inconclusive literature search

Based on clinical experience and expert opinion after literature review yielded insufficient evidence for an evidence-based recommendation

Key evidence considered:

- Watts et al. 2012[12]
- Capsomidis & Tighe. 2010[13]
- Schuh et al. 2009[14]
- Robertson et al. 2007[15]
- Nwokoro et al. 2014[16]
- Valovirta et al. 2011[17]
- Bacharier et al. 2008[18]
- Harmanci et al. 2006[19]

Last reviewed version 2.0

More information

Short-acting beta-2 agonist relievers for children: 1–5 years

Infants under 12 months

In infants under 12 months, bronchiolitis is the most likely cause of acute respiratory distress. Bronchodilators are not recommended in children under 12 months old, consistent with current guidelines for the management of acute bronchiolitis.[20]

Children aged 1–5 years

Inhaled short-acting beta$_2$ agonists are effective bronchodilators in children aged 1–5 years.[21]

Short-acting beta$_2$ agonists may be less effective for wheezing in children under 2 years old than in older children.[22] However, many clinical trials in infants have included those with bronchiolitis, so there is limited evidence for the effects of short-acting beta$_2$ agonists specifically in asthma.[22] Studies conducted in emergency departments have shown that short-acting beta$_2$ agonists are more effective than placebo in controlling acute wheeze in children under 2 years, but may not achieve clinically significant improvements.[22]

Inhaled short-acting beta$_2$ agonists are generally well tolerated in children aged 1–5 years.[21] Adverse effects can include muscle tremor, headache, palpitations and agitation. Muscle tremor and agitation are common with initial use of standard doses, but often settle over time. Serious adverse effects such as hypokalaemia have been reported at very high doses.[21]

Oral short-acting beta$_2$ agonists are associated with adverse effects[21] and should not be used for the treatment of asthma in any age group.

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Administration of inhaled medicines in children: 1-5 years

To use inhaler devices correctly, parents and children need training in inhaler technique and in the care and cleaning of inhalers and spacers.

Children need careful supervision when taking their inhaled medicines (e.g. at preschool), especially when using a reliever for acute asthma symptoms.

Types of inhalers suitable for preschool children

Preschool children cannot use pressurised metered-dose inhalers properly unless a spacer is attached (with mask when necessary), because it is difficult for them to coordinate inspiratory effort with actuating the device.[21] Note that breath-actuated pressurised metered-dose inhalers cannot be used with a spacer.

Dry-powder inhalers are usually ineffective for preschool children because they cannot generate sufficient inspiratory air flow.[21]

Drug delivery is very variable in young children with any type of inhaler, including pressurised metered dose inhalers and spacers.[23] Filter studies have shown high day-to-day variability in delivered doses in preschool children.[21] This variation might explain fluctuations in effectiveness, even if the child's parents have been trained to use the device correctly.

Table. Types of inhaler devices for delivering asthma and COPD medicines

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/75

Pressurised metered-dose inhalers plus spacers for relievers

During acute wheezing episodes, delivery of short-acting beta2 agonist to airways is more effective with a pressurised metered-dose inhaler plus spacer than with a nebuliser.[21] In older children, salbutamol has also been associated with a greater increase in heart rate when delivered by nebuliser than when delivered by pressurised metered-dose inhaler plus spacer.[24]

When administering salbutamol to relieve asthma symptoms in a preschool child, the standard recommendation is to shake the inhaler, actuate one puff at a time into the spacer and have the child take 4–6 breaths in and out of the spacer (tidal breathing).[25] Fewer breaths may suffice; in children with asthma aged 2–7 years (not tested during an acute asthma episode), the number of tidal breaths needed to inhale salbutamol adequately from a spacer has been estimated at 2 breaths for small-volume spacers, 2 breaths for a spacer made from a 500-mL modified soft drink bottle, and 3 breaths for a large (Volumatic) spacer.[26]

Face masks for infants

When using a spacer with face mask (e.g. for an infant too young or uncooperative to be able to use a mouthpiece), effective delivery of medicine to the airways depends on a tight seal around the face.

When masks are used for inhaled corticosteroids, there is a risk of exposure to eyes and skin if the seal over the mouth and nose is not adequate. Parents should be advised to wash the child's face after administering inhaled corticosteroids by mask.

Babies are unlikely to inhale enough medicine while crying.[24] The use of a spacer and face mask for a crying infant may require patience and skill: the child can be comforted (e.g. held by a parent, in own pram, or sitting on the floor) while the mask is kept on, and the actuation carefully timed just before the next intake of breath. Most infants will tolerate the spacer and mask eventually. The child may be more likely to accept the spacer and mask if allowed to handle them first (and at other times), if the devices are personalised (e.g. with stickers), or if the mask has a scent associated with the mother (e.g. lip gloss). The use of a spacer with a coloured valve allows parents to see the valve move as the child breathes in and out.

▶ Go to: National Asthma Council Australia's information paper for health professionals on *Inhaler technique for people with asthma or COPD*

Last reviewed version 2.0

Preparation of new spacers before first use

Spacers are made of plastic, antistatic polymer/polycarbonate polyurethane, or cardboard.

Plastic spacers (e.g. Breath-A-Tech, Volumatic)

Electrostatic surface charge on new spacers made of plastic (e.g. *Breath-A-Tech*, *Volumatic*) reduces the proportion of medicine available for delivery to the airway. This charge can be reduced by washing the plastic spacer in dishwashing liquid and allowing it to air dry or drip-dry without rinsing or wiping.[21]

Alternatively, priming the spacer by actuating the device several times into the spacer also overcomes the charge, but this wastes medicine. The optimal number of actuations for priming is not known and the findings of in vitro studies vary widely. One study (using older, CFC-based formulations of asthma medicines) reported that up to 40 actuations fired into a new plastic spacer overcame the effect of the electrostatic charge.[27] Others have concluded that the electrostatic charge on plastic spacers does not reduce in vivo efficacy of bronchodilator therapy in children with asthma.[28] The number of actuations necessary may be known when the results of recent studies become available.

When a new plastic spacer must be used immediately (e.g. for a person with asthma symptoms), patients, parents and carers should follow the manufacturer's priming instructions. In hospitals and emergency departments, a new spacer that has not been pre-treated by washing can be primed using multiple (at least 10) puffs of salbutamol. (This is an arbitrary number of actuations in the absence of evidence that would enable a precise guideline.)

Non-plastic spacers

Disposable cardboard spacers (e.g. DispozABLE, LiteAire) and polyurethane/antistatic polymer spacers (e.g. *Able A2A*, *AeroChamber Plus*, *La Petite E-Chamber*, *La Grande E-Chamber*) do not require preparation before first use.[21]

Note: The term 'priming' is also used for the preparation process that is necessary for new pressurised metered-dose inhalers that have not been used for more than a week. This involves first actuating the inhaler into the air (away from the patient). Users should follow the manufacturer's instructions for the particular brand of inhaler, which specify the number of actuations required.

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Parent/carer-initiated oral corticosteroids for wheezing and asthma flare-ups

▶ See also: Managing acute asthma in clinical settings

- Oral corticosteroids are associated with adverse effects on behaviour and bone health. Frequent courses may affect the hypothalamus–pituitary–adrenal axis.

Children aged 1–5 years

Short courses of oral corticosteroids initiated by parents/carers in response to children's wheezing, or at the first sign of a cold, are not effective in managing symptoms in preschool children.[29, 30, 4]

There is inconsistent evidence for the benefits of systemic corticosteroids in preschool children with acute viral-induced wheezing presenting to acute care services.[4, 1, 31] Current evidence does not strongly support their use in this age group.[2]

The Thoracic Society of Australia and New Zealand position statement on the use of corticosteroids in children[3] recommends that oral corticosteroid treatment in preschool children, particularly those with intermittent viral-induced wheezing, should be limited to children with wheeze severe enough to need admission to hospital.

Children aged 6 years and over

A Cochrane systematic review found that there was insufficient evidence supporting the use of parent-initiated courses of oral corticosteroids in school-aged children,[32] although some clinical trials have reported benefits.

In a clinical trial in children aged 6–14 years with a history of recurrent episodes of acute asthma, short courses of oral prednisolone (1 mg/kg a day), initiated by parents in response to an asthma flare-ups, reduced asthma symptoms and the number of missed school

days.[33] Another quasi-experimental study found that home initiation of corticosteroids reduced the rate of emergency department visits among school-aged children with moderate-to-severe persistent asthma, compared with rates pre-intervention.[34]

The Thoracic Society of Australia and New Zealand position statement on the use of corticosteroids in children[3] recommends a short course of systemic corticosteroid therapy for children with moderate-to-severe acute asthma or when there is an incomplete response to beta-agonists, and does not recommend against parent/carer-initiated courses.

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Oral corticosteroids for children: adverse effects

Oral corticosteroids may have adverse psychiatric effects in children, including aggression and hyperactivity.[35] Effects in the general population include euphoria, hypomania, depression, disturbances of mood, cognition, sleep and behaviour.[36]

A short course of oral corticosteroid therapy (less than 2 weeks) is associated with little risk of long-term suppression of the hypothalamus–pituitary–adrenal axis.[3] However, risk can accumulate if frequent courses (four or more per year) are given.[3]

Recurrent courses of oral corticosteroids may also affect bone mineral density, especially in boys.[3,37]

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Increasing the inhaled corticosteroid dose to control flare-ups in children

In children taking regular inhaled corticosteroid-containing preventers, there is conflicting evidence for whether, and by how much, the dose should be increased when symptoms worsen or at the onset of an acute flare-up.

Overall, current evidence from highly controlled randomised controlled trials does not support increasing the dose of inhaled corticosteroid as part of a self-initiated action plan to manage flare-ups in children younger than 12 years.[38]

There is some evidence that high doses of inhaled steroids used pre-emptively might be effective in preventing severe acute asthma in children aged under 5 years, based on studies in children not taking regular inhaled corticosteroids.[39] However, very high pre-emptive doses affect children's growth[40] and are not recommended.

Recent randomised controlled trials reported a lack of effect with a range of dose increases:

- A five-fold increase in the inhaled corticosteroid dose at early signs of worsening asthma did not reduce the rate of severe acute asthma in children aged 5–11 years with well-controlled asthma while taking maintenance inhaled corticosteroid treatment (with high adherence).[41] This strategy was associated with a small reduction in linear growth.[41]
- Dose increases of four or eight times usual inhaled corticosteroid maintenance dose at the onset of an acute flare-up in children aged 2–17 years did not reduce requirement for oral corticosteroids, compared with doubling the dose.[11]

A Cochrane systematic review[38] in children and adults reported that increasing the inhaled corticosteroid dose did not prevent severe flare-ups, regardless of how soon the increase was initiated after the onset of symptoms or the magnitude of the dose increase (doubling versus quadrupling). The results did not differ between children under 15 and adults or older adolescents.[38] However, there were too few studies in children to make firm conclusions.

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Montelukast for children: efficacy

- Montelukast use has been associated with behavioural and/or neuropsychiatric adverse effects, including suicidality.

▶ Go to: TGA alert

Overview

Montelukast is a leukotriene receptor antagonist preventer. It is registered by the TGA for the treatment of asthma in children aged 2 years and older, and for the symptomatic treatment of allergic rhinitis.[42]

Montelukast can be used as an alternative to inhaled corticosteroids or as an add-on treatment in a child already taking regular inhaled corticosteroids.

However, it is not effective for all children. Overall, only approximately 20–30% of children will respond to montelukast treatment. The effect is thought to depend mainly on the child's genotype.[43, 16, 44] Clinically, it is not possible to predict accurately which children will benefit most from montelukast treatment.

Montelukast as first-line preventer in children aged 2–5 years

Viral-induced wheezing

Overall, regular maintenance montelukast treatment does not reduce the risk of wheezing episodes requiring oral corticosteroid treatment among preschool children who only have wheezing episodes when they have viral upper respiratory tract infections.[45]

However, montelukast may be effective for some children. Some randomised controlled trials have reported a reduction the risk of flare-ups in preschool children with intermittent asthma/wheeze,[46, 47] while others have not.[17]

Persistent asthma or wheezing

A systematic review comparing montelukast with inhaled corticosteroids in preschoolers with asthma or recurrent wheezing requiring daily preventer treatment[48] reported that inhaled corticosteroids appeared to achieve better symptom control and reduce flare-ups (including severe flare-ups requiring treatment with systemic corticosteroids). However, results were inconsistent and meta-analysis was not possible due to heterogeneity of outcomes measured in available clinical trials.[48]

Some preschool children with persistent asthma/wheeze respond to montelukast. A crossover study in preschool children with persistent asthma/wheeze reported that some children showed their best response to montelukast, while most responded better to regular inhaled corticosteroids.[49] Predictors of a better response to inhaled corticosteroids than montelukast were aeroallergen hypersensitivity and blood eosinophilia (eosinophil counts ≥ 300/μL).[49] However, routine blood eosinophil count is not feasible or recommended for this purpose.

Montelukast as first-line preventer children aged 6 years and over

In school-aged children with persistent asthma, inhaled corticosteroids are more effective overall than montelukast in improving lung function and controlling asthma symptoms.[50, 52]

However, symptoms will respond to a treatment trial of montelukast in approximately one-quarter to one-third of children,[50, 53,54] and some may benefit more than from an inhaled corticosteroid.[50] More severe asthma and markers of allergic inflammation may predict a better response to inhaled corticosteroids.[50]

Montelukast as add-on treatment

A systematic review of studies in children over 6 years and adolescents with mild-to-moderate persistent asthma found that the addition of montelukast to inhaled corticosteroids did reduce flare-ups requiring oral corticosteroids or hospital admissions for asthma, compared with the same or an increased dose.[52]

In a study comparing step-up treatments in children with asthma symptoms uncontrolled by low-dose inhaled corticosteroids, the addition of a long-acting beta$_2$ agonist was effective in more children than either montelukast or increasing the dose of inhaled corticosteroid for controlling asthma symptoms and preventing flare-ups requiring systemic corticosteroids.[55] However, some studies in school-aged children with persistent asthma already taking regular inhaled corticosteroids have reported that add-on montelukast reduced the risk of flare-ups[55, 56] and exercise-induced asthma symptoms.[56] Not all children will respond.

In a small study in children with persistent asthma already taking regular inhaled corticosteroids who were homozygous for the Arg16 genotype, montelukast was more effective as an add-on therapy than long-acting beta$_2$ agonist in reducing symptoms, reliever use and days absent from school due to asthma, depending on the child's beta receptor genotype.[44] However, children were given inhaled corticosteroid and long-acting beta$_2$ agonists in separate inhalers, which is which is known to be associated with increased risks.

However, genotyping it is not currently feasible in clinical practice. In practice, a treatment trial of 4–6 weeks can determine which preventer is suitable for controlling a child's asthma symptoms,[50] but longer treatment may be required to evaluate effect on flare-ups, because flare-ups may be independent of symptom control.

Exercise-induced symptoms

In school-aged children who experience exercise-induced symptoms despite taking regular inhaled corticosteroids, the addition of montelukast is effective in controlling symptoms, but not all children experience a response.[57, 58]

See: *Investigation and management of exercise-induced bronchoconstriction*

Short-term use in the management of flare-ups

Some, but not all studies suggest that a short course of montelukast, introduced at the first signs of an upper respiratory tract infection, may be effective in controlling flare-ups. An Australian study reported that this strategy could achieve a small reduction in symptoms, school absence and medical consultations in preschool and school-aged children with episodic wheeze.[15]

However, the evidence is inconsistent, with some studies showing no benefit.[17,12, 13, 14, 18] The findings of one study suggested that whether or not intermittent montelukast is effective in wheezing children aged 5 years and under depends on genotype.[16]

Montelukast is not TGA-approved or PBS-subsidised for intermittent use.

Note: PBS status as at March 2019: Montelukast is not subsidised by the PBS for adolescents 15 years and over.

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Thunderstorm asthma

Certain types of thunderstorms in spring or early summer in regions with high grass pollen concentrations in the air can cause life-threatening allergic asthma flare-ups in individuals sensitised to rye grass, even if they have not had asthma before.[59, 60, 61, 62, 63]

Sensitisation to rye grass allergen is almost universal in patients who have reported flare-ups consistent with thunderstorm asthma in Australia.

People with allergic rhinitis and allergy to ryegrass pollen (i.e. most people with springtime allergic rhinitis symptoms) are at risk of thunderstorm asthma if they live in, or are travelling to, a region with seasonal high grass pollen levels – even if they have never had asthma symptoms before. This includes people with undiagnosed asthma, no previous asthma, known asthma.[59, 60] Lack of inhaled corticosteroid preventer treatment has been identified as a risk factor.[59]

Epidemics of thunderstorm asthma can occur when such a storm travels across a region and triggers asthma in many susceptible individuals. Epidemic thunderstorm asthma events are uncommon, but when they occur can they make a high demand on ambulance and health services.[64, 63, 65]

Data from thunderstorm asthma epidemics suggest that the risk of asthma flare-ups being triggered by a thunderstorm is highest in adults who are sensitised to grass pollen and have seasonal allergic rhinitis (with or without known asthma).[59]

The worst outcomes are seen in people with poorly controlled asthma.[64] Treatment with an inhaled corticosteroid asthma preventer was significantly protective in a well-conducted Australian case-control study.[60]

There is insufficient evidence to determine whether intranasal corticosteroids help protect against thunderstorm asthma. Intranasal corticosteroids reduce symptoms of allergic rhinitis and limited indirect evidence suggests they may protect against asthma flare-ups in people not taking inhaled corticosteroids.[66]

The effectiveness of specific allergen immunotherapy in protecting against thunderstorm asthma has not been evaluated in randomised clinical trials, but data from a small Australian open-label study suggest that short-term treatment with five-grass sublingual immunotherapy may have been protective in individuals.[67]

▶ Go to: National Asthma Council Australia's *Epidemic thunderstorm asthma* information paper
Go to: ASCIA's *Pollen calendar*
Go to: *Vic Emergency's Thunderstorm asthma forecast (Victoria only)*

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Asthma triggers in children: respiratory tract infections

Viral respiratory infections, such as the common cold, are a frequent cause of wheezing and asthma flare-ups in children, especially in preschool children.

The findings of observational cohort studies and limited randomised controlled trials show that influenza vaccination reduces the number, frequency and duration of asthma flare-ups in children, and lower the rate of emergency department visits and hospitalisation for asthma.[68]

Although bacterial respiratory infections may also trigger wheezing, antibiotics are not routinely indicated for asthma flare-ups or wheezing, and should only be given if they would otherwise be indicated.

▶ See: Preventive care

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Asthma triggers in children: environmental allergens

There is insufficient evidence on which to base recommendations for the reduction of exposure to environmental allergens in the treatment of wheezing in preschool children.[21]

▶ See: *Allergies and asthma*
See: *Asthma triggers*

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Asthma triggers in children: tobacco smoke

There is consistent, high-quality evidence that exposure to environmental tobacco smoke can both cause and worsen wheezing in preschool children.[21, 69]

The Introduction of environmental tobacco controls has led to significant reduction in asthma hospitalisations among children.

▶ See: *Smoking and asthma*
See: *Asthma triggers*

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References

1. Foster SJ, Cooper MN, Oosterhof S, Borland ML. Oral prednisolone in preschool children with virus-associated wheeze: a prospective, randomised, double-blind, placebo-controlled trial. *Lancet Respir Med*. 2018; 6: 97-106. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29373235
2. Castro-Rodriguez JA, Beckhaus AA, Forno E. Efficacy of oral corticosteroids in the treatment of acute wheezing episodes in asthmatic preschoolers: Systematic review with meta-analysis. *Pediatric pulmonology* 2016; 51: 868-76. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27074244
3. van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma*. The Thoracic Society of Australia and New Zealand, 2010. Available from: https://www.thoracic.org.au/journal-publishing/command/download_file/id/25/filename/The_role_of_corticosteroids_in_the_management_of_childhood_asthma_-_2010.pdf
4. Panickar J, Lakhanpaul M, Lambert PC, *et al*. Oral prednisolone for preschool children with acute virus-induced wheezing. *N Engl J Med*. 2009; 360: 329-328. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19164186
5. Chang, A B, Clark, R, Sloots, T P, *et al*. A 5- versus 3-day course of oral corticosteroids for children with asthma exacerbations who are not hospitalised: a randomised controlled trial. *Med J Aust*. 2008; 189: 306-310.Available from: https://www.ncbi.nlm.nih.gov/pubmed/18803532/
6. Smith M, Iqbal S, Elliot TM et al. Corticosteroids for hospitalised children with acute asthma. *Cochrane Database Syst Rev*. 2003; Issue 2: CD002886. Available from: https://www.ncbi.nlm.nih.gov/pubmed/12804441
7. Rowe BH, Spooner C, Ducharme F, *et al*. Early emergency department treatment of acute asthma with systemic corticosteroids. *Cochrane Database Syst Rev*. 2001; Issue 1: CD002178. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11279756
8. Brand PL, Caudri D, Eber E et al. Classification and pharmacological treatment of preschool wheezing: changes since 2008. *Eur Respir J*. 2014; 43: 1172-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24525447
9. Kew, KM; Quinn, M; Quon, B. S; Ducharme, FM;. Increased versus stable doses of inhaled corticosteroids for exacerbations of chronic asthma in adults and children. *Cochrane Database Syst Rev*. 2016; Issue 6: CD007524: . Available from: https://www.ncbi.nlm.nih.gov/pubmed/27272563
10. Chong J, Haran C, Chauhan BF, Asher I. Intermittent inhaled corticosteroid therapy versus placebo for persistent asthma in children and adults. *Cochrane Database Syst Rev*. 2015; : Cd011032. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26197430
11. Yousef, E., Hossain, J., Mannan, S., *et al*. Early intervention with high-dose inhaled corticosteroids for control of acute asthma exacerbations at home and improved outcomes: a randomized controlled trial. *Allergy Asthma Proc*. 2012; 33: 508-13. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23394509
12. Watts, K, Chavasse, R J P G. Leukotriene receptor antagonists in addition to usual care for acute asthma in adults and children. *Cochrane Database Syst Rev*. 2012; Issue 5: . Available from: http://cochranelibrary-wiley.com/doi/10.1002/14651858.CD006100.pub2/full
13. Capsomidis, A., Tighe, M.. Archimedes. Question 2. Is oral montelukast beneficial in treating acute asthma exacerbations in children?. *Arch Dis Child*. 2010; 95: 948-50. Available from: http://adc.bmj.com/content/95/11/948.long
14. Schuh, S, Willan, AR, Stephens, D, *et al*. Can montelukast shorten prednisolone therapy in children with mild to moderate acute asthma? A randomized controlled trial. *J Pediatr*. 2009; 155: 795-800. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19656525
15. Robertson CF, Price D, Henry R, *et al*. Short-course montelukast for intermittent asthma in children: a randomized controlled trial. *Am J Respir Crit Care Med*. 2007; 175: 323-329. Available from: http://ajrccm.atsjournals.org/content/175/4/323.long
16. Nwokoro C, Pandya H, Turner S, *et al*. Intermittent montelukast in children aged 10 months to 5 years with wheeze (WAIT trial): a multicentre, randomised, placebo-controlled trial. *Lancet Respir Med*. 2014; 2: 796-803. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25212745
17. Valovirta, E., Boza, M. L., Robertson, C. F., *et al*. Intermittent or daily montelukast versus placebo for episodic asthma in children. *Ann Allergy Asthma Immunol*. 2011; 106: 518-26. Available from: https://www.ncbi.nlm.nih.gov/pubmed/21624752
18. Bacharier LB, Phillips BR, Zeiger RS, *et al*. Episodic use of an inhaled corticosteroid or leukotriene receptor antagonist in preschool children with moderate-to-severe intermittent wheezing. *J Allergy Clin Immunol*. 2008; 122: 1127-1135. Available from: https://www.ncbi.nlm.nih.gov/pubmed/18973936
19. Harmanci, K, Bakirtas, A, Turktas, I, Degim, T. Oral montelukast treatment of preschool-aged children with acute asthma. *Ann Allergy Asthma Immunol*. 2006; 96: 731-735. Available from: https://www.ncbi.nlm.nih.gov/pubmed/16729788
20. Paediatric Research in Emergency Departments International Collaborative. *Australasian bronchiolitis guideline*. PREDICT; 2016. Available from: http://www.predict.org.au/publications/2016-pubs/
21. Brand PL, Baraldi E, Bisgaard H, *et al*. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. *Eur Respir J*. 2008; 32: 1096-1110. Available from: http://erj.ersjournals.com/content/32/4/1096.full
22. Chavasse RJ, Bara A, McKean MC. Short acting beta2-agonists for recurrent wheeze in children under two years of age. *Cochrane Database Syst Rev*. 2002; Issue 2: CD002873. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002873/full
23. Schultz A, Sly PD, Zhang G, *et al*. Incentive device improves spacer technique but not clinical outcome in preschool children with asthma. *J Paediatr Child Health*. 2012; 48: 52-6. Available from: http://onlinelibrary.wiley.com/doi/10.1111/j.1440-1754.2011.02190.x/full

24. Schuh, S., Johnson, D. W., Stephens, D., *et al*. Comparison of albuterol delivered by a metered dose inhaler with spacer versus a nebulizer in children with mild acute asthma. *The Journal of pediatrics*. 1999; 135: 22-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/10393599
25. National Asthma Council Australia. *Kids' First Aid for Asthma*. National Asthma Council Australia, Melbourne, 2011. Available from: http://www.nationalasthma.org.au/first-aid
26. Schultz A, Le Souëf TJ, Venter A, *et al*. Aerosol inhalation from spacers and valved holding chambers requires few tidal breaths for children. *Pediatrics*. 2010; 126: e1493-8. Available from: http://pediatrics.aappublications.org/content/126/6/e1493.long
27. Berg E. In vitro properties of pressurized metered dose inhalers with and without spacer devices. *J Aerosol Med*. 1995; 8 Suppl 3: S3-10; discussion S11. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10157897
28. Dompeling E, Oudesluys-Murphy AM, Janssens HM, *et al*. Randomised controlled study of clinical efficacy of spacer therapy in asthma with regard to electrostatic charge. *Arch Dis Child*. 2001; 84: 178-182. Available from: http://adc.bmj.com/content/84/2/178.full
29. Beigelman A, King TS, Mauger D, *et al*. Do oral corticosteroids reduce the severity of acute lower respiratory tract illnesses in preschool children with recurrent wheezing?. *J Allergy Clin Immunol*. 2013; 131: 1518-1525. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23498594
30. Oommen A, Lambert PC, Grigg J. Efficacy of a short course of parent-initiated oral prednisolone for viral wheeze in children aged 1-5 years: randomised controlled trial. *Lancet*. 2003; 362: 1433-1438. Available from: http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(03)14685-5/fulltext
31. Therapeutic guidelines [Electronic book]: Therapeutic Guidelines Limited; 2018 [cited 2018 April].
32. Ganaie MB, Munavvar M, Gordon M et al. Patient- and parent-initiated oral steroids for asthma exacerbations. *Cochrane Database Syst Rev* 2016; 12: Cd012195. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27943237
33. Vuillermin P, Robertson CF, Carlin JB, *et al*. Parent initiated prednisolone for acute asthma in children of school age: randomised controlled crossover trial. *BMJ*. 2010; 340: c843. Available from: http://www.bmj.com/content/340/bmj.c843.long
34. Sarzynski LM, Turner T, Stukus DR, Allen E. Home supply of emergency oral steroids and reduction in asthma healthcare utilization. *Pediatr Pulmonol* 2017; 52: 1546-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29034999
35. Stuart, F. A., Segal, T. Y., Keady, S.. Adverse psychological effects of corticosteroids in children and adolescents. *Arch Dis Child*. 2005; 90: 500-6. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1720409/
36. Australian Medicines Handbook. Last modified July 2018: *Australian Medicines Handbook Pty Ltd*. 2018
37. Kelly, H. W., Van Natta, M. L., Covar, R. A., *et al*. Effect of long-term corticosteroid use on bone mineral density in children: a prospective longitudinal assessment in the childhood Asthma Management Program (CAMP) study. *Pediatrics*. 2008; 122: e53-61. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/18595975/
38. Kew KM, Quinn M, Quon BS, Ducharme FM. Increased versus stable doses of inhaled corticosteroids for exacerbations of chronic asthma in adults and children. *Cochrane Database Syst Rev* 2016; Issue 6: CD007524. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27272563
39. Kaiser SV, Huynh T, Bacharier LB et al. Preventing exacerbations in preschoolers with recurrent wheeze: a meta-analysis. *Pediatrics* 2016; 137: Available from: https://www.ncbi.nlm.nih.gov/pubmed/27230765
40. Ducharme FM, Lemire C, Noya FJ, *et al*. Preemptive use of high-dose fluticasone for virus-induced wheezing in young children. *N Engl J Med*. 2009; 360: 339-353. Available from: http://www.nejm.org/doi/full/10.1056/NEJMoa0808907#t=article
41. Jackson DJ, Bacharier LB, Mauger DT et al. Quintupling Inhaled Glucocorticoids to Prevent Childhood Asthma Exacerbations. *N Engl J Med* 2018; 378: 891-901. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29504498
42. Merck, Sharp and Dohme Australia Pty Ltd. *Product Information: Singulair (montelukast sodium) Tablets*. Therapeutic Goods Administration, Canberra, 2013. Available from: https://www.ebs.tga.gov.au/
43. Bush A. Montelukast in paediatric asthma: where we are now and what still needs to be done? *Paediatr Respir Rev*. 2015; 16: 97-100. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25499571
44. Lipworth BJ, Basu K, Donald HP, *et al*. Tailored second-line therapy in asthmatic children with the Arg(16) genotype. *Clin Sci (Lond)*. 2013; 124: 521-528. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23126384
45. Brodlie M, Gupta A, Rodriguez-Martinez CE, *et al*. Leukotriene receptor antagonists as maintenance and intermittent therapy for episodic viral wheeze in children. *Cochrane Database Syst Rev*. 2015; Issue 10: CD008202. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26482324
46. Bisgaard H, Zielen S, Garcia-Garcia ML, *et al*. Montelukast reduces asthma exacerbations in 2- to 5-year-old children with intermittent asthma. *Am J Respir Crit Care Med*. 2005; 171: 315-322. Available from: http://ajrccm.atsjournals.org/content/171/4/315.long
47. Nagao M, Ikeda M, Fukuda N, *et al*. Early control treatment with montelukast in preschool children with asthma: a randomized controlled trial. *Allergol Int*. 2018; 67: 72-78. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28526210
48. Castro-Rodriguez JA, Rodriguez-Martinez CE, Ducharme FM. Daily inhaled corticosteroids or montelukast for preschoolers with asthma or recurrent wheezing: A systematic review. *Pediatr Pulmonol*. 2018; Epub ahead of print 6 November. Available from: https://www.ncbi.nlm.nih.gov/pubmed/30394700
49. Fitzpatrick AM, Jackson DJ, Mauger DT et al. Individualized therapy for persistent asthma in young children. *J Allergy Clin Immunol*. 2016; 138: 1608-18.e12. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27777180
50. Jartti T. Inhaled corticosteroids or montelukast as the preferred primary long-term treatment for pediatric asthma? *Eur J Pediatr*. 2008; 167: 731-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/18214538
51. Benard, B., Bastien, V., Vinet, B., *et al*. Neuropsychiatric adverse drug reactions in children initiated on montelukast in real-life practice. *Eur Respir J*. 2017; 50: . Available from: https://www.ncbi.nlm.nih.gov/pubmed/28818882
52. Chauhan BF, Ben Salah R, Ducharme FM. Addition of anti-leukotriene agents to inhaled corticosteroids in children with persistent

asthma. *Cochrane Database Syst Rev*. 2013; Issue 10: CD009585. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24089325
53. Maspero, J, Guerra, F, Cuevas, F, *et al*. Efficacy and tolerability of salmeterol/fluticasone propionate versus montelukast in childhood asthma: a prospective, randomized, double-blind, double-dummy, parallel-group study. *Clin Ther*. 2008; 30: 1492-1504.
54. Pedersen S, Maspero J, Gul N, Sharma R. Components of asthma control and treatment response of individual control criteria in children: analysis of the PEACE study. *Pediatr Pulmonol*. 2011; 46: 1182-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/21751432
55. Malka J, Mauger DT, Covar R, *et al*. Eczema and race as combined determinants for differential response to step-up asthma therapy. *J Allergy Clin Immunol*. 2014; 134: 483-5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24835502
56. Stelmach I, Ozarek-Hanc A, Zaczeniuk M et al. Do children with stable asthma benefit from addition of montelukast to inhaled corticosteroids: randomized, placebo controlled trial. *Pulm Pharmacol Ther*. 2015; 31: 42-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25640020
57. Grzelewski, T, Stelmach, I. Exercise-induced bronchoconstriction in asthmatic children: a comparative systematic review of the available treatment options. *Drugs*. 2009; 69: 1533-1553. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19678711
58. Fogel RB, Rosario N, Aristizabal G, *et al*. Effect of montelukast or salmeterol added to inhaled fluticasone on exercise-induced bronchoconstriction in children. *Ann Allergy Asthma Immunol*. 2010; 104: 511-517. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20568384
59. Davies J, Queensland University of Technology. Literature review on thunderstorm asthma and its implications for public health advice. Final report. Melbourne: *Victorian State Government Department of Health and Human Services*; 2017. Available from: https://www2.health.vic.gov.au/about/publications/researchandreports/thunderstorm-asthma-literature-review-may-2107/
60. Girgis ST, Marks GB, Downs SH et al. Thunderstorm-associated asthma in an inland town in south-eastern Australia. Who is at risk? *Eur Respir J* 2000; 16: 3-8.
61. Marks GB, Colquhoun JR, Girgis ST, *et al*. Thunderstorm outflows preceding epidemics of asthma during spring and summer. *Thorax*. 2001; 56: 468-71.
62. D'Amato G, Vitale C, D'Amato M et al. Thunderstorm-related asthma: what happens and why. *Clin Exp Allergy* 2016; 46: 390-6.
63. Victoria State Government Department of Health and Human Services. *The November 2016 Victorian epidemic thunderstorm asthma event: an assessment of the health impacts. The Chief Health Officer's Report, 27 April 2017*. Melbourne: Victorian Government; 2017.
64. Thien F, Beggs PJ, Csutoros D et al. The Melbourne epidemic thunderstorm asthma event 2016: an investigation of environmental triggers, effect on health services, and patient risk factors. *Lancet Planet Health* 2018; 2: e255-e63. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29880157/
65. Andrew E, Nehme Z, Bernard S et al. Stormy weather: a retrospective analysis of demand for emergency medical services during epidemic thunderstorm asthma. *BMJ* 2017; 359: j5636. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29237604/
66. Lohia S, Schlosser RJ, Soler ZM. Impact of intranasal corticosteroids on asthma outcomes in allergic rhinitis: a meta-analysis. *Allergy*. 2013; 68: 569-79. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23590215/
67. O'Hehir RE, Varese NP, Deckert K et al. Epidemic thunderstorm asthma protection with five-grass pollen tablet sublingual immunotherapy: a clinical trial. *Am J Respir Crit Care Med* 2018; 198: 126-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29461859/
68. Vasileiou, E., Sheikh, A., Butler, C., *et al*. Effectiveness of influenza vaccines in asthma: a systematic review and meta-analysis. *Clin Infect Dis*. 2017; 65: 1388-1395. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28591866 Full text at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5850022
69. Burke H, Leonardi-Bee J, Hashim A, *et al*. Prenatal and passive smoke exposure and incidence of asthma and wheeze: systematic review and meta-analysis. *Pediatrics*. 2012; 129: 735-744. Available from: http://pediatrics.aappublications.org/content/129/4/735.long

Managing severe asthma in children aged 1–5 years

Recommendations

If asthma symptoms remain uncontrolled (persisting symptoms or flare-ups) despite maximal regular preventer treatment:

- **assess adherence**
- **check inhaler technique**
- **review the diagnosis**
- **assess comorbidity (e.g. allergic rhinitis)**
- **check whether the child is exposed to environmental triggers (e.g. allergens, cigarette smoke)**
- **check that the dose and regimen is appropriate.**

Table. Reviewing and adjusting preventer treatment for children aged 1–5 years

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/25

Figure. Stepped approach to adjusting asthma medication in children aged 1-5 years

Please view and print this figure separately: http://www.asthmahandbook.org.au/figure/show/18

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Chung et al. 2014[1]
- Bush et al. 2011[2]
- Bush et al. 2010[3]

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If good asthma control is still not achieved after eliminating common reasons for treatment failure, consider referral to a paediatric respiratory physician or paediatrician.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

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More information

Step-up options in children with asthma that is not controlled by low-dose inhaled corticosteroids

In children whose asthma is inadequately controlled by low-dose inhaled corticosteroids alone (and adherence is good, inhaler technique is correct and diagnosis has been confirmed), treatment options include:

- increasing the inhaled corticosteroid dose
- adding montelukast
- switching to inhaled corticosteroid/long-acting beta$_2$ agonist combination.

Table. Step-up options for children when good asthma control is not achieved with low-dose ICS

Option	TGA-registered indications for add-on therapy	PBS considerations
High-dose ICS	N/A	Subsidised
ICS plus montelukast	2 years and over	2–5 years: not subsidised* 6–14 years: not subsidised unless for exercise-induced bronchoconstriction despite ICS treatment† 15 years and over: not subsidised‡
ICS/long-acting beta$_2$ agonist combination	4 years and over for fluticasone propionate/ salmeterol xinafoate 12 years and over for budesonide/formoterol fumarate dihydrate	Subsidised

- Advise parents about potential adverse psychiatric effects of montelukast

* Montelukast is not subsidised for use in combination with other preventers or for children who require inhaled corticosteroids.

† Montelukast is subsidised for prevention of exercise-induced asthma if asthma is otherwise well controlled while taking optimal-dose inhaled corticosteroids – it is not otherwise subsidised in combination with inhaled corticosteroids (or inhaled corticosteroid/long-acting beta$_2$ agonist combinations).

‡ Montelukast is not subsidised for people aged over 15 years.

Asset ID: 27

In the majority of children with persistent asthma that requires preventive treatment, control can be achieved with one of these options.[4]

Few studies have been conducted in preschool-aged children. The preferred step-up option for children aged 6–12 years is controversial and guidelines differ in their recommendations.[5]

Increasing inhaled corticosteroid dose versus adding a long-acting beta$_2$ agonist

In school-aged children with persistent asthma taking regular inhaled corticosteroid, the addition of a long-acting beta$_2$ agonist does not reduce the rate of asthma flare-ups requiring systemic steroids compared with the same or higher doses of inhaled corticosteroid.[6, 7] However, the long-acting beta$_2$ agonist–inhaled corticosteroid was superior for improving lung function.[6] Growth is reduced in children treated with higher-dose inhaled corticosteroid, compared with those taking same dose plus a long-acting beta$_2$ agonist.[6]

Adolescents may benefit more from combination inhaled corticosteroid/long-acting beta$_2$ agonist treatment than children under 12 years. In adolescents with persistent asthma that is not controlled by a low dose of inhaled corticosteroids, the combination of a long-acting beta$_2$ agonist and an inhaled corticosteroid is modestly more effective in reducing the risk of flare-ups requiring oral corticosteroids than a higher dose of inhaled corticosteroids.[8]

Adding montelukast versus adding a long-acting beta-2 agonist or increasing inhaled corticosteroid dose

Children aged 1–5 years

In one study in children aged 5 years or less with persistent asthma/wheeze requiring preventer treatment, raised blood eosinophil levels and atopy predicted better short-term response to high-dose inhaled corticosteroid than to montelukast.[9] However, routine eosinophil counts are currently not recommended to guide treatment in children.

In children aged 1–5 years with asthma/wheeze that is not adequately controlled by low-dose inhaled corticosteroid alone, adding montelukast is preferable to increasing the dose of inhaled corticosteroids when the safety profiles of these options are compared.[10]

Long-acting beta$_2$ agonists are not recommended for this age group.

- Montelukast use has been associated with behavioural and/or neuropsychiatric adverse effects.

▶ Go to: TGA alert

Note: Montelukast is TGA-approved for children aged 2 years and over.

Children aged 6 years and over

Among children 6 years and over with asthma that is not controlled by low-dose inhaled corticosteroids, the optimal regimen varies between individuals.[11] In one study of children selected for high adherence with maintenance treatment, short-term responses varied between individuals: in some children the best response was achieved by adding a long-acting beta$_2$ agonist, in others by adding montelukast, and in others by increasing the dose of inhaled corticosteroid.[11]

Note: The use of inhaled corticosteroids and long-acting beta$_2$ agonists in separate inhalers is not recommended for either children or adults because of the potential for increased risk due to selective non-adherence to the inhaled corticosteroid.[12]

Overall, the addition of montelukast to an inhaled corticosteroid does not reduce the need for rescue oral corticosteroids or hospital admission, compared with the same or an increased dose of inhaled corticosteroids, in children aged 6 years and over or adolescents with mild-to-moderate asthma.[13]

For children aged 6–14 years with persistent asthma and exercise-induced bronchoconstriction, adding montelukast is more effective in protecting against exercise-induced bronchoconstriction than switching to a combination of inhaled corticosteroid and a long-acting beta$_2$ agonist.[14] The use of montelukast also avoids beta-receptor tolerance associated with long-acting beta$_2$ agonists, so a short-acting beta$_2$ agonist taken after exercise produces a greater bronchodilator response than it does in children taking regular long-acting beta$_2$ agonist.[14]

A treatment trial of montelukast for 4–6 weeks is the best option when effects on exercise-induced symptoms and safety are also considered.[10]

- Montelukast use has been associated with behavioural and/or neuropsychiatric adverse effects.

▶ Go to: TGA alert

See: *Investigation and management of exercise-induced bronchoconstriction*

Genetic influence on effect of long-acting beta$_2$ agonists

Clinical response to long-acting beta$_2$ agonists partly depends on genetics. A beta$_2$receptor genotype (Arg16 polymorphism in the beta$_2$ receptor gene) pre-disposes children with asthma to down-regulation of the beta$_2$ receptor and increased susceptibility to flare-ups during regular treatment with regular long-acting beta$_2$agonists.[15] However, routine genetic testing to tailor asthma therapy is not yet available in clinical practice.

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Definitions of severe and difficult-to-treat asthma

Although most people's asthma can be effectively treated with currently available medicines, a substantial subset of people have uncontrolled asthma (as indicated by persisting symptoms, low lung function and/or flare-ups) despite treatment. These patients are described as having difficult-to-treat asthma.

Some patients with difficult-to-treat asthma have severe asthma. Asthma severity is classified retrospectively according to the level of treatment needed to achieve or maintain good asthma control, rather than by the intensity or frequency of symptoms.[16] International guidelines have been published for the assessment and management of patients with severe asthma.[1] 'Severe asthma' (also called severe refractory asthma' or 'severe treatment-resistant asthma') is defined as asthma for which good control is not achieved despite the highest level of recommended treatment, or asthma for which control can be maintained only with the highest level of recommended treatment.[1] It is estimated that 5-10% of patients with asthma have severe asthma.[1]

Not all patients with difficult-to-treat asthma have severe asthma. 'Difficult-to-treat asthma' includes asthma that is uncontrolled due to adherence issues, inappropriate or incorrect use of medicines, environmental triggers or comorbidities. Patients whose asthma control improves rapidly with correction of such problems are not considered to have severe asthma.[1]

Treatment-resistant asthma or severe refractory asthma can only be diagnosed after confirming the diagnosis, confirming good adherence to high-dose inhaled corticosteroid and correct inhaler technique, excluding alternative or overlapping diagnoses, identifying and minimising exposure to preventable triggers including allergens, irritants and medicines that cause bronchoconstriction, managing comorbidities, and closely monitoring for at least 6 months.[17, 1]

Omalizumab is a treatment option for some adults, adolescents and children with severe asthma.

The definition of severe asthma proposed by the World Health Organization (WHO) Consultation on Severe Asthma for global use is 'uncontrolled asthma which can result in risk of frequent severe exacerbations (or death) and/or adverse reactions to medications and/or chronic morbidity (including impaired lung function or reduced lung growth in children)'.[18] The WHO definition of severe asthma includes a category called 'severe untreated asthma', a term recommended only for use in countries that lack access to standard asthma medications such as inhaled corticosteroids.

Patients with severe symptoms due to untreated asthma may be found, after starting regular treatment, to have mild asthma (i.e. asthma that is easily controlled with low-dose inhaled corticosteroids).[16]

▶ Go to: European Respiratory Society and American Thoracic Society guidelines on *definition, evaluation and treatment of severe asthma*

Common reasons for poor response to preventer treatment

Apparent lack of response to asthma treatment is commonly due to one or more of the following:[3]

- poor adherence (which may be due to lack of perceived need for the medication, concern about potential or actual side-effects, cost of medicines, a busy lifestyle, misunderstanding of the purpose and effects of asthma medicines, or inability to follow the medical instructions)
- poor inhaler technique
- mishandling devices (e.g. failure to clean spacer, allowing mouthpiece of dry-powder inhalers to become blocked)
- incorrect dose or frequency
- empty inhaler
- expired medicines
- continued exposure to smoke or allergen triggers.

Failure to identify these causes before adjusting medicines could result in over-medication with preventers.

▶ See: *Management challenges*

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Correct use of inhaler devices

Checking and correcting inhaler technique is essential to effective asthma management.

Most patients with asthma or COPD do not use their inhalers properly,[19, 20,21, 21, 22] and most have not had their technique checked or corrected by a health professional.

Incorrect inhaler technique when using maintenance treatments increases the risk of severe flare-ups and hospitalisation for people with asthma or COPD.[19, 20, 23, 24, 25, 26]

Poor asthma symptom control is often due to incorrect inhaler technique.[27, 28]

Incorrect inhaler technique when using inhaled corticosteroids increases the risk of local side effects like dysphonia and oral thrush.

The steps for using an inhaler device correctly differ between brands. Checklists of correct steps for each inhaler type and how-to videos are available from the National Asthma Council website.

▶ Go to: National Asthma Council Australia's *Using your inhaler* webpage for information, patient resources and videos on inhaler technique
Go to: National Asthma Council Australia's information paper for health professionals on *Inhaler technique for people with asthma or COPD*
Go to: NPS MedicineWise information on *Inhaler devices for respiratory medicines*

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Inhaled corticosteroid/long-acting beta-2 agonist combinations for children aged 4–11 years

The combination of salmeterol plus fluticasone propionate in a single inhaler is TGA-registered for use in children 4 years and older.

Efficacy

A very large (n=6208) randomised controlled trial in children aged 4–11 years reported that, unlike in adults, the combination of inhaled corticosteroid and long-acting $beta_2$ agonist was not associated with a significant reduction in severe flare-ups, compared with inhaled corticosteroid alone.[29] Combination treatment was not associated with an increase in in symptom-free days or a reduction in reliever use, compared with inhaled corticosteroid alone.[29]

Safety

Clinical response to long-acting beta$_2$ agonists partly depends on genetics. A beta$_2$receptor genotype (Arg16 polymorphism in the beta$_2$ receptor gene) pre-disposes children with asthma to down-regulation of the beta$_2$ receptor and increased susceptibility to flare-ups during regular treatment with regular long-acting beta$_2$agonists.[15, 30] However, routine genetic testing to tailor asthma therapy is not yet available in clinical practice.

Earlier systematic reviews and meta-analyses led to concern about the possibility that the use of long-acting beta-agonists (even in combination with inhaled corticosteroids) might even increase the risk of flare-ups that require treatment with oral steroids or hospital admission, or of severe flare-ups.[4,10, 12] A meta-analysis commissioned by the US Food and Drug Administration found that the use of long-acting beta$_2$ agonists was associated with increased risk of severe asthma-associated adverse events (both overall and among the subset of people using concomitant inhaled corticosteroid and long-acting beta$_2$ agonist), and that this risk was greatest in children aged 4–11 years.[12] However, the increased risk was only seen in studies where inhaled corticosteroid was not provided, or where inhaled corticosteroid and long-acting beta$_2$ agonist were not combined in a single inhaler (i.e. where there was the possibility of selective non-adherence to the inhaled corticosteroid).

The PBAC Post-market review of medicines used to treat asthma in children[31] concluded that there was insufficient evidence to ascertain whether tolerance to long-acting beta$_2$ agonist could explain why it is less effective than montelukast and inhaled corticosteroids in managing exercise-induced asthma symptoms.[31]

A very large randomised controlled trial of children aged 4–11 years, stratified by asthma symptom control and pre-study treatment, found no increased risk of serious adverse outcomes with combination fluticasone propionate and salmeterol in a single inhaler, compared with fluticasone propionate alone.[29] Subsequent to the publication of this and similar studies in adults,[32] regulators in the USA and Australia removed previous 'black box' warnings from combination inhaled corticosteroid–long-acting beta$_2$ agonist products for asthma.[33]

PBS status as at March 2019: All formulations that contain a combination of inhaled corticosteroid plus long-acting beta$_2$ agonist are listed as 'Authority required - streamlined'. Patient using these combinations for asthma must have previously had frequent episodes of asthma while receiving treatment with oral corticosteroids or optimal doses of inhaled corticosteroids.

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Specific allergen immunotherapy (desensitisation)

- Specific allergen immunotherapy should not be started unless the patient has stable asthma, including spirometry-demonstrated forced expiratory volume in 1 second (FEV_1) greater than 80% predicted for subcutaneous immunotherapy and greater than 70% predicted for sublingual immunotherapy.[34, 35] For patients with unstable asthma (e.g. frequent symptoms, marked variability in airflow measured by spirometry or peak flow monitor), the risks of treatment should be considered. These patients will need specialist supervision during treatment.

Options available in Australia

Two forms of specific allergen immunotherapy are available:

- sublingual immunotherapy
- subcutaneous immunotherapy.

Both forms of specific allergen immunotherapy require 3–5 years of treatment. Specific allergy immunotherapy can be repeated.

Although some specific allergen therapies can be prescribed by primary care health professionals, it is recommended that they are initiated under the care of an allergy specialist (allergist or clinical immunologist), where possible.

Commercial allergen preparations for immunotherapy are available in Australia for aeroallergens including house dust mite, pollens (e.g. grass, tree and weed pollens), animal dander and moulds.

▶ Go to: ASCIA's *Allergen Immunotherapy* fact sheet for patients
Go to: ASCIA's *Allergen immunotherapy e-training for health professionals*

Overview of efficacy

There is strong evidence that allergen immunotherapy is effective in the treatment of seasonal and perennial allergic rhinitis.[36, 37, 38] There is less evidence supporting specific allergen immunotherapy in children than in adults.[37] Specific allergen immunotherapy in children with seasonal allergic rhinoconjunctivitis might prevent development of asthma.[39, 40, 41]

Single-allergen specific allergen immunotherapy is effective in patients sensitised to one allergen and those sensitised to multiple allergens.[42, 43, 44] In selected cases more than one allergen may be administered as separate extracts. There is weak evidence for the efficacy of allergen mixes.[45]

A systematic review of studies directly comparing subcutaneous immunotherapy and sublingual immunotherapy in the treatment of allergic rhinoconjunctivitis and asthma found:[46]

- low-grade evidence that subcutaneous immunotherapy is more effective than sublingual immunotherapy for reducing asthma symptoms and for reducing a combined measure of rhinitis symptoms and medication use
- moderate-grade evidence that subcutaneous immunotherapy is more effective than sublingual immunotherapy for reducing nasal and/or eye symptoms.

Sublingual immunotherapy is associated with a lower rate of severe adverse effects (anaphylaxis and death) than subcutaneous immunotherapy, based on indirect comparison.[47, 48, 49]

Sublingual immunotherapy

Sublingual immunotherapy (self-administered at home) is effective for the treatment of allergic rhinitis in adults and children.[50, 51] The greatest benefits have been demonstrated in those with allergies to temperate grass pollens or house dust mite.[51] Therapeutic Goods Administration (TGA)-approved indications for commercially available preparations vary according to age group.

The extract must be held under the tongue without swallowing for 2 minutes (liquid extracts) or 1 minute (tablets).

Sublingual immunotherapy is generally well tolerated.[50] Local adverse effects are common in children receiving sublingual immunotherapy.[47] Systemic adverse reactions, such as anaphylaxis, are very rare.[47] The majority of adverse events occur soon after beginning treatment.[51]

TGA-approved indications

Asthma: Acarizax (house dust mite) is indicated for adults 18–65 years with house dust mite allergic asthma that is not well controlled by inhaled corticosteroids and is associated with mild-to-severe house dust mite allergic rhinitis.[52] It is contraindicated in patients with FEV_1 <70% predicted after adequate treatment, and for patients who have experienced a severe flare-up within the previous 3 months.[52]

Allergic rhinitis: Several commercial preparations of aeroallergens for sublingual immunotherapy in patients with allergic rhinitis are used in Australia, including:

- *Acarizax* (house dust mite) – indicated for adults 18–65 years with persistent moderate to severe house dust mite allergic rhinitis despite symptomatic treatment.[52]
- *Actair* (house dust mite) – indicated for the treatment of house dust mite allergic rhinitis with or without conjunctivitis in adults and adolescents over 12 years diagnosed with house dust mite allergy.[53]
- *Grazax* (Timothy grass *[Phleum pratense]* pollen extract) – indicated for adults, adolescents and children older than 5 years with allergic rhinitis induced by Timothy grass[54]
- *Oralair* tablets (mix of grass pollens) – indicated for adults and children over 5 years with grass pollen allergic rhinitis.[55]

Various single allergens and/or multiple allergen mixes are available for use as advised by the treating allergist, available as liquid extracts. Age restrictions vary between products.

Note: PBS status as at October 2016: Treatment with sublingual immunotherapy specific allergen preparations is not subsidised by the PBS.

Subcutaneous immunotherapy

Subcutaneous immunotherapy involves injections in which the dose is gradually increased at regular intervals (usually weekly), or until a therapeutic/maintenance dose is reached. This can take approximately 3–6 months.[56] Treatment is then continued for a further 3–5 years.

Subcutaneous immunotherapy is generally not suitable for younger children (e.g. less than 7 years) because they may not be able to tolerate frequent injections.

Several commercial preparations of aeroallergens for subcutaneous immunotherapy are available in Australia, including various single allergens and/or multiple allergen mixes for use as advised by the treating allergist. Age restrictions vary between products.

Subcutaneous immunotherapy is effective for the treatment of allergic rhinitis and asthma, particularly when single-allergen immunotherapy regimens are used.[48] There is strong evidence that it reduces asthma symptoms, asthma medication usage, rhinitis/rhinoconjunctivitis symptoms, conjunctivitis symptoms, and rhinitis/rhinoconjunctivitis disease-specific quality of life, in comparison to placebo or usual care.[48] There is also moderate evidence that subcutaneous immunotherapy reduces rhinitis/rhinoconjunctivitis medication usage.[48]

Subcutaneous immunotherapy is associated with local adverse effects (e.g. injection-site swelling) and, less frequently, serious systemic adverse effects.[47, 51] The most common systemic reactions are respiratory symtoms. There have been few reports of anaphylaxis.[47]

Note: PBS status as at March 2019: Treatment with subcutaneous specific allergen immunotherapy preparations is not subsidised by the PBS.

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Oral corticosteroids for children: adverse effects

Oral corticosteroids may have adverse psychiatric effects in children, including aggression and hyperactivity.[57] Effects in the general population include euphoria, hypomania, depression, disturbances of mood, cognition, sleep and behaviour.[58]

A short course of oral corticosteroid therapy (less than 2 weeks) is associated with little risk of long-term suppression of the hypothalamus–pituitary–adrenal axis.[4] However, risk can accumulate if frequent courses (four or more per year) are given.[4]

Recurrent courses of oral corticosteroids may also affect bone mineral density, especially in boys.[4,59]

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References

1. Chung, K. F., Wenzel, S. E., Brozek, J. L., *et al*. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *The European respiratory journal*. 2014; 43: 343-73. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24337046
2. Bush, A, Pedersen, S, Hedlin, G, *et al*. Pharmacological treatment of severe, therapy-resistant asthma in children: what can we learn from where?. *Eur Respir J*. 2011; 38: 947-958. Available from: http://erj.ersjournals.com/content/38/4/947.long
3. Bush A, Saglani S. Management of severe asthma in children. *Lancet*. 2010; 376: 814-25. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20816548
4. van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma*. The Thoracic Society of Australia and New Zealand, 2010. Available from: https://www.thoracic.org.au/journal-publishing/command/download_file/id/25/filename/The_role_of_corticosteroids_in_the_management_of_childhood_asthma_-_2010.pdf
5. Papi, A., Brightling, C., Pedersen, S. E., Reddel, H. K.. Asthma. *Lancet*. 2018; 391: 783-800. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29273246
6. Chauhan BF, Chartrand C, Ni Chroinin M et al. Addition of long-acting beta2-agonists to inhaled corticosteroids for chronic asthma in children. *Cochrane Database Syst Rev* 2015; Volume 11: CD007949. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26594816
7. Castro-Rodriguez, J. A., Rodrigo, G. J., Rodriguez-Martinez, C. E.. Principal findings of systematic reviews for chronic treatment in childhood asthma. *J Asthma*. 2015; 52: 1038-45. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26303207
8. Ducharme FM, Ni Chroinin M, Greenstone I, Lasserson TJ. Addition of long-acting beta2-agonists to inhaled corticosteroids versus same dose inhaled corticosteroids for chronic asthma in adults and children. *Cochrane Database Syst Rev*. 2010; Issue 5: CD005535. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005535.pub2/full
9. Fitzpatrick AM, Jackson DJ, Mauger DT et al. Individualized therapy for persistent asthma in young children. *J Allergy Clin Immunol*. 2016; 138: 1608-18.e12. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27777180
10. van Asperen PP. Long-acting beta agonists for childhood asthma. *Aust Prescr*. 2012; 35: 111-3. Available from: https://www.nps.org.au/australian-prescriber/articles/long-acting-beta2-agonists-for-childhood-asthma
11. Lemanske RF, Mauger DT, Sorkness CA, *et al*. Step-up therapy for children with uncontrolled asthma receiving inhaled corticosteroids. *N Engl J Med*. 2010; 362: 975-985. Available from: http://www.nejm.org/doi/full/10.1056/NEJMoa1001278#t=article
12. McMahon AW, Levenson MS, McEvoy BW, *et al*. Age and risks of FDA-approved long-acting β2-adrenergic receptor agonists. *Pediatrics*. 2011; 128: e1147-1154. Available from: http://pediatrics.aappublications.org/content/128/5/e1147.long
13. Chauhan BF, Ben Salah R, Ducharme FM. Addition of anti-leukotriene agents to inhaled corticosteroids in children with persistent asthma. *Cochrane Database Syst Rev*. 2013; Issue 10: CD009585. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24089325
14. Fogel RB, Rosario N, Aristizabal G et al. Effect of montelukast or salmeterol added to inhaled fluticasone on exercise-induced bronchoconstriction in children. *Ann Allergy Asthma Immunol* 2010; 104: 511-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20568384
15. Lipworth BJ, Basu K, Donald HP, *et al*. Tailored second-line therapy in asthmatic children with the Arg(16) genotype. *Clin Sci (Lond)*. 2013; 124: 521-528. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23126384
16. Reddel HK, Taylor DR, Bateman ED, *et al*. An official American Thoracic Society/European Respiratory Society statement: asthma control and exacerbations: standardizing endpoints for clinical asthma trials and clinical practice. *Am J Respir Crit Care Med*. 2009; 180: 59-99. Available from: http://ajrccm.atsjournals.org/content/180/1/59.long
17. Bel EH, Sousa A, Fleming L, *et al*. Diagnosis and definition of severe refractory asthma: an international consensus statement from the Innovative Medicine Initiative (IMI). *Thorax*. 2011; 66: 910-917. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21106547
18. Bousquet J, Mantzouranis E, Cruz AA, *et al*. Uniform definition of asthma severity, control, and exacerbations: document presented for the World Health Organization Consultation on Severe Asthma. *J Allergy Clin Immunol*. 2010; 126: 926-38. Available from: http://www.jacionline.org/article/S0091-6749(10)01126-7/fulltext
19. The Inhaler Error Steering Committee,, Price, D., Bosnic-Anticevich, S., *et al*. Inhaler competence in asthma: common errors, barriers to use and recommended solutions. *Respir Med*. 2013; 107: 37-46. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23098685
20. Bjermer, L.. The importance of continuity in inhaler device choice for asthma and chronic obstructive pulmonary disease. *Respiration; international review of thoracic diseases*. 2014; 88: 346-52. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25195762
21. Basheti, I A, Armour, C L, Bosnic-Anticevich, S Z, Reddel, H K. Evaluation of a novel educational strategy, including inhaler-based reminder labels, to improve asthma inhaler technique. *Patient Educ Couns*. 2008; 72: 26-33. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18314294
22. Bosnic-Anticevich, S. Z., Sinha, H., So, S., Reddel, H. K.. Metered-dose inhaler technique: the effect of two educational interventions

delivered in community pharmacy over time. *The Journal of asthma : official journal of the Association for the Care of Asthma*. 2010; 47: 251-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20394511
23. Melani AS, Bonavia M, Cilenti V, *et al*. Inhaler mishandling remains common in real life and is associated with reduced disease control. *Respir Med*. 2011; 105: 930-8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21367593
24. Levy ML, Dekhuijzen PN, Barnes PJ, *et al*. Inhaler technique: facts and fantasies. A view from the Aerosol Drug Management Improvement Team (ADMIT). *NPJ Prim Care Respir Med*. 2016; 26: 16017. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27098045
25. Haughney, J., Price, D., Barnes, N. C., *et al*. Choosing inhaler devices for people with asthma: current knowledge and outstanding research needs. *Respiratory medicine*. 2010; 104: 1237-45. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20472415
26. Giraud, V., Roche, N.. Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability. *The European respiratory journal*. 2002; 19: 246-51. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11866004
27. Harnett, C. M., Hunt, E. B., Bowen, B. R., *et al*. A study to assess inhaler technique and its potential impact on asthma control in patients attending an asthma clinic. *J Asthma*. 2014; 51: 440-5.
28. Hardwell, A., Barber, V., Hargadon, T., *et al*. Technique training does not improve the ability of most patients to use pressurised metered-dose inhalers (pMDIs). *Prim Care Respir J*. 2011; 20: 92-6. Available from: http://www.nature.com/articles/pcrj201088
29. Stempel, D. A., Szefler, S. J., Pedersen, S., *et al*. Safety of adding salmeterol to fluticasone propionate in children with asthma. *N Engl J Med*. 2016; 375: 840-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27579634
30. Finkelstein Y, Bournissen FG, Hutson JR, Shannon M. Polymorphism of the ADRB2 gene and response to inhaled beta- agonists in children with asthma: a meta-analysis. *J Asthma* 2009; 46: 900-5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19905915
31. Pharmaceutical Benefits Scheme,. *Post-market review. PBS medicines used to treat asthma in children. Report to PBAC. Final Report*. 2017.
32. Busse WW, Bateman ED, Caplan AL et al. Combined analysis of asthma safety trials of long-acting beta2-agonists. *N Engl J Med* 2018; 378: 2497-505. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29949492
33. Seymour SM, Lim R, Xia C et al. Inhaled corticosteroids and LABAs - removal of the FDA's boxed warning. *N Engl J Med* 2018; 378: 2461-3. Available from: https://www.nejm.org/doi/10.1056/NEJMp1716858
34. Ciolkowski, J., Mazurek, H., Stasiowska, B.. Evaluation of step-down therapy from an inhaled steroid to montelukast in childhood asthma. *Allergol Immunopathol (Madr)*. 2014; 42: 282-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23684855
35. Nagao M, Ikeda M, Fukuda N, *et al*. Early control treatment with montelukast in preschool children with asthma: a randomized controlled trial. *Allergol Int*. 2018; 67: 72-78. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28526210
36. Kew KM, Beggs S, Ahmad S. Stopping long-acting beta2-agonists (LABA) for children with asthma well controlled on LABA and inhaled corticosteroids. *Cochrane Database Syst Rev*. 2015; Issue 5: CD011316. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25997166
37. Kew, KM; Quinn, M; Quon, B. S; Ducharme, FM;. Increased versus stable doses of inhaled corticosteroids for exacerbations of chronic asthma in adults and children. *Cochrane Database Syst Rev*. 2016; Issue 6: CD007524: . Available from: https://www.ncbi.nlm.nih.gov/pubmed/27272563
38. Basheti, IA; Obeidat, NM; Reddel, HK;. Effect of novel inhaler technique reminder labels on the retention of inhaler technique skills in asthma: a single-blind randomized controlled trial.. *NPJ Prim Care Respir Med*. 2017; 27: 9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28184045
39. Rank, M. A., Johnson, R., Branda, M., *et al*. Long-term outcomes after stepping down asthma controller medications: a claims-based, time-to-event analysis. *Chest*. 2015; 148: 630-639. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4556120/
40. Jacobsen, L., Niggemann, B., Dreborg, S., *et al*. Specific immunotherapy has long-term preventive effect of seasonal and perennial asthma: 10-year follow-up on the PAT study. *Allergy*. 2007; 62: 943-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/17620073
41. Pike, K. C., Akhbari, M., Kneale, D., Harris, K. M.. Interventions for autumn exacerbations of asthma in children. *Cochrane Database Syst Rev*. 2018; Issue 3: Cd012393. Available from: http://cochranelibrary-wiley.com/doi/10.1002/14651858.CD012393.pub2/full
42. Mann, RD; Pearce, GL; Dunn, N; Shakir, S. Sedation with "non-sedating" antihistamines: four prescription-event monitoring studies in general practice. *BMJ (Clinical research ed)*. 2000; 320: 1184-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/10784544
43. Ducharme, F. M., Noya, F. J., Allen-Ramey, F. C., *et al*. Clinical effectiveness of inhaled corticosteroids versus montelukast in children with asthma: prescription patterns and patient adherence as key factors. *Curr Med Res Opin*. 2012; 28: 111-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/22077107
44. Garcia Garcia, ML, Wahn, U, Gilles, L, *et al*. Montelukast, compared with fluticasone, for control of asthma among 6- to 14-year-old patients with mild asthma: The MOSAIC Study. *Pediatrics*. 2005; 116: 360-369. Available from: https://www.ncbi.nlm.nih.gov/pubmed/16061590
45. Fonseca-Aten, M, Okada, P J, Bowlware, K L, *et al*. Effect of clarithromycin on cytokines and chemokines in children with an acute exacerbation of recurrent wheezing: a double-blind, randomized, placebo-controlled trial. *Ann Allergy Asthma Immunol*. 2006; 97: 457-463.
46. Philip, G, Hustad, C, Noonan, G, *et al*. Reports of suicidality in clinical trials of montelukast. *J Allergy Clin Immunol*. 2009; 124: 691-696. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19815114
47. Brożek JL, Bousquet J, Baena-Cagnani CE, *et al*. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 Revision. *J Allergy Clin Immunol*. 2010; 126: 466-476. Available from: http://www.jacionline.org/article/S0091-6749(10)01057-2/fulltext
48. Philip, G., Hustad, C. M., Malice, M. P., *et al*. Analysis of behavior-related adverse experiences in clinical trials of montelukast. *J Allergy Clin Immunol*. 2009; 124: 699-706. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19815116
49. Ali, M. M., O'Brien, C. E., Cleves, M. A., Martin, B. C.. Exploring the possible association between montelukast and neuropsychiatric events among children with asthma: a matched nested case-control study. *Pharmacoepidemiol Drug Saf*. 2015; 24: 435-45. Available

from: https://www.ncbi.nlm.nih.gov/pubmed/25683909
50. Therapeutic Goods Administration,. Montelukast – neuropsychiatric risks. *Aust Prescr*. 2013; 36: 168-171. Available from: https://www.nps.org.au/australian-prescriber/articles/medicines-safety-update-2-58#article
51. Schumock, G T, Stayner, L T, Valuck, R J, *et al*. Risk of suicide attempt in asthmatic children and young adults prescribed leukotriene-modifying agents: a nested case-control study. *J Allergy Clin Immunol*. 2012; 130: 368-375. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22698520
52. Seqirus. *Product Information: Acarizax (standardised allergen extract from the house dust mites*. Therapeutic Goods Administration, Canberra, 2016. Available from: https://www.ebs.tga.gov.au/
53. Stallergenes. *Product Information: Actair Initiation Sublingual Tablets 100 IR & 300 IR and Actair Continuation Treatment Sublingual Tablets 300 IR (mixture of*. Therapeutic Goods Administration, Canberra, 2016. Available from: https://www.ebs.tga.gov.au/
54. Seqirus. *Product Information: Grazax*. Therapeutic Goods Administration, Canberra, 2017. Available from: https://www.ebs.tga.gov.au
55. Stallergenes. *Product Information: Oralair (allergen pollen extract of five grasses)*. Therapeutic Goods Administration, Canberra, 2016. Available from: https://www.ebs.tga.gov.au/
56. Australasian Society of Clinical Immunology and Allergy (ASCIA). *Allergen Immunotherapy*. ASCIA, Sydney, 2013. Available from: http://www.allergy.org.au/patients/allergy-treatment/immunotherapy
57. Stuart, F. A., Segal, T. Y., Keady, S.. Adverse psychological effects of corticosteroids in children and adolescents. *Arch Dis Child*. 2005; 90: 500-6. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1720409/
58. Australian Medicines Handbook. Last modified July 2018: *Australian Medicines Handbook Pty Ltd*. 2018
59. Kelly, H. W., Van Natta, M. L., Covar, R. A., *et al*. Effect of long-term corticosteroid use on bone mineral density in children: a prospective longitudinal assessment in the childhood Asthma Management Program (CAMP) study. *Pediatrics*. 2008; 122: e53-61. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/18595975/

Managing asthma in children aged 6 years and over

In this section

Assessing symptoms and control in children 6 years and over

Recommendations

For children with a new asthma diagnosis or those not taking regular preventer treatment, assess frequency and severity of symptoms and flare-ups.

Note: This assessment should be based on overall pattern of symptoms including frequency of flare-ups and symptoms between flare-ups, not on symptoms seen during a flare-up.

Table. Classification of asthma and indications for initiating preventer treatment in children aged 6–11

	Average frequency of flare-ups and symptoms between flare-ups		
Severity of flare-ups	*Infrequent intermittent* **Flare-ups every 6 weeks or less and no symptoms between flare-ups**	*Frequent intermittent* **Flare-ups more than once every 6 weeks and no symptoms between flare-ups**	*Persistent* **Between flare-ups (any of):** • **Daytime symptoms‡ more than once per week** • **Night-time symptoms‡ more than twice per month** • **Symptoms restrict activity or sleep**
Mild flare-ups *(almost always managed with salbutamol in community)*	**Not indicated**	**Consider**	**Indicated**
Moderate–severe flare-ups *(>2 in past year requiring ED or oral corticosteroids)*	**Consider**	**Indicated**	**Indicated**

Life-threatening flare-ups *(require hospitalisation or PICU)*	**Indicated**	**Indicated**	**Indicated**

Preventer should be started as a treatment trial. Assess response after 4–6 weeks and review before prescribing long term.

ED: emergency department

Indicated: Prescribe preventer and monitor as a treatment trial. At follow-up, discontinue if ineffective

Not indicated: Preventer is unlikely to be beneficial

Consider prescribing preventer according to overall risk for severe flare-ups

‡ Symptoms between flare-ups. A flare-up is defined as a period of worsening asthma symptoms, from mild (e.g. symptoms that are just outside the normal range of variation for the child, documented when well) to severe (e.g. events that require urgent action by parents/carers and health professionals to prevent a serious outcome such as hospitalisation or death from asthma).

Last reviewed version 2.0

Asset ID: 16

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

Assess level of recent asthma symptom control.

Notes: If reliable equipment and appropriately trained staff are available, spirometry can be performed in primary care. If not, refer to an appropriate provider such as an accredited respiratory function laboratory.

Most children aged 6 and older can perform spirometry reliably.

Table. Definition of levels of recent asthma symptom control in children (regardless of current treatment regimen)

Good control	Partial control	Poor control
All of: • **Daytime symptoms† ≤2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator)** • **No limitation of activities‡** • **No symptoms§ during night or when wakes up** • **Need for SABA reliever# ≤2 days per week**	**Any of:** • **Daytime symptoms† >2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator)** • **Any limitation of activities*** • **Any symptoms during night or when wakes up††** • **Need for SABA reliever# >2 days per week**	**Either of:** • **Daytime symptoms† >2 days per week (lasting from minutes to hours or recurring, and partially or fully relieved by SABA reliever)** • **≥3 features of partial control within the same week**

SABA: short-acting beta$_2$ agonist

† e.g. wheezing or breathing problems

‡ child is fully active; runs and plays without symptoms

§ including no coughing during sleep

 # not including doses taken prophylactically before exercise. (Record this separately and take into account when assessing management.)

*** e.g. wheeze or breathlessness during exercise, vigorous play or laughing**

†† e.g. waking with symptoms of wheezing or breathing problems

Notes:

Recent asthma control is based on symptoms over the previous 4 weeks. Each child's risk factors for future asthma outcomes should also be assessed and taken into account in management.

Validated questionnaires can be used for assessing recent symptom control:
Test for Respiratory and Asthma Control in Kids (TRACK) for children < 5 years
Childhood Asthma Control Test (C-ACT) for children aged 4–11 years

Last reviewed version 2.0

Asset ID: 23

How this recommendation was developed

Consensus recommendation following inconclusive literature search

Based on clinical experience and expert opinion after literature review yielded insufficient evidence for an evidence-based recommendation

Key evidence considered:

- Abramson et al. 2015[1]
- Deschildre et al. 2012[2]
- Haahtela et al. 2006[3]

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Assess risk factors for flare-ups.

Table. Risk factors for life-threatening asthma flare-ups in children

Asthma-related factors

Poor asthma control

Admission to hospital in preceding 12 months

History of intubation for acute asthma

Over-use of short-acting beta$_2$ agonist reliever

Abnormal spirometry findings

Reversible expiratory airflow limitation on spirometry despite treatment

Poor adherence to preventer

Incorrect inhaler technique for preventer

Poor adherence to asthma action plan

Exposure to clinically relevant allergens

Exposure to tobacco smoke

Other clinical factors

Allergies to foods, insects, medicines

Obesity

Family-related factors

Frequent failure to attend consultations/lack of follow-up after an acute flare-up

Significant parental psychological or socioeconomic problems

Parent/carer unequipped to manage asthma emergency

Last reviewed version 2.0

Asset ID: 116

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

Perform spirometry in children able to do this test reliably.

If spirometry is normal, it should be repeated at planned asthma reviews at least yearly.

If spirometry is abnormal, it should be checked again 4–6 weeks after starting treatment or changing the treatment regimen.

How this recommendation was developed

Consensus recommendation following inconclusive literature search

Based on clinical experience and expert opinion after literature review yielded insufficient evidence for an evidence-based recommendation

Key evidence considered:

- Abramson et al. 2015[1]
- Deschildre et al. 2012[2]
- Haahtela et al. 2006[3]

Last reviewed version 2.0

If the diagnosis of asthma was made elsewhere, confirm the diagnosis, if possible.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

More information

Classification of symptom patterns in children

The pattern and severity of symptoms in a child with asthma or preschool wheeze is a guide to initial treatment.

Table. Classification of preschool wheeze and indications for preventer treatment in children aged 1–5

Severity of flare-ups	Frequency of symptoms			
	Symptoms every 6 months or less	**Symptoms every 3–4 months**	**Symptoms every 4–6 weeks**	**Symptoms at least once per week**
Mild flare-ups *(managed with salbutamol in community)*	Not indicated	Not indicated	Consider	Indicated
Moderate–severe flare-ups *(require ED care/oral corticosteroids)*	Indicated	Indicated	Indicated	Indicated
Life-threatening flare-ups *(require hospitalisation or PICU)*	Indicated	Indicated	Indicated	Indicated

PICU: paediatric intensive care unit; ED: emergency department

Indicated: Prescribe preventer and monitor as a treatment trial. Discontinue if ineffective.

Not indicated: Preventer is unlikely to be beneficial

Consider prescribing preventer according to overall risk for severe flare-ups

Symptoms: wheeze, cough or breathlessness. May be triggered by viral infection, exercise or inhaled allergens

Flare-up: increase in symptoms from usual day-to-day symptoms (ranging from worsening asthma over a few days to an acute asthma episode)

Preventer options: an inhaled corticosteroid (low dose) or montelukast

[!] Advise parents/carers about potential adverse behavioural and/or neuropsychiatric effects of montelukast

Notes:

Preventer medication is unlikely to be beneficial in a child whose symptoms do not generally respond to salbutamol

In children taking preventer, symptoms should be managed with a short-acting inhaled beta$_2$ agonist reliever (e.g. when child shows difficulty breathing).

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Asset ID: 20

Table. Definitions of asthma patterns in children aged 6 years and over not taking regular preventer

Category		**Pattern and intensity of symptoms (when not taking regular treatment)**
Infrequent intermittent asthma †		Symptom-free for at least 6 weeks at a time (flare-ups up to once every 6 weeks on average but no symptoms between flare-ups)
Frequent intermittent asthma		Flare-ups more than once every 6 weeks on average but no symptoms between flare-ups
Persistent asthma	*Mild*	FEV_1 ≥80% predicted and at least one of: • Daytime symptoms‡ more than once per week but not every day • Night-time symptoms‡ more than twice per month but not every week
	Moderate	Any of: • FEV_1 <80% predicted‡ • Daytime symptoms‡ daily • Night-time symptoms‡ more than once per week • Symptoms sometimes restrict activity or sleep
	Severe	Any of: • FEV_1 ≤60% predicted‡ • Daytime symptoms‡ continual • Night-time symptoms‡ frequent • Flare-ups frequent • Symptoms frequently restrict activity or sleep

† It may not be appropriate to make the diagnosis of asthma in children aged 6 or older who wheeze only during upper respiratory tract infections. These children can be considered to have episodic (viral) wheeze.

‡ Symptoms between flare-ups. A flare-up is defined as a period of worsening asthma symptoms, from mild (e.g. symptoms that are just outside the normal range of variation for the child, documented when well) to severe (e.g. events that require urgent action by parents and health professionals to prevent a serious outcome such as hospitalisation or death from asthma).

Asset ID: 15

Table. Classification of asthma and indications for initiating preventer treatment in children aged 6–11

	Average frequency of flare-ups and symptoms between flare-ups

Severity of flare-ups	*Infrequent intermittent* **Flare-ups every 6 weeks or less and no symptoms between flare-ups**	*Frequent intermittent* **Flare-ups more than once every 6 weeks and no symptoms between flare-ups**	*Persistent* **Between flare-ups (any of):** • **Daytime symptoms‡ more than once per week** • **Night-time symptoms‡ more than twice per month** • **Symptoms restrict activity or sleep**
Mild flare-ups *(almost always managed with salbutamol in community)*	Not indicated	Consider	Indicated
Moderate–severe flare-ups *(>2 in past year requiring ED or oral corticosteroids)*	Consider	Indicated	Indicated
Life-threatening flare-ups *(require hospitalisation or PICU)*	Indicated	Indicated	Indicated

Preventer should be started as a treatment trial. Assess response after 4–6 weeks and review before prescribing long term.

ED: emergency department

Indicated: Prescribe preventer and monitor as a treatment trial. At follow-up, discontinue if ineffective

Not indicated: Preventer is unlikely to be beneficial

Consider prescribing preventer according to overall risk for severe flare-ups

‡ Symptoms between flare-ups. A flare-up is defined as a period of worsening asthma symptoms, from mild (e.g. symptoms that are just outside the normal range of variation for the child, documented when well) to severe (e.g. events that require urgent action by parents/carers and health professionals to prevent a serious outcome such as hospitalisation or death from asthma).

Last reviewed version 2.0

Asset ID: 16

For children already taking regular preventer treatment, adjustments to the treatment regimen are based on finding the lowest dose of medicines that will maintain good control of symptoms.

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Approaches to assessment and monitoring of asthma control in children

Assessment of asthma control in children is based mainly on:

- recent asthma symptom control (assessed by the frequency and severity of symptoms between flare-ups
- the degree to which asthma symptoms affect daily activities such as interference with physical activity or missed school days)
- the frequency of flare-ups
- spirometry in children who are able to perform the test reliably.

Standardised questionnaires

Questionnaire-based instruments have been validated for assessing asthma control in children:

▶ *Test for Respiratory and Asthma Control in Kids (TRACK)* for children less than 5 years old – consists of five questions about frequency of respiratory symptoms (wheeze, cough, shortness of breath), activity limitation, and night-time awakenings in the past 4 weeks, rescue medication use in the past 3 months, and oral corticosteroid use in the previous year.[4, 5] A lower score indicates worse asthma control.

Childhood Asthma Control Test (C-ACT) for children aged 4–11 years – consists of seven items: three for the parent/carer (about the child's symptoms over the previous 4 weeks) and four for the child.[6, 7] A lower score indicates worse asthma control. **Note:** C-ACT is intended for US use.

Lung function tests

Frequent spirometry to guide asthma treatment in children has not been shown to achieve superior outcomes to symptom-based treatment.[8] Current evidence does not support use of home spirometers to guide asthma treatment in children.[2] However, low FEV_1 predicts clinically significant flare-ups, so spirometry should be performed at asthma reviews for children who are old enough to do the test.
The quality and utility of spirometry depends on the skill, clinical expertise and experience of the person doing and interpreting spirometry.

The results of one study in children aged 6–16 years with moderate atopic asthma suggest that asthma treatment guided by airway hyperresponsiveness (measured by bronchial provocation testing) may have a benefit over symptom-guided treatment in improving lung, but this effect was lost after 3–7 years of usual care.[9, 10] Repeated bronchial provocation testing is not feasible in clinical practice.

Measures of airway inflammation

Measures of airway inflammation (e.g. sputum eosinophil count, exhaled nitric oxide measurement) are not recommended in primary care to guide treatment decisions, but are increasingly used in specialist clinics.

Asthma treatment guided by sputum eosinophil count has been shown to reduce the frequency of flare-ups in adults with asthma, but there is insufficient evidence to ascertain its value for children.[11]

Exhaled nitric oxide measurement may be useful in guiding asthma management in some children. In children not taking inhaled corticosteroid, a high nitric oxide level probably predicts a good short-term response to inhaled corticosteroid treatment,[12] but it does not distinguish between asthma and eosinophilic bronchitis and is often high in children with atopy. There is insufficient evidence to ascertain whether a low exhaled nitric oxide level predicts successful withdrawal from inhaled corticosteroids without asthma relapse,[12] or safety of treating asthma without inhaled corticosteroids.

A Cochrane review[13] found that exhaled nitric oxide-guided management was significantly better than other approaches to adjusting medicines for reducing the number of children with flare-ups and the number of children who needed oral corticosteroids, but did not reduce the frequency of flare-ups or the rate of flare-ups requiring hospitalisation, improve lung function or symptoms scores, or reduce inhaled corticosteroid doses. The authors concluded that it could not be recommended for all children but may be beneficial for a subset not yet defined.[13]

Towards personalised asthma care

Emerging understanding of asthma phenotypes and of genetic factors that predict therapeutic response to preventer options is leading to the possibility of personalised, genomics-based treatment for asthma in children.[14] In the near future, individual tailored therapy is may replace the standardised step model based on population data.

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Role of spirometry in the diagnosis of asthma in children

Generally, spirometry cannot be performed to acceptable standards in children younger than 4–5 years.[15]

Some older children cannot perform spirometry either. However, children who are unable to perform spirometry satisfactorily on their first visit are often able to perform the test correctly at the next visit.[15]

Normal spirometry in a child, especially when asymptomatic, does not exclude the diagnosis of asthma. FEV_1 is often normal in children with persistent asthma.

Reduced FEV_1 alone does not indicate that a child has asthma, because it may be seen with other lung diseases (or be due to poor spirometric technique). However, reduced ratio of FEV_1 to FVC for age indicates expiratory airflow limitation.

A significant increase in FEV_1 (>12% from baseline) after administering a bronchodilator (e.g. 2–4 puffs of salbutamol 100 microg/actuation) indicates that airflow limitation is reversible and supports the diagnosis of asthma. However, an absent response to bronchodilators does not exclude asthma.

In children with asthma, bronchodilator reversibility is also predictive of a good lung function response to inhaled corticosteroids.[16]

- Go to: National Asthma Council Australia's *Spirometry Resources*

Last reviewed version 2.0

Managing cough in children

When cough is the predominant symptom in a young child, careful assessment is needed to avoid making an incorrect diagnosis of asthma, or instigating inappropriate treatment.[17] Cough alone (recurrent non-specific cough) is most likely due to recurrent viral bronchitis, which is unresponsive to both bronchodilators and preventive therapy including inhaled corticosteroids. Recurrent non-specific cough usually resolves by age 6 or 7 years and leaves no residual pulmonary pathology.

If cough is a problem for a child with known asthma, it should be managed according to national *Cough in Children and Adults: Diagnosis and Assessment (CICADA)* guidelines.[17]

- There are significant concerns about use of cough medicines in children.

▶ Go to: *Australian Cough Guidelines*
Go to: *Therapeutic Goods Administration (TGA) recommendations on the use of cough and cold medicines in children*

Last reviewed version 2.0

References

1. Abramson, M. J., Schattner, R. L., Holton, C., *et al*. Spirometry and regular follow-up do not improve quality of life in children or adolescents with asthma: Cluster randomized controlled trials. *Pediatr Pulmonol*. 2015; 50: 947-54. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25200397
2. Deschildre A, Beghin L, Salleron J, *et al*. Home telemonitoring (forced expiratory volume in 1 s) in children with severe asthma does not reduce exacerbations. *Eur Respir J*. 2012; 39: 290-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/21852334
3. Haahtela, T., Tuomisto, L. E., Pietinalho, A., *et al*. A 10 year asthma programme in Finland: major change for the better. *Thorax*. 2006; 61: 663-70. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/16877690/
4. Murphy KR, Zeiger RS, Kosinski M, *et al*. Test for respiratory and asthma control in kids (TRACK): a caregiver-completed questionnaire for preschool-aged children. *J Allergy Clin Immunol*. 2009; 123: 833-9. Available from: http://www.jacionline.org/article/S0091-6749(09)00212-7/fulltext
5. Zeiger RS, Mellon M, Chipps B, *et al*. Test for Respiratory and Asthma Control in Kids (TRACK): clinically meaningful changes in score. *J Allergy Clin Immunol*. 2011; 128: 983-8. Available from: http://www.jacionline.org/article/S0091-6749(11)01287-5/fulltext
6. Liu AH, Zeiger R, Sorkness C, *et al*. Development and cross-sectional validation of the Childhood Asthma Control Test. *J Allergy Clin Immunol*. 2007; 119: 817-25. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17353040
7. Liu AH, Zeiger RS, Sorkness CA, *et al*. The Childhood Asthma Control Test: retrospective determination and clinical validation of a cut point to identify children with very poorly controlled asthma. *J Allergy Clin Immunol*. 2010; 126: 267-73, 273.e1. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20624640
8. Abramson MJ, Schattner RL, Holton C et al. Spirometry and regular follow-up do not improve quality of life in children or adolescents with asthma: Cluster randomized controlled trials. *Pediatr Pulmonol* 2015; 50: 947-54. (Available from: https://www.ncbi.nlm.nih.gov/pubmed/25200397
9. Nuijsink M, Hop WC, Sterk PJ et al. Long-term asthma treatment guided by airway hyperresponsiveness in children: a randomised controlled trial. *Eur Respir J* 2007; 30: 457-66. (Available from: https://www.ncbi.nlm.nih.gov/pubmed/17537770
10. Nuijsink M, Vaessen-Verberne AA, Hop WC et al. Long-term follow-up after two years of asthma treatment guided by airway responsiveness in children. *Respir Med* 2013; 107: 981-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23672993
11. Petsky HL, Li A, Chang AB. Tailored interventions based on sputum eosinophils versus clinical symptoms for asthma in children and adults. *Cochrane Database Syst Rev* 2017; 8: Cd005603. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28837221
12. Lehtimaki L, Csonka P, Makinen E et al. Predictive value of exhaled nitric oxide in the management of asthma: a systematic review. *Eur Respir J* 2016; 48: 706-14. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27492830
13. Petsky HL, Kew KM, Chang AB. Exhaled nitric oxide levels to guide treatment for children with asthma. *Cochrane Database Syst*. Rev 2016; Issue 11: CD011439. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27825189/

14. Turner S, Francis B, Vijverberg S et al. Childhood asthma exacerbations and the Arg16 beta2-receptor polymorphism: A meta-analysis stratified by treatment. *J Allergy Clin Immunol* 2016; 138: 107-13.e5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26774659
15. Johns DP, Pierce R. *Pocket guide to spirometry*. 3rd edn. McGraw Hill, North Ryde, 2011.
16. Szefler, SJ, Phillips, BR, Martinez, FD, *et al*. Characterization of within-subject responses to fluticasone and montelukast in childhood asthma. *J Allergy Clin Immunol*. 2005; 115: 233-242. Available from: https://www.ncbi.nlm.nih.gov/pubmed/15696076
17. Gibson PG, Chang AB, Glasgow NJ, *et al*. CICADA: cough in children and adults: diagnosis and assessment. Australian cough guidelines summary statement. *Med J Aust*. 2010; 192: 265-271. Available from: https://www.mja.com.au/journal/2010/192/5/cicada-cough-children-and-adults-diagnosis-and-assessment-australian-cough

Prescribing reliever and considering regular preventer treatment for children 6 years and over

Recommendations

Discuss the goals of asthma treatment with the child's parents/carers and the child (as appropriate to the child's age and maturity). Explain that the overall aims of treatment are to reduce the risk of flare-ups, make sure asthma does not interfere with sport, play or school attendance, and to minimise the side effects of treatment by using the lowest level of medication required to maintain good asthma control.

Figure. Stepped approach to adjusting asthma medication in children aged 6-11 years

Please view and print this figure separately: http://www.asthmahandbook.org.au/figure/show/120

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

For all children, prescribe a reliever for as-needed relief of symptoms. Educate children and parents/carers how and when to use reliever, and advise them to carry reliever (and spacer) at all times.

Advise that reliever should not be used regularly.

Table. Non-emergency use of bronchodilators (relievers) in children aged 6–11 years

Option	Dose	Mode of delivery
Salbutamol 100 microg per actuation (puff)	**2–4 puffs as needed (one at a time)** **Repeat if needed**	**Pressurised metered-dose inhaler plus spacer**
Terbutaline 500 microg/actuation	**1–2 actuations** **Repeat if needed**	**Dry-powder inhaler†**

Note: This table lists usual doses to be administered by parents/carers in the community to manage symptoms as needed. Higher during may be given during acute asthma, including emergencies.

† If able to use this type of inhaler correctly

- **Do not prescribe oral salbutamol.**

Last reviewed version 2.0

Asset ID: 28

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

Consider regular preventer treatment according to pattern of symptoms. Explain to parents/carers that preventer treatment should be taken every day and continued long term.

Table. Classification of asthma and indications for initiating preventer treatment in children aged 6–11

	Average frequency of flare-ups and symptoms between flare-ups		
Severity of flare-ups	*Infrequent intermittent* **Flare-ups every 6 weeks or less and no symptoms between flare-ups**	*Frequent intermittent* **Flare-ups more than once every 6 weeks and no symptoms between flare-ups**	*Persistent* **Between flare-ups (any of):** • **Daytime symptoms‡ more than once per week** • **Night-time symptoms‡ more than twice per month** • **Symptoms restrict activity or sleep**
Mild flare-ups *(almost always managed with salbutamol in community)*	**Not indicated**	**Consider**	**Indicated**
Moderate–severe flare-ups *(>2 in past year requiring ED or oral corticosteroids)*	**Consider**	**Indicated**	**Indicated**
Life-threatening flare-ups *(require hospitalisation or PICU)*	**Indicated**	**Indicated**	**Indicated**

Preventer should be started as a treatment trial. Assess response after 4–6 weeks and review before prescribing long term.

ED: emergency department

Indicated: Prescribe preventer and monitor as a treatment trial. At follow-up, discontinue if ineffective

Not indicated: Preventer is unlikely to be beneficial

Consider prescribing preventer according to overall risk for severe flare-ups

‡ Symptoms between flare-ups. A flare-up is defined as a period of worsening asthma symptoms, from mild (e.g. symptoms that are just outside the normal range of variation for the child, documented when well) to severe (e.g. events that require urgent action by parents/carers and health professionals to prevent a serious outcome such as hospitalisation or death from asthma).

Last reviewed version 2.0

Asset ID: 16

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- van Asperen et al. 2010[1]

Last reviewed version 2.0

If a short-acting beta$_2$ agonist reliever is needed more than twice per week or always needed before exercise, consider starting regular preventer treatment with either of:

- **an inhaled corticosteroid (low dose)**
- **montelukast.**

- **Advise parents/carers about potential adverse psychiatric effects of montelukast.**

▶ Go to: TGA alert

Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)	
	Low	High
Beclometasone dipropionate †	100–200	>200 (maximum 400)
Budesonide	200–400	>400 (maximum 800)
Ciclesonide ‡	80–160	>160 (maximum 320)
Fluticasone propionate	100–200	>200 (maximum 500)

† Dose equivalents for *Qvar* (TGA-registered CFC-free formulation of beclometasone dipropionate)

‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

Source

van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma*. **The Thoracic Society of Australia and New Zealand, 2010. Available from: http://www.thoracic.org.au/clinical-documents/area?command=record&id=14**

Last reviewed version 2.0

Asset ID: 21

How this recommendation was developed

Consensus recommendation following inconclusive literature search

Based on clinical experience and expert opinion after literature review yielded insufficient evidence for an evidence-based recommendation

Key evidence considered:

- Chauhan et al. 2013[2]
- Ciółkowski et al. 2014[3]
- Nagao et al. 2018[4]
- Nwokoro et al. 2014[5]
- Valovirta et al. 2011[6]
- Pike et al. 2018[7]
- Ducharme et al. 2012[8]
- Garcia Garcia et al. 2005[9]
- Luskin et al. 2003[10]
- Sorkness et al. 2007[11]
- Zeiger et al. 2006[12]
- Ostrom et al. 2005[13]

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When starting preventer for the first time, the choice of agent can be guided by the following considerations.

An inhaled corticosteroid should be considered as the first choice preventer for those with symptoms that are frequent (e.g. daytime or night-time symptoms at least once per week), symptoms that restrict activity or sleep), or a history of severe flare-ups (e.g. requiring treatment in the emergency department or hospital admission).

An inhaled corticosteroid could also be preferable when either of the following are present:

- **atopy**
- **raised blood eosinophil count (if known; this test is not recommended routinely).**

When starting preventer for the first time for a child aged 2 years or over, the choice of agent can be guided by the following considerations.

Montelukast might be considered as alternative to an inhaled corticosteroid when any of the following apply:

- **The child is unable or refuses to use to pMDI + spacer/mask.**
- **The child has significant allergic rhinitis that requires treatment.**
- **Parents, despite education about risks and benefits, decline inhaled corticosteroids or are significantly concerned about their adverse effects (poor adherence is likely in this context).**

How this recommendation was developed

Consensus recommendation following inconclusive literature search

Based on clinical experience and expert opinion after literature review yielded insufficient evidence for an evidence-based recommendation

Key evidence considered:

- Chauhan et al. 2013[2]
- Ciółkowski et al. 2014[3]
- Nagao et al. 2018[4]
- Nwokoro et al. 2014[5]
- Valovirta et al. 2011[6]
- Pike et al. 2018[7]
- Ducharme et al. 2012[8]
- Garcia Garcia et al. 2005[9]
- Luskin et al. 2003[10]
- Sorkness et al. 2007[11]
- Zeiger et al. 2006[14]
- Ostrom et al. 2005[13]
- Grzelewski & Stelmach 2009[15]

- Stelmach et al. 2008[16]

Last reviewed version 2.0

When prescribing montelukast, start as a treatment trial. Review effects at 4–6 weeks and discontinue if no response. (The response to montelukast may be genotype dependent.)

- **Advise parents/carers about potential adverse psychiatric effects of montelukast.**

▶ Go to: TGA alert

How this recommendation was developed

Evidence-based recommendation

Based on literature search and formulated by multidisciplinary working group

Key evidence considered:

- Chauhan et al. 2013[2]
- Ciółkowski et al. 2014[3]
- Nagao et al. 2018[4]
- Nwokoro et al. 2014[5]
- Valovirta et al. 2011[6]
- Pike et al. 2018[7]
- Ducharme et al. 2012[8]
- Garcia Garcia et al. 2005[9]
- Luskin et al. 2003[10]
- Sorkness et al. 2007[17]
- Zeiger et al. 2006[12]
- Ostrom et al. 2005[13]
- Grzelewski & Stelmach 2009[15]
- Stelmach et al. 2008[18]
- Knorr et al. 1998[19]
- Becker et al. 2004[20]

Last reviewed version 2.0

When prescribing montelukast, warn parents/carers that behavioural and/or neuropsychiatric effects of montelukast are possible, but do not occur in the majority of children. Explain that if these adverse effects occur, they are typically seen within the first 2 weeks of starting regular treatment but resolve soon after discontinuing.

When dispensing montelukast in pharmacies, counsel parents/carers about behavioural and/or neuropsychiatric effects of montelukast and provide the consumer medicines information leaflet.

▶ Go to: TGA alert

How this recommendation was developed

Evidence-based recommendation

Based on literature search and formulated by multidisciplinary working group

Key evidence considered:

- Bernard et al. 2017[21]
- Aldea Perona et al. 2016[22]
- Wallerstedt et al. 2009[23]
- Philip et al. 2009[24]
- Philip et al. 2009[25]
- Ali et al. 2015[26]
- Therapeutic Goods Administration[27]
- Schumock et al. 2012[28]

Last reviewed version 2.0

When prescribing regular inhaled corticosteroids, begin with a low dose.

Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)	
	Low	High
Beclometasone dipropionate †	100–200	>200 (maximum 400)
Budesonide	200–400	>400 (maximum 800)
Ciclesonide ‡	80–160	>160 (maximum 320)
Fluticasone propionate	100–200	>200 (maximum 500)

† Dose equivalents for *Qvar* **(TGA-registered CFC-free formulation of beclometasone dipropionate)**

‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

Source

van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma***. The Thoracic Society of Australia and New Zealand, 2010. Available from:**
http://www.thoracic.org.au/clinical-documents/area?command=record&id=14

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Asset ID: 21

Table. Classification of asthma and indications for initiating preventer treatment in children aged 6–11

	Average frequency of flare-ups and symptoms between flare-ups		
Severity of flare-ups	*Infrequent intermittent* **Flare-ups every 6 weeks or less and no symptoms between flare-ups**	*Frequent intermittent* **Flare-ups more than once every 6 weeks and no symptoms between flare-ups**	*Persistent* **Between flare-ups (any of):** • **Daytime symptoms‡ more than once per week** • **Night-time symptoms‡ more than twice per month** • **Symptoms restrict activity or sleep**

Mild flare-ups *(almost always managed with salbutamol in community)*	**Not indicated**	**Consider**	**Indicated**
Moderate–severe flare-ups *(>2 in past year requiring ED or oral corticosteroids)*	**Consider**	**Indicated**	**Indicated**
Life-threatening flare-ups *(require hospitalisation or PICU)*	**Indicated**	**Indicated**	**Indicated**

Preventer should be started as a treatment trial. Assess response after 4–6 weeks and review before prescribing long term.

ED: emergency department

Indicated: Prescribe preventer and monitor as a treatment trial. At follow-up, discontinue if ineffective

Not indicated: Preventer is unlikely to be beneficial

Consider prescribing preventer according to overall risk for severe flare-ups

‡ Symptoms between flare-ups. A flare-up is defined as a period of worsening asthma symptoms, from mild (e.g. symptoms that are just outside the normal range of variation for the child, documented when well) to severe (e.g. events that require urgent action by parents/carers and health professionals to prevent a serious outcome such as hospitalisation or death from asthma).

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Asset ID: 16

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- van Asperen et al. 2010[1]

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Do not routinely prescribe theophyllines (aminophylline or theophylline) for children.

Note: Theophyllines are sometimes prescribed by specialists for children with severe asthma.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

Ipratropium is not recommended for the regular management of asthma in children.

Note: Ipratropium is used in the management of acute asthma.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- McDonald et al. 2003[29]

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More information

Classification of recent asthma symptom control in children

Ongoing review of asthma involves both assessing recent asthma symptom control and assessing risks for poor asthma outcomes such as flare-ups and adverse effects of medicines.

Recent asthma symptom control is assessed according to the frequency of asthma symptoms over the previous 4 weeks.

Table. Definition of levels of recent asthma symptom control in children (regardless of current treatment regimen)

Good control	Partial control	Poor control
All of: • Daytime symptoms† ≤2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • No limitation of activities‡ • No symptoms§ during night or when wakes up • Need for SABA reliever# ≤2 days per week	Any of: • Daytime symptoms† >2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • Any limitation of activities* • Any symptoms during night or when wakes up†† • Need for SABA reliever# >2 days per week	Either of: • Daytime symptoms† >2 days per week (lasting from minutes to hours or recurring, and partially or fully relieved by SABA reliever) • ≥3 features of partial control within the same week

SABA: short-acting beta$_2$ agonist

† e.g. wheezing or breathing problems

‡ child is fully active; runs and plays without symptoms

§ including no coughing during sleep

not including doses taken prophylactically before exercise. (Record this separately and take into account when assessing management.)

* e.g. wheeze or breathlessness during exercise, vigorous play or laughing

†† e.g. waking with symptoms of wheezing or breathing problems

Notes:

Recent asthma control is based on symptoms over the previous 4 weeks. Each child's risk factors for future asthma outcomes should also be assessed and taken into account in management.

Validated questionnaires can be used for assessing recent symptom control:
Test for Respiratory and Asthma Control in Kids (TRACK) for children < 5 years
Childhood Asthma Control Test (C-ACT) for children aged 4–11 years

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Asset ID: 23

Table. Risk factors for life-threatening asthma flare-ups in children
Asthma-related factors

Poor asthma control

Admission to hospital in preceding 12 months

History of intubation for acute asthma

Over-use of short-acting beta$_2$ agonist reliever

Abnormal spirometry findings

Reversible expiratory airflow limitation on spirometry despite treatment

Poor adherence to preventer

Incorrect inhaler technique for preventer

Poor adherence to asthma action plan

Exposure to clinically relevant allergens

Exposure to tobacco smoke

Other clinical factors

Allergies to foods, insects, medicines

Obesity

Family-related factors

Frequent failure to attend consultations/lack of follow-up after an acute flare-up

Significant parental psychological or socioeconomic problems

Parent/carer unequipped to manage asthma emergency

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Asset ID: 116

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Short-acting beta-2 agonist relievers for children: 6 years and over

Inhaled short-acting beta$_2$ agonists is the major class of bronchodilators used for relief of symptoms in asthma.[30]

Children with well-controlled asthma need little or no reliever (on no more than 2 days per week).

Increased use of short-acting beta$_2$ agonists for relief of asthma symptoms, especially daily use, indicates deterioration of asthma control.[31, 32]

Dispensing of 3 or more canisters in a year (average 1.6 puffs per day) is associated with increased risk of flare-ups.[33] Dispensing 12 or more canisters in a year (average 6.6 puffs per day) is associated with increased risk of asthma death.[2]

Table. Definition of levels of recent asthma symptom control in children (regardless of current treatment regimen)

Good control	Partial control	Poor control
All of: • Daytime symptoms† ≤2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • No limitation of activities‡ • No symptoms§ during night or when wakes up • Need for SABA reliever# ≤2 days per week	Any of: • Daytime symptoms† >2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • Any limitation of activities* • Any symptoms during night or when wakes up†† • Need for SABA reliever# >2 days per week	Either of: • Daytime symptoms† >2 days per week (lasting from minutes to hours or recurring, and partially or fully relieved by SABA reliever) • ≥3 features of partial control within the same week

SABA: short-acting beta$_2$ agonist

† e.g. wheezing or breathing problems

‡ child is fully active; runs and plays without symptoms

§ including no coughing during sleep

not including doses taken prophylactically before exercise. (Record this separately and take into account when assessing management.)

* e.g. wheeze or breathlessness during exercise, vigorous play or laughing

†† e.g. waking with symptoms of wheezing or breathing problems

Notes:

Recent asthma control is based on symptoms over the previous 4 weeks. Each child's risk factors for future asthma outcomes should also be assessed and taken into account in management.

Validated questionnaires can be used for assessing recent symptom control:
Test for Respiratory and Asthma Control in Kids (TRACK) for children < 5 years
Childhood Asthma Control Test (C-ACT) for children aged 4–11 years

Last reviewed version 2.0

Asset ID: 23

Last reviewed version 2.0

Administration of inhaled medicines in children: 6 years and over

Parents, carers and children need training to use inhaler devices correctly, including inhaler technique, and care and cleaning of inhalers and spacers.

School-aged children (depending on the child's age, ability, and with individualised training) can learn to use a range of inhaler types, including manually actuated pressurised metered-dose inhalers with spacers, breath-actuated pressurised metered-dose inhalers (e.g. Autohaler), and dry-powder inhalers (e.g. Accuhaler, Turbuhaler).[34, 35, 36, 37, 38]

Table. Types of inhaler devices for delivering asthma and COPD medicines

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/75

A pressurised metered-dose inhaler and spacer is an appropriate first choice for most children.[36]

School-aged children are unlikely to use their inhaler device correctly without careful training and repeated checking.[39]

▶ Go to: National Asthma Council Australia's *How to use a puffer and spacer for kids* video
Go to: National Asthma Council Australia's information paper for health professionals on *Inhaler technique for people with asthma or COPD*

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Correct use of inhaler devices

Checking and correcting inhaler technique is essential to effective asthma management.

Most patients with asthma or COPD do not use their inhalers properly,[40, 41,42, 42, 43] and most have not had their technique checked or corrected by a health professional.

Incorrect inhaler technique when using maintenance treatments increases the risk of severe flare-ups and hospitalisation for people with asthma or COPD.[40, 41, 44, 45, 46, 47]

Poor asthma symptom control is often due to incorrect inhaler technique.[48, 49]

Incorrect inhaler technique when using inhaled corticosteroids increases the risk of local side effects like dysphonia and oral thrush.

The steps for using an inhaler device correctly differ between brands. Checklists of correct steps for each inhaler type and how-to videos are available from the National Asthma Council website.

▶ Go to: National Asthma Council Australia's *Using your inhaler* webpage for information, patient resources and videos on inhaler technique
Go to: National Asthma Council Australia's information paper for health professionals on *Inhaler technique for people with asthma or COPD*
Go to: NPS MedicineWise information on *Inhaler devices for respiratory medicines*

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Preparation of new spacers before first use

Spacers are made of plastic, antistatic polymer/polycarbonate polyurethane, or cardboard.

Plastic spacers (e.g. Breath-A-Tech, Volumatic)

Electrostatic surface charge on new spacers made of plastic (e.g. *Breath-A-Tech*, *Volumatic*) reduces the proportion of medicine available for delivery to the airway. This charge can be reduced by washing the plastic spacer in dishwashing liquid and allowing it to air dry or drip-dry without rinsing or wiping.[50]

Alternatively, priming the spacer by actuating the device several times into the spacer also overcomes the charge, but this wastes medicine. The optimal number of actuations for priming is not known and the findings of in vitro studies vary widely. One study (using older, CFC-based formulations of asthma medicines) reported that up to 40 actuations fired into a new plastic spacer overcame the effect of the electrostatic charge.[51] Others have concluded that the electrostatic charge on plastic spacers does not reduce in vivo efficacy of bronchodilator therapy in children with asthma.[52] The number of actuations necessary may be known when the results of recent studies become available.

When a new plastic spacer must be used immediately (e.g. for a person with asthma symptoms), patients, parents and carers should follow the manufacturer's priming instructions. In hospitals and emergency departments, a new spacer that has not been pre-treated by washing can be primed using multiple (at least 10) puffs of salbutamol. (This is an arbitrary number of actuations in the absence of evidence that would enable a precise guideline.)

Non-plastic spacers

Disposable cardboard spacers (e.g. DispozABLE, LiteAire) and polyurethane/antistatic polymer spacers (e.g. *Able A2A*, *AeroChamber Plus*, *La Petite E-Chamber*, *La Grande E-Chamber*) do not require preparation before first use.[50]

Note: The term 'priming' is also used for the preparation process that is necessary for new pressurised metered-dose inhalers that have not been used for more than a week. This involves first actuating the inhaler into the air (away from the patient). Users should follow the manufacturer's instructions for the particular brand of inhaler, which specify the number of actuations required.

Last reviewed version 2.0

Montelukast for children: efficacy

- Montelukast use has been associated with behavioural and/or neuropsychiatric adverse effects, including suicidality.

▶ Go to: TGA alert

Overview

Montelukast is a leukotriene receptor antagonist preventer. It is registered by the TGA for the treatment of asthma in children aged 2 years and older, and for the symptomatic treatment of allergic rhinitis.[53]

Montelukast can be used as an alternative to inhaled corticosteroids or as an add-on treatment in a child already taking regular inhaled corticosteroids.

However, it is not effective for all children. Overall, only approximately 20–30% of children will respond to montelukast treatment. The effect is thought to depend mainly on the child's genotype.[54, 5, 55] Clinically, it is not possible to predict accurately which children will benefit most from montelukast treatment.

Montelukast as first-line preventer in children aged 2–5 years

Viral-induced wheezing

Overall, regular maintenance montelukast treatment does not reduce the risk of wheezing episodes requiring oral corticosteroid treatment among preschool children who only have wheezing episodes when they have viral upper respiratory tract infections.[56]

However, montelukast may be effective for some children. Some randomised controlled trials have reported a reduction the risk of flare-ups in preschool children with intermittent asthma/wheeze,[57, 4] while others have not.[6]

Persistent asthma or wheezing

A systematic review comparing montelukast with inhaled corticosteroids in preschoolers with asthma or recurrent wheezing requiring daily preventer treatment[58] reported that inhaled corticosteroids appeared to achieve better symptom control and reduce flare-ups (including severe flare-ups requiring treatment with systemic corticosteroids). However, results were inconsistent and meta-analysis was not possible due to heterogeneity of outcomes measured in available clinical trials.[58]

Some preschool children with persistent asthma/wheeze respond to montelukast. A crossover study in preschool children with persistent asthma/wheeze reported that some children showed their best response to montelukast, while most responded better to

regular inhaled corticosteroids.[59] Predictors of a better response to inhaled corticosteroids than montelukast were aeroallergen hypersensitivity and blood eosinophilia (eosinophil counts ≥ 300/μL).[59] However, routine blood eosinophil count is not feasible or recommended for this purpose.

Montelukast as first-line preventer children aged 6 years and over

In school-aged children with persistent asthma, inhaled corticosteroids are more effective overall than montelukast in improving lung function and controlling asthma symptoms.[60, 2]

However, symptoms will respond to a treatment trial of montelukast in approximately one-quarter to one-third of children,[60, 61,62] and some may benefit more than from an inhaled corticosteroid.[60] More severe asthma and markers of allergic inflammation may predict a better response to inhaled corticosteroids.[60]

Montelukast as add-on treatment

A systematic review of studies in children over 6 years and adolescents with mild-to-moderate persistent asthma found that the addition of montelukast to inhaled corticosteroids did reduce flare-ups requiring oral corticosteroids or hospital admissions for asthma, compared with the same or an increased dose.[2]

In a study comparing step-up treatments in children with asthma symptoms uncontrolled by low-dose inhaled corticosteroids, the addition of a long-acting beta$_2$ agonist was effective in more children than either montelukast or increasing the dose of inhaled corticosteroid for controlling asthma symptoms and preventing flare-ups requiring systemic corticosteroids.[63] However, some studies in school-aged children with persistent asthma already taking regular inhaled corticosteroids have reported that add-on montelukast reduced the risk of flare-ups[63, 64] and exercise-induced asthma symptoms.[64] Not all children will respond.

In a small study in children with persistent asthma already taking regular inhaled corticosteroids who were homozygous for the Arg16 genotype, montelukast was more effective as an add-on therapy than long-acting beta$_2$ agonist in reducing symptoms, reliever use and days absent from school due to asthma, depending on the child's beta receptor genotype.[55] However, children were given inhaled corticosteroid and long-acting beta$_2$ agonists in separate inhalers, which is which is known to be associated with increased risks.

However, genotyping it is not currently feasible in clinical practice. In practice, a treatment trial of 4–6 weeks can determine which preventer is suitable for controlling a child's asthma symptoms,[60] but longer treatment may be required to evaluate effect on flare-ups, because flare-ups may be independent of symptom control.

Exercise-induced symptoms

In school-aged children who experience exercise-induced symptoms despite taking regular inhaled corticosteroids, the addition of montelukast is effective in controlling symptoms, but not all children experience a response.[15, 65]

See: *Investigation and management of exercise-induced bronchoconstriction*

Short-term use in the management of flare-ups

Some, but not all studies suggest that a short course of montelukast, introduced at the first signs of an upper respiratory tract infection, may be effective in controlling flare-ups. An Australian study reported that this strategy could achieve a small reduction in symptoms, school absence and medical consultations in preschool and school-aged children with episodic wheeze.[66]

However, the evidence is inconsistent, with some studies showing no benefit.[6,67, 68, 69, 70] The findings of one study suggested that whether or not intermittent montelukast is effective in wheezing children aged 5 years and under depends on genotype.[5]

Montelukast is not TGA-approved or PBS-subsidised for intermittent use.

Note: PBS status as at March 2019: Montelukast is not subsidised by the PBS for adolescents 15 years and over.

Last reviewed version 2.0

Montelukast for children: behavioural and/or neuropsychiatric adverse effects

Montelukast is generally very well tolerated. Behavioural and psychiatric adverse effects were rare in clinical trials.[71, 72] However, post-marketing surveillance reports have identified behavioural and/or neuropsychiatric adverse effects associated with montelukast use in some children.[23]

Behavioural treatment-associated effects are difficult to assess in young children. No factors have been identified to predict which children are at risk.

Reported adverse events include nightmares, sleep disturbance, anxiety, irritability, aggression and depression.[23, 73, 21, 22]

Suicidal ideation has been reported in adolescents and adults taking montelukast.[22] A nested case-control study concluded that children with asthma aged 5–18 years taking leukotriene receptor antagonists were not at increased risk of suicide attempts.[75]

Reported adverse effects are usually mild.[21] The majority occur within 7–14 days of starting montelukast,[23, 21] but some may appear after several months.[22]

Behavioural and/or neuropsychiatric adverse effects typically disappear within 4 days of stopping montelukast treatment.[21] There is no evidence of long term effects.

The TGA recommends that clinicians treating children with montelukast should educate caregivers about these potential adverse effects and should consider providing them with the CMI. Advise them to seek medical advice if they have any concerns.

▶ Go to: TGA's 2018 safety review of montelukast

Last reviewed version 2.0

Inhaled corticosteroids for children: efficacy

Role in treatment asthma in children

The effectiveness of ICS in children appears to depend on several factors including the child's age, which triggers are causing symptoms, wheezing phenotype, tobacco smoke exposure and genotype.[76] Overall, inhaled corticosteroids seem to be more effective in older children and those with more severe disease.[1]

Early introduction of inhaled corticosteroid for children with recurrent wheeze does not prevent airway remodelling, improve long-term lung function or prevent the onset of persistent asthma, according to current evidence from long-term randomised controlled clinical trials in preschool children and school-aged children with intermittent or mild persistent asthma.[1]

Current evidence does not support planned seasonal use of inhaled corticosteroids in children not taking preventer at other times.[77]

Children aged 1–5 years

Intermittent wheeze/asthma

In preschool children who only have wheezing episodes with viral respiratory infections, limited available evidence suggests that regular treatment with inhaled corticosteroids does not reduce the risk of hospitalisation, flare-ups that require oral corticosteroid use, or reduce the frequency and duration of acute episodes.[76, 78] Inhaled corticosteroid treatment does not reduce these children's risk of developing persistent wheeze by age 6 years.[50]

Persistent wheeze/asthma

In preschool children who have episodes of wheezing from time to time, but also cough and wheezes at other times when they do not have a viral cold (e.g. when cries, plays or laughs), regular inhaled corticosteroids are moderately effective in controlling symptoms, though less effective than in older children.[50] When wheeze improves markedly during a short treatment trial (e.g. 3 months), it is not possible to tell whether improvement was due to the treatment or spontaneous resolution of symptoms.[50] However, this can be clarified by stopping inhaled corticosteroid treatment, monitoring symptoms, and re-starting.

In infants and preschoolers with persistent wheezing or asthma of at least 6 months' duration, regular treatment with inhaled corticosteroids improves wheezing, asthma symptoms and lung function, and reduces flare-ups.[1, 79]

Children aged 6 years and over

Most clinical trials of regular inhaled corticosteroid treatment in children have been conducted among children with asthma symptoms every week or more often ('persistent asthma').[1]

Beclometasone dipropionate, budesonide, ciclesonide and fluticasone propionate have all been shown to be effective in children. There have been relatively fewer studies of ciclesonide in children,[1] but, overall, randomised clinical trials show that it is equally effective as budesonide or fluticasone propionate in improving asthma symptoms and reducing flare-ups.[80] In some studies, ciclesonide was associated with less adrenal suppression or height than comparator inhaled corticosteroids.[80]

In a study of school-aged children with more than 2 days per week with symptoms, night waking more than twice per month due to asthma symptoms, or needing regular preventer, regular low-dose daily inhaled corticosteroid treatment reduced the rate of flare-ups that require treatment with oral corticosteroids, compared with no regular preventer treatment and as-needed short-acting beta$_2$agonist for wheezing episodes.[81]

In a study of children aged 4–11 years with asthma diagnosed within the previous 2 years and symptoms more than weekly in the previous 3 months, regular preventer was associated with a reduction in serious flare-ups, school absence due to asthma, an increase in symptom-free days, and improved lung function, compared with placebo.[82, 83]

The Thoracic Society of Australia and New Zealand's current position statement on the use of inhaled corticosteroids in children[1] recommends regular treatment with inhaled corticosteroid:

- as a first-choice preventer for children with asthma symptoms at least daily or night-time symptoms at least twice per week between flare-ups
- as an alternative to cromones (nedocromil or sodium cromoglycate) or montelukast in children with any daytime or night-time

symptoms between flare-ups, or those with flare-ups every 6 weeks or more.

Doses

In the majority of children, asthma control can be achieved with any of the following initial doses:[1]

- budesonide up to 400 microg/day
- beclometasone (*Qvar*) up to 200 microg/day
- ciclesonide up to 160 microg/day
- fluticasone propionate up to 200 microg/day.

If these doses do not achieve control of symptoms, possible explanations include alternative diagnoses, adherence, incorrect inhaler technique, psychosocial factors and exposure to tobacco smoke or other triggers such as allergens.[1]

Dose–response studies of inhaled corticosteroids show that the maximal efficacy is generally achieved at a dose equivalent to approximately 200 microg/day fluticasone propionate,[1] while the risk of adrenal suppression increases exponentially at doses above 500 microg/day.[1] Therefore (based on theoretical equivalents between different agents), upper limits of daily doses for children are:

- budesonide 800 microg/day
- beclometasone dipropionate [*Qvar*] 400 microg/day
- ciclesonide 320 microg/day
- fluticasone propionate 500 microg/day.

Higher doses are unlikely to be more effective, and are likely to cause systemic effects.[1]

Most studies of inhaled corticosteroids in children have used twice-daily dosing.[1] Fluticasone propionate is only approved for twice-daily dosing, but the other inhaled corticosteroids are approved for once daily dosing. Ciclesonide is effective when given once daily.[1]

Note: Do not use beclometasone dose recommendations from outdated or overseas guidelines based on older formulations containing CFC propellant – doses are different.

Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)	
	Low	**High**
Beclometasone dipropionate †	100–200	>200 (maximum 400)
Budesonide	200–400	>400 (maximum 800)
Ciclesonide ‡	80–160	>160 (maximum 320)
Fluticasone propionate	100–200	>200 (maximum 500)

† Dose equivalents for *Qvar* (TGA-registered CFC-free formulation of beclometasone dipropionate)

‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

Source

van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma.* The Thoracic Society of Australia and New Zealand, 2010. Available from: http://www.thoracic.org.au/clinical-documents/area?command=record&id=14

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Inhaled corticosteroids for children: adverse effects

Local adverse effects

Hoarseness and pharyngeal candidiasis are not commonly reported among preschool children or school-aged children talking inhaled

corticosteroids. [50, 1, 84]

Topical effects can be reduced by use of spacer devices (which reduce oropharyngeal deposition), and by mouth-rinsing and spitting after use.[1] Immediate quick mouth-rinsing removes more residual medicine in the mouth than delayed rinsing.[85]

There is limited evidence that inhaled asthma medication can affect dental health.[1, 86] Mouth rinsing might reduce this risk.

Systemic adverse effects

Systemic effects of inhaled corticosteroids in children depend on the dose, but clinically significant adverse effects are uncommon.[1]

The use of spacers and mouth rinsing will not reduce systemic effects, but the use of a spacer may increase efficacy so that a lower dose is required.

Growth

Short-term suppression of linear growth has been demonstrated in children taking inhaled corticosteroids.[87,88] The effect seems to be maximal during the first year of therapy and only one study has reported an effect in subsequent years of treatment.[88] A Cochrane systematic review concluded that regular use of inhaled corticosteroid at low or medium daily doses is associated with a mean reduction of 0.48 cm per year in linear growth velocity and 0.61 cm less gain in height during 1 year of treatment in children with mild to moderate persistent asthma.[88]

One study of patients who participated in a clinical trial of inhaled corticosteroids as children, reported a reduction in adult height of approximately 1 cm,[87, 89, 90, 91] whereas several studies have reported that children taking inhaled corticosteroids attained normal adult height.[92, 93, 94]

The effect is dose-dependent[90,91] and may be more likely in children who begin inhaled corticosteroid treatment before age 10.[89]

Other factors affect growth in children with asthma. Uncontrolled asthma itself reduces growth and final adult height.[93] One study found that inhaled corticosteroid equivalent to budesonide 400 microg/day affected growth less than low socioeconomic status.[94]

Bone density

Inhaled corticosteroids have not been associated with effects on bone density or fractures in children. [1] However, data from a recent study in Australia suggested asthma itself is associated with increased incidence of fractures in children, independent of medication.[95]

Given that the total dose of corticosteroids (both inhaled corticosteroids and oral corticosteroids) influences bone health, the aim of asthma management is to maintain symptom control using the lowest inhaled corticosteroid dose required, and to avoid repeated courses of oral corticosteroids.

Adrenal suppression

Biochemical testing in a research setting suggests that hypothalamic–pituitary–adrenal axis suppression may occur in up to two-thirds of children treated with inhaled corticosteroids, and may occur at even low doses.[96] The risk is higher among children receiving concomitant intranasal steroids and those with lower body mass index,[96] and is influenced by genetics.[97]

Clinical adrenal insufficiency in children taking inhaled corticosteroids is rare but has been reported, [98, 99, 100] including cases in Australia.[100] Most cases have involved children given more than 500 microg per day fluticasone propionate.[98]

Adrenal suppression is associated with hypoglycaemia, hypotension, weakness, failure to grow, and is potentially fatal. Hypothalamic–pituitary–adrenal axis suppression may not be detected until adrenal crisis is precipitated by physical stress.[101]

Written information (e.g. a steroid alert card) can be prepared for children receiving long-term high-dose inhaled corticosteroids. Parents/carers can be instructed to present the card if the child ever needs to go to the emergency department (for any reason) or be admitted to hospital. A steroid alert card should state that child has asthma and the inhaled corticosteroid dose. A medical alert bracelet could also be considered.

There are no nationally accepted protocols for routine assessment of adrenal function in primary care because it has not yet been possible to identify precisely which children should be tested, to interpret test results reliably, to identify the appropriate interval for retesting, and because a clinical benefit has not been clearly demonstrated.

Regular monitoring of height might help detect adrenal suppression, based on the findings of a study in which a reduction in linear growth velocity occurred before adrenal suppression.[102]

Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)	
	Low	High

Inhaled corticosteroid	Daily dose (microg)	
	Low	**High**
Beclometasone dipropionate †	100–200	>200 (maximum 400)
Budesonide	200–400	>400 (maximum 800)
Ciclesonide ‡	80–160	>160 (maximum 320)
Fluticasone propionate	100–200	>200 (maximum 500)

† Dose equivalents for *Qvar* (TGA-registered CFC-free formulation of beclometasone dipropionate)

‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

Source

van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma*. The Thoracic Society of Australia and New Zealand, 2010. Available from: http://www.thoracic.org.au/clinical-documents/area?command=record&id=14

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Asset ID: 21

▶ Go to: The Thoracic Society of Australia and New Zealand's *Position Statement: The role of corticosteroids in the management of childhood asthma*

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Tiotropium for children aged 6 years and over

Tiotropium (5 microg administered via mist inhaler as two puffs once daily) is approved by TGA for use in children aged 6 years and older with moderate-to-severe asthma.

Tiotropium is subsidised by then PBS for children aged 6–17 years when used in combination with maintenance ICS+LABA treatment, for patients with severe asthma treated by, or in consultation with, a specialist (respiratory physician, paediatric respiratory physician, clinical immunologist, allergist, paediatrician or general physician experienced in severe asthma management), with frequent moderate exacerbations or ≥ one documented severe exacerbation that required systemic corticosteroids in the previous 12 months despite maintenance treatment with a medium-to-high dose of inhaled corticosteroid in combination with a long-acting beta2 agonist, and correct inhaler technique has been assessed, demonstrated and documented (see PBS for details).

▶ Go to: *PBS listings*

Children aged 6–11

A systematic review of three randomised controlled trials reported that, in children aged 6–11 years with moderate-to-severe symptomatic asthma, tiotropium improved lung function, improved symptoms, and reduced the rate of flare-ups.[103] Tiotropium was generally well tolerated.[103]

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Managing cough in children

When cough is the predominant symptom in a young child, careful assessment is needed to avoid making an incorrect diagnosis of asthma, or instigating inappropriate treatment.[104] Cough alone (recurrent non-specific cough) is most likely due to recurrent viral bronchitis, which is unresponsive to both bronchodilators and preventive therapy including inhaled corticosteroids. Recurrent non-specific cough usually resolves by age 6 or 7 years and leaves no residual pulmonary pathology.

If cough is a problem for a child with known asthma, it should be managed according to national *Cough in Children and Adults: Diagnosis and Assessment (CICADA)* guidelines.[104]

- There are significant concerns about use of cough medicines in children.

▶ Go to: *Australian Cough Guidelines*

Go to: *Therapeutic Goods Administration (TGA) recommendations on the use of cough and cold medicines in children*

Last reviewed version 2.0

References

1. van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma*. The Thoracic Society of Australia and New Zealand, 2010. Available from: https://www.thoracic.org.au/journal-publishing/command/download_file/id/25/filename/The_role_of_corticosteroids_in_the_management_of_childhood_asthma_-_2010.pdf
2. Chauhan BF, Ben Salah R, Ducharme FM. Addition of anti-leukotriene agents to inhaled corticosteroids in children with persistent asthma. *Cochrane Database Syst Rev*. 2013; Issue 10: CD009585. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24089325
3. Ciolkowski, J., Mazurek, H., Stasiowska, B.. Evaluation of step-down therapy from an inhaled steroid to montelukast in childhood asthma. *Allergol Immunopathol (Madr)*. 2014; 42: 282-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23684855
4. Nagao M, Ikeda M, Fukuda N, *et al*. Early control treatment with montelukast in preschool children with asthma: a randomized controlled trial. *Allergol Int*. 2018; 67: 72-78. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28526210
5. Nwokoro C, Pandya H, Turner S, *et al*. Intermittent montelukast in children aged 10 months to 5 years with wheeze (WAIT trial): a multicentre, randomised, placebo-controlled trial. *Lancet Respir Med*. 2014; 2: 796-803. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25212745
6. Valovirta, E., Boza, M. L., Robertson, C. F., *et al*. Intermittent or daily montelukast versus placebo for episodic asthma in children. *Ann Allergy Asthma Immunol*. 2011; 106: 518-26. Available from: https://www.ncbi.nlm.nih.gov/pubmed/21624752
7. Pike, K. C., Akhbari, M., Kneale, D., Harris, K. M.. Interventions for autumn exacerbations of asthma in children. *Cochrane Database Syst Rev*. 2018; Issue 3: Cd012393. Available from: http://cochranelibrary-wiley.com/doi/10.1002/14651858.CD012393.pub2/full
8. Ducharme, F. M., Noya, F. J., Allen-Ramey, F. C., *et al*. Clinical effectiveness of inhaled corticosteroids versus montelukast in children with asthma: prescription patterns and patient adherence as key factors. *Curr Med Res Opin*. 2012; 28: 111-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/22077107
9. Garcia Garcia, ML, Wahn, U, Gilles, L, *et al*. Montelukast, compared with fluticasone, for control of asthma among 6- to 14-year-old patients with mild asthma: The MOSAIC Study. *Pediatrics*. 2005; 116: 360-369. Available from: https://www.ncbi.nlm.nih.gov/pubmed/16061590
10. Bukstein, DE, Luskin, AT, Bernstein, A. 'Real-world' effectiveness of daily controller medicine in children with mild persistent asthma. *Ann Allergy Asthma Immunol*. 2003; 90: 543-549. Available from: https://www.ncbi.nlm.nih.gov/pubmed/12775136
11. Sorkness, CA, Lemanske, RF, Mauger, DT, *et al*. Long-term comparison of 3 controller regimens for mild-moderate persistent childhood asthma: The Pediatric Asthma Controller Trial. *J Allergy Clin Immunol*. 2007; 119: 64-72. Available from: https://www.ncbi.nlm.nih.gov/pubmed/17140647
12. Zeiger, RS, Szefler, SJ, Phillips, BR, *et al*. Response profiles to fluticasone and montelukast in mild-to-moderate persistent childhood asthma. *J Allergy Clin Immunol*. 2006; 117: 45-52. Available from: https://www.ncbi.nlm.nih.gov/pubmed/16387583
13. Ostrom, NK, Decotiis, BA, Lincourt, WR, *et al*. Comparative efficacy and safety of low-dose fluticasone propionate and montelukast in children with persistent asthma. *J Pediatr*. 2005; 147: 213-220. Available from: https://www.ncbi.nlm.nih.gov/pubmed/16126052
14. Zeiger, RS, Szefler, SJ, Phillips, BR, *et al*. Response profiles to fluticasone and montelukast in mild-to-moderate persistent childhood asthma. *J Allergy Clin Immunol*. 2006; 117: 45-52.
15. Grzelewski, T, Stelmach, I. Exercise-induced bronchoconstriction in asthmatic children: a comparative systematic review of the available treatment options. *Drugs*. 2009; 69: 1533-1553. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19678711
16. Stelmach I, Grzelewski T, Majak P, *et al*. Effect of different antiasthmatic treatments on exercise-induced bronchoconstriction in children with asthma. *J Allergy Clin Immunol*. 2008; 121: 383-389. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17980416
17. Sorkness, CA, Lemanske, RF, Mauger, DT, *et al*. Long-term comparison of 3 controller regimens for mild-moderate persistent childhood asthma: The Pediatric Asthma Controller Trial. *J Allergy Clin Immunol*. 2007; 119: 64-72. Available from: https://www.ncbi.nlm.nih.gov/pubmed/17140647
18. Stelmach, I., Grzelewski, T., Majak, P., *et al*. Effect of different antiasthmatic treatments on exercise-induced bronchoconstriction in children with asthma. *J Allergy Clin Immunol*. 2008; 121: 383-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/17980416
19. Knorr, B, Matz, J, Bernstein, JA, *et al*. Montelukast for chronic asthma in 6- to 14-year-old children: a randomized, double-blind trial. Pediatric Montelukast Study Group. *JAMA*. 1998; 279: 1181-1186. Available from: https://www.ncbi.nlm.nih.gov/pubmed/9555757
20. Becker, A, Swern, A, Tozzi, C A, *et al*. Montelukast in asthmatic patients 6 years-14 years old with an FEV1 > 75%. *Curr Med Res Opin*. 2004; 20: 1651-1659. Available from: https://www.ncbi.nlm.nih.gov/pubmed/15462699
21. Benard, B., Bastien, V., Vinet, B., *et al*. Neuropsychiatric adverse drug reactions in children initiated on montelukast in real-life practice. *Eur Respir J*. 2017; 50: . Available from: https://www.ncbi.nlm.nih.gov/pubmed/28818882
22. Aldea Perona, A., Garcia-Saiz, M., Sanz Alvarez, E.. Psychiatric disorders and montelukast in children: a disproportionality analysis of the VigiBase®. *Drug Saf*. 2016; 39: 69-78. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26620206
23. Wallerstedt, S. M., Brunlof, G., Sundstrom, A., Eriksson, A. L.. Montelukast and psychiatric disorders in children. *Pharmacoepidemiol Drug Saf*. 2009; 18: 858-64. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19551697
24. Philip, G, Hustad, C, Noonan, G, *et al*. Reports of suicidality in clinical trials of montelukast. *J Allergy Clin Immunol*. 2009; 124: 691-696. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19815114

25. Philip, G., Hustad, C. M., Malice, M. P., *et al*. Analysis of behavior-related adverse experiences in clinical trials of montelukast. *J Allergy Clin Immunol*. 2009; 124: 699-706. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19815116
26. Ali, M. M., O'Brien, C. E., Cleves, M. A., Martin, B. C.. Exploring the possible association between montelukast and neuropsychiatric events among children with asthma: a matched nested case-control study. *Pharmacoepidemiol Drug Saf*. 2015; 24: 435-45. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25683909
27. Therapeutic Goods Administration,. Montelukast – neuropsychiatric risks. *Aust Prescr*. 2013; 36: 168-171. Available from: https://www.nps.org.au/australian-prescriber/articles/medicines-safety-update-2-58#article
28. Schumock, G T, Stayner, L T, Valuck, R J, *et al*. Risk of suicide attempt in asthmatic children and young adults prescribed leukotriene-modifying agents: a nested case-control study. *J Allergy Clin Immunol*. 2012; 130: 368-375. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22698520
29. McDonald N, Bara A, McKean MC. Anticholinergic therapy for chronic asthma in children over two years of age. *Cochrane Database Syst Rev*. 2003; Issue 1: CD003535. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003535/full
30. Walters EH, Walters JA, Gibson PG, Jones P. Inhaled short acting beta2-agonist use in chronic asthma: regular versus as needed treatment. *Cochrane Database Syst Rev*. 2003; Issue 1: CD001285. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001285/full
31. Global Initiative for Asthma (GINA). *Global strategy for asthma management and prevention*. GINA, 2012. Available from: http://www.ginasthma.org
32. British Thoracic Society (BTS) Scottish Intercollegiate Guidelines Network (SIGN). *British Guideline on the Management of Asthma. Quick Reference Guide*. Revised May 2011. BTS, SIGN, Edinburgh, 2008.
33. Stanford, R. H., Shah, M. B., D'Souza, A. O., *et al*. Short-acting beta-agonist use and its ability to predict future asthma-related outcomes. *Ann Allergy Asthma Immunol*. 2012; 109: 403-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23176877
34. Gillette, C., Rockich-Winston, N., Kuhn, J. A., *et al*. Inhaler technique in children with asthma: a systematic review. *Acad Pediatr*. 2016; 16: 605-15. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27130811
35. Capanoglu, M., Dibek Misirlioglu, E., Toyran, M., *et al*. Evaluation of inhaler technique, adherence to therapy and their effect on disease control among children with asthma using metered dose or dry powder inhalers. *J Asthma*. 2015; 52: 838-45. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26037396
36. Ram, F S F, Brocklebank, D D M, White, J, *et al*. Pressurised metered dose inhalers versus all other hand-held inhaler devices to deliver beta-2 agonist bronchodilators for non-acute asthma. *Cochrane Database Syst Rev*. 2002; Issue 2: .
37. Nikander, K, Turpeinen, M, Pelkonen, A S, *et al*. True adherence with the Turbuhaler in young children with asthma. *Arch Dis Child*. 2011; 96: 168-173.
38. Pedersen, S., Mortensen, S.. Use of different inhalation devices in children. *Lung*. 1990; 168 Suppl: 653-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/2117175
39. Sleath, B, Ayala, G X, Gillette, C, *et al*. Provider demonstration and assessment of child device technique during pediatric asthma visits. *Pediatrics*. 2011; 127: 642-648.
40. The Inhaler Error Steering Committee,, Price, D., Bosnic-Anticevich, S., *et al*. Inhaler competence in asthma: common errors, barriers to use and recommended solutions. *Respir Med*. 2013; 107: 37-46. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23098685
41. Bjermer, L.. The importance of continuity in inhaler device choice for asthma and chronic obstructive pulmonary disease. *Respiration; international review of thoracic diseases*. 2014; 88: 346-52. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25195762
42. Basheti, I A, Armour, C L, Bosnic-Anticevich, S Z, Reddel, H K. Evaluation of a novel educational strategy, including inhaler-based reminder labels, to improve asthma inhaler technique. *Patient Educ Couns*. 2008; 72: 26-33. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18314294
43. Bosnic-Anticevich, S. Z., Sinha, H., So, S., Reddel, H. K.. Metered-dose inhaler technique: the effect of two educational interventions delivered in community pharmacy over time. *The Journal of asthma : official journal of the Association for the Care of Asthma*. 2010; 47: 251-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20394511
44. Melani AS, Bonavia M, Cilenti V, *et al*. Inhaler mishandling remains common in real life and is associated with reduced disease control. *Respir Med*. 2011; 105: 930-8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21367593
45. Levy ML, Dekhuijzen PN, Barnes PJ, *et al*. Inhaler technique: facts and fantasies. A view from the Aerosol Drug Management Improvement Team (ADMIT). *NPJ Prim Care Respir Med*. 2016; 26: 16017. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27098045
46. Haughney, J., Price, D., Barnes, N. C., *et al*. Choosing inhaler devices for people with asthma: current knowledge and outstanding research needs. *Respiratory medicine*. 2010; 104: 1237-45. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20472415
47. Giraud, V., Roche, N.. Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability. *The European respiratory journal*. 2002; 19: 246-51. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11866004
48. Harnett, C. M., Hunt, E. B., Bowen, B. R., *et al*. A study to assess inhaler technique and its potential impact on asthma control in patients attending an asthma clinic. *J Asthma*. 2014; 51: 440-5.
49. Hardwell, A., Barber, V., Hargadon, T., *et al*. Technique training does not improve the ability of most patients to use pressurised metered-dose inhalers (pMDIs). *Prim Care Respir J*. 2011; 20: 92-6. Available from: http://www.nature.com/articles/pcrj201088
50. Brand PL, Baraldi E, Bisgaard H, *et al*. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. *Eur Respir J*. 2008; 32: 1096-1110. Available from: http://erj.ersjournals.com/content/32/4/1096.full
51. Berg E. In vitro properties of pressurized metered dose inhalers with and without spacer devices. *J Aerosol Med*. 1995; 8 Suppl 3: S3-10; discussion S11. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10157897
52. Dompeling E, Oudesluys-Murphy AM, Janssens HM, *et al*. Randomised controlled study of clinical efficacy of spacer therapy in

asthma with regard to electrostatic charge. *Arch Dis Child*. 2001; 84: 178-182. Available from: http://adc.bmj.com/content/84/2/178.full
53. Merck, Sharp and Dohme Australia Pty Ltd. *Product Information: Singulair (montelukast sodium) Tablets*. Therapeutic Goods Administration, Canberra, 2013. Available from: https://www.ebs.tga.gov.au/
54. Bush A. Montelukast in paediatric asthma: where we are now and what still needs to be done? *Paediatr Respir Rev*. 2015; 16: 97-100. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25499571
55. Lipworth BJ, Basu K, Donald HP, *et al*. Tailored second-line therapy in asthmatic children with the Arg(16) genotype. *Clin Sci (Lond)*. 2013; 124: 521-528. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23126384
56. Brodlie M, Gupta A, Rodriguez-Martinez CE, *et al*. Leukotriene receptor antagonists as maintenance and intermittent therapy for episodic viral wheeze in children. *Cochrane Database Syst Rev*. 2015; Issue 10: CD008202. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26482324
57. Bisgaard H, Zielen S, Garcia-Garcia ML, *et al*. Montelukast reduces asthma exacerbations in 2- to 5-year-old children with intermittent asthma. *Am J Respir Crit Care Med*. 2005; 171: 315-322. Available from: http://ajrccm.atsjournals.org/content/171/4/315.long
58. Castro-Rodriguez JA, Rodriguez-Martinez CE, Ducharme FM. Daily inhaled corticosteroids or montelukast for preschoolers with asthma or recurrent wheezing: A systematic review. *Pediatr Pulmonol*. 2018; Epub ahead of print 6 November. Available from: https://www.ncbi.nlm.nih.gov/pubmed/30394700
59. Fitzpatrick AM, Jackson DJ, Mauger DT et al. Individualized therapy for persistent asthma in young children. *J Allergy Clin Immunol*. 2016; 138: 1608-18.e12. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27777180
60. Jartti T. Inhaled corticosteroids or montelukast as the preferred primary long-term treatment for pediatric asthma? *Eur J Pediatr*. 2008; 167: 731-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/18214538
61. Maspero, J, Guerra, F, Cuevas, F, *et al*. Efficacy and tolerability of salmeterol/fluticasone propionate versus montelukast in childhood asthma: a prospective, randomized, double-blind, double-dummy, parallel-group study. *Clin Ther*. 2008; 30: 1492-1504.
62. Pedersen S, Maspero J, Gul N, Sharma R. Components of asthma control and treatment response of individual control criteria in children: analysis of the PEACE study. *Pediatr Pulmonol*. 2011; 46: 1182-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/21751432
63. Malka J, Mauger DT, Covar R, *et al*. Eczema and race as combined determinants for differential response to step-up asthma therapy. *J Allergy Clin Immunol*. 2014; 134: 483-5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24835502
64. Stelmach I, Ozarek-Hanc A, Zaczeniuk M et al. Do children with stable asthma benefit from addition of montelukast to inhaled corticosteroids: randomized, placebo controlled trial. *Pulm Pharmacol Ther*. 2015; 31: 42-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25640020
65. Fogel RB, Rosario N, Aristizabal G, *et al*. Effect of montelukast or salmeterol added to inhaled fluticasone on exercise-induced bronchoconstriction in children. *Ann Allergy Asthma Immunol*. 2010; 104: 511-517. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20568384
66. Robertson CF, Price D, Henry R, *et al*. Short-course montelukast for intermittent asthma in children: a randomized controlled trial. *Am J Respir Crit Care Med*. 2007; 175: 323-329. Available from: http://ajrccm.atsjournals.org/content/175/4/323.long
67. Watts, K, Chavasse, R J P G. Leukotriene receptor antagonists in addition to usual care for acute asthma in adults and children. *Cochrane Database Syst Rev*. 2012; Issue 5: . Available from: http://cochranelibrary-wiley.com/doi/10.1002/14651858.CD006100.pub2/full
68. Capsomidis, A., Tighe, M.. Archimedes. Question 2. Is oral montelukast beneficial in treating acute asthma exacerbations in children?. *Arch Dis Child*. 2010; 95: 948-50. Available from: http://adc.bmj.com/content/95/11/948.long
69. Schuh, S, Willan, AR, Stephens, D, *et al*. Can montelukast shorten prednisolone therapy in children with mild to moderate acute asthma? A randomized controlled trial. *J Pediatr*. 2009; 155: 795-800. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19656525
70. Bacharier LB, Phillips BR, Zeiger RS, *et al*. Episodic use of an inhaled corticosteroid or leukotriene receptor antagonist in preschool children with moderate-to-severe intermittent wheezing. *J Allergy Clin Immunol*. 2008; 122: 1127-1135. Available from: https://www.ncbi.nlm.nih.gov/pubmed/18973936
71. Philip G, Hustad C, Noonan G, *et al*. Reports of suicidality in clinical trials of montelukast. *J Allergy Clin Immunol*. 2009; 124: 691-6.e6. Available from: http://www.jacionline.org/article/S0091-6749(09)01247-0/fulltext
72. Philip G, Hustad CM, Malice MP, *et al*. Analysis of behavior-related adverse experiences in clinical trials of montelukast. *J Allergy Clin Immunol*. 2009; 124: 699-706.e8. Available from: http://www.jacionline.org/article/S0091-6749(09)01248-2/fulltext
73. Haarman M, van Hunsel F, de Vries T. Adverse drug reactions of montelukast in children and adults. *Pharmacol Res Perspect* 2017; 5: e00341. Available from: http://onlinelibrary.wiley.com/doi/10.1002/prp2.341/full
74. Robertson, CF, Price, D, Henry, R, *et al*. Short-course montelukast for intermittent asthma in children: a randomized controlled trial. *Am J Respir Crit Care Med*. 2007; 175: 323-329. Available from: https://www.ncbi.nlm.nih.gov/pubmed/17110643
75. Schumock GT, Stayner LT, Valuck RJ, *et al*. Risk of suicide attempt in asthmatic children and young adults prescribed leukotriene-modifying agents: a nested case-control study. *J Allergy Clin Immunol*. 2012; 130: 368-75. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22698520
76. Ducharme FM, Krajinovic M. Steroid responsiveness and wheezing phenotypes. *Paediatr Respir Rev*. 2011; 12: 170-176. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21722845
77. Chong J, Haran C, Chauhan BF, Asher I. Intermittent inhaled corticosteroid therapy versus placebo for persistent asthma in children and adults. *Cochrane Database Syst Rev*. 2015; : Cd011032. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26197430
78. McKean MC, Ducharme F. Inhaled steroids for episodic viral wheeze of childhood. *Cochrane Database Syst Rev*. 2000; 2: CD001107.

Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001107/full
79. Castro-Rodriguez JA, Rodrigo GJ. Efficacy of inhaled corticosteroids in infants and preschoolers with recurrent wheezing and asthma: A systematic review with meta-analysis. *Pediatrics*. 2009; 123: e519-e525. Available from: http://pediatrics.aappublications.org/content/123/3/e519.full
80. Kramer S, Rottier BL, Scholten RJ, Boluyt N. Ciclesonide versus other inhaled corticosteroids for chronic asthma in children. *Cochrane Database Syst Rev*. 2013; Issue 2: CD010352. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010352/full
81. Martinez FD, Chinchilli VM, Morgan WJ, *et al*. Use of beclomethasone dipropionate as rescue treatment for children with mild persistent asthma (TREXA): a randomised, double-blind, placebo-controlled trial. *Lancet*. 2011; 377: 650-7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21324520
82. Weiss K, Buxton M, Andersson FL et al. Cost-effectiveness of early intervention with once-daily budesonide in children with mild persistent asthma: results from the START study. *Pediatr Allergy Immunol* 2006; 17 Suppl 17: 21-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/16573705
83. Chen YZ, Busse WW, Pedersen S et al. Early intervention of recent onset mild persistent asthma in children aged under 11 yrs: the Steroid Treatment As Regular Therapy in early asthma (START) trial. *Pediatr Allergy Immunol* 2006; 17 Suppl 17: 7-13. Available from: https://www.ncbi.nlm.nih.gov/pubmed/16573703
84. Cazeiro C, Silva C, Mayer S et al. Inhaled corticosteroids and respiratory infections in children with asthma: a meta-analysis. *Pediatrics*. 2017; 139. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28235797
85. Yokoyama H, Yamamura Y, Ozeki T, *et al*. Effects of mouth washing procedures on removal of budesonide inhaled by using Turbuhaler. *Yakugaku Zasshi*. 2007; 127: 1245-1249. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17666876
86. Godara N, Godara R, Khullar M. Impact of inhalation therapy on oral health. *Lung India*. 2011; 28: 272-5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/22084541
87. Loke YK, Blanco P, Thavarajah M, Wilson AM. Impact of inhaled corticosteroids on growth in children with asthma: systematic review and meta-analysis. *PloS One*. 2015; 10: e0133428. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26191797
88. Zhang L, Prietsch SO, Ducharme FM. Inhaled corticosteroids in children with persistent asthma: effects on growth. *Cochrane Database Syst Rev*. 2014: Cd009471. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25030198
89. Kelly HW, Sternberg AL, Lescher R, *et al*. Effect of inhaled glucocorticoids in childhood on adult height. *N Engl J Med*. 2012; 367: 904-12. Available from: http://www.nejm.org/doi/full/10.1056/NEJMoa1203229
90. Pruteanu AI, Chauhan BF, Zhang L et al. Inhaled corticosteroids in children with persistent asthma: dose-response effects on growth. *Cochrane Database Syst Rev*. 2014: Cd009878. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25030199
91. De Leonibus C, Attanasi M, Roze Z et al. Influence of inhaled corticosteroids on pubertal growth and final height in asthmatic children. *Pediatr Allergy Immunol*. 2016; 27: 499-506. Available from:https://www.ncbi.nlm.nih.gov/pubmed/26919136
92. Pauwels RA, Pedersen S, Busse WW, *et al*. Early intervention with budesonide in mild persistent asthma: a randomised, double-blind trial. *Lancet*. 2003; 361: 1071-1076. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12672309
93. Pedersen S. Do inhaled corticosteroids inhibit growth in children? *Am J Respir Crit Care Med*. 2001; 164: 521-35. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11520710
94. Agertoft L, Pedersen S. Effect of long-term treatment with inhaled budesonide on adult height in children with asthma. *N Engl J Med*. 2000; 343: 1064-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11027740
95. Degabriele EL, Holloway KL, Pasco JA et al. Associations between asthma status and radiologically confirmed fracture in children: A data-linkage study. *J Paediatr Child Health*. 2018; 54(8): 855-860. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29614205
96. Zöllner EW, Lombard CJ, Galal U, *et al*. Hypothalamic-adrenal-pituitary axis suppression in asthmatic school children. *Pediatrics*. 2012; 130: e1512-19. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23147980
97. Hawcutt DB, Francis B, Carr DF et al. Susceptibility to corticosteroid-induced adrenal suppression: a genome-wide association study. *Lancet Respir Med*. 2018; 6:442-450. Available from: https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(18)30058-4/fulltext
98. Ahmet A, Kim H, Spier S. Adrenal suppression: A practical guide to the screening and management of this under-recognized complication of inhaled corticosteroid therapy. *Allergy Asthma Clin Immunol*. 2011; 7: 13. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3177893/
99. Priftis, K N, Papadimitriou, A, Anthracopoulos, M B, Fretzayas, A, Chrousos, G P. Endocrine-immune interactions in adrenal function of asthmatic children on inhaled corticosteroids. *Neuroimmunomodulation* 2008; 16: 333-339.
100. Macdessi JS, Randell TL, Donaghue KC, *et al*. Adrenal crises in children treated with high-dose inhaled corticosteroids for asthma. *Med J Aust*. 2003; 178: 214-6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12603184
101. Rao Bondugulapati LN, Rees DA. Inhaled corticosteroids and HPA axis suppression: how important is it and how should it be managed? *Clin Endocrinol (Oxf)*. 2016; 85: 165-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27038017
102. Liddell BS, Oberlin JM, Hsu DP. Inhaled corticosteroid related adrenal suppression detected by poor growth and reversed with ciclesonide. *J Asthma*. 2017; 54: 99-104. Available from:https://www.ncbi.nlm.nih.gov/pubmed/27284755
103. Rodrigo GJ, Neffen H. Efficacy and safety of tiotropium in school-age children with moderate-to-severe symptomatic asthma: A systematic review. *Pediatr Allergy Immunol* 2017; 28: 573-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28692145
104. Gibson PG, Chang AB, Glasgow NJ, *et al*. CICADA: cough in children and adults: diagnosis and assessment. Australian cough guidelines summary statement. *Med J Aust*. 2010; 192: 265-271. Available from: https://www.mja.com.au/journal/2010/192/5/cicada-cough-children-and-adults-diagnosis-and-assessment-australian-cough

Reviewing initial treatment in children aged 6 years and over

Recommendations

When prescribing any preventer medicine for a child, consider each adjustment to the regimen as a treatment trial: monitor response continually, review within 4–6 weeks (or earlier as needed in response to parents' concerns), and adjust treatment according to response.

Table. Reviewing and adjusting preventer treatment for children aged 6–11 years

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/26

Figure. Stepped approach to adjusting asthma medication in children aged 6-11 years

Please view and print this figure separately: http://www.asthmahandbook.org.au/figure/show/120

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

If good asthma symptom control has not been achieved by an initial low dose of inhaled corticosteroids, do not increase the dose or change the regimen until you have (all of):

- **checked adherence to the inhaled corticosteroid**
- **checked the child's inhaler technique**
- **assessed exposure to environmental triggers (e.g. allergens, cigarette smoke)**
- **reviewed the diagnosis (consider whether symptoms may be due to a comorbidity or alternative diagnosis such as rhinosinusitis, de-conditioning, obesity or upper airway dysfunction).**

Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)	
	Low	High
Beclometasone dipropionate †	100–200	>200 (maximum 400)
Budesonide	200–400	>400 (maximum 800)
Ciclesonide ‡	80–160	>160 (maximum 320)
Fluticasone propionate	100–200	>200 (maximum 500)

† Dose equivalents for *Qvar* **(TGA-registered CFC-free formulation of beclometasone dipropionate)**

‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

Source

van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma*. **The Thoracic Society of Australia and New Zealand, 2010. Available from:**
http://www.thoracic.org.au/clinical-documents/area?command=record&id=14

Last reviewed version 2.0

Asset ID: 21

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- van Asperen et al. 2010[1]

Last reviewed version 2.0

If asthma is not well controlled by regular low-dose inhaled corticosteroid treatment (and adherence is good, inhaler technique is correct and diagnosis has been confirmed), consider one of the following options:

- **Increase the inhaled corticosteroid dose.**
- **Continue low-dose inhaled corticosteroid and add montelukast.**
- **Switch to an inhaled corticosteroid/long-acting beta$_2$ agonist combination at low dose.**

Note: TGA-registered indications for inhaled corticosteroid/long-acting beta2 agonist combinations differ between products.

- **Advise parents/carers about potential adverse psychiatric effects of montelukast.**
- **Go to: TGA alert**

Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)	
	Low	High
Beclometasone dipropionate †	100–200	>200 (maximum 400)
Budesonide	200–400	>400 (maximum 800)
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Fluticasone propionate	100–200	>200 (maximum 500)

† Dose equivalents for *Qvar* (TGA-registered CFC-free formulation of beclometasone dipropionate)

‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

Source

van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma*. **The Thoracic Society of Australia and New Zealand, 2010. Available from:**
http://www.thoracic.org.au/clinical-documents/area?command=record&id=14

Last reviewed version 2.0

Asset ID: 21

How this recommendation was developed

Consensus recommendation following inconclusive literature search

Based on clinical experience and expert opinion after literature review yielded insufficient evidence for an evidence-based recommendation

Key evidence considered:

- Stempel et al. 2016[2]
- Chang et al. 2014[3]
- Malka et al. 2014[4]
- Rabinovitch et al. 2014[5]
- van Asperen et al. 2010[1]
- Lemanske et al. 2010[6]
- Papadopoulos et al. 2009[7]

Last reviewed version 2.0

In children taking regular inhaled corticosteroid treatment, the dose of inhaled corticosteroid should be adjusted to the lowest dose needed to maintain control.

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- van Asperen et al. 2010[1]

Last reviewed version 2.0

Long-acting beta$_2$ agonists for children must not be prescribed in a separate inhaler, but only as a fixed-dose combination with an inhaled corticosteroids.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

When reviewing treatment for a child taking a combination of inhaled corticosteroid and long acting beta$_2$ agonist, ask parents/carers whether symptoms of wheeze or breathlessness resolve rapidly when the child is given short-acting beta$_2$ agonist reliever.

If you suspect reduced response to short-acting beta$_2$ agonist in a child treated with combination inhaled corticosteroid and long-acting beta$_2$ agonist, consider obtaining a specialist opinion.

How this recommendation was developed

Consensus recommendation following inconclusive literature search

Based on clinical experience and expert opinion after literature review yielded insufficient evidence for an evidence-based recommendation

Key evidence considered:

- Carroll et al. 2010[8]
- Fogel et al. 2010[9]
- Adler et al. 2006[10]
- PBS 2017[11]

Last reviewed version 2.0

In children with persistent exercise-induced respiratory symptoms despite regular treatment with inhaled corticosteroids, consider adding montelukast (children 6–14 years).

Advise parents/carers that not all children experience asthma improvement with montelukast.

Review response within 4–6 weeks and discontinue if no response.

- **Advise parents/carers about potential adverse psychiatric effects of montelukast**

▶ **Go to: TGA alert**

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- van Asperen et al. 2010[1]
- Fogel et al. 2010[9]
- Grzelewski et al. 2009[12]

Last reviewed version 2.0

If treatment-related behavioural and/or neuropsychiatric symptoms are suspected in a child taking montelukast, discontinue treatment and advise parents/carers to monitor and treat asthma symptoms while off treatment.

If unsure whether a change in behaviour could be due to medication, consider stopping for a short time (e.g. 1 week or more) and re-starting to monitor effects.

▶ **Go to: TGA alert**

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

If parents/carers report behavioural changes possibly related to treatment in a child taking regular inhaled corticosteroids, consider reducing the dose, changing to a different corticosteroid and monitoring effect, or trialling a different preventer.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

More information

Approaches to assessment and monitoring of asthma control in children

Assessment of asthma control in children is based mainly on:

- recent asthma symptom control (assessed by the frequency and severity of symptoms between flare-ups
- the degree to which asthma symptoms affect daily activities such as interference with physical activity or missed school days)
- the frequency of flare-ups
- spirometry in children who are able to perform the test reliably.

Standardised questionnaires

Questionnaire-based instruments have been validated for assessing asthma control in children:

▶ *Test for Respiratory and Asthma Control in Kids (TRACK)* for children less than 5 years old – consists of five questions about frequency of respiratory symptoms (wheeze, cough, shortness of breath), activity limitation, and night-time awakenings in the past 4 weeks, rescue medication use in the past 3 months, and oral corticosteroid use in the previous year.[13, 14] A lower score indicates worse asthma control.

Childhood Asthma Control Test (C-ACT) for children aged 4–11 years – consists of seven items: three for the parent/carer (about the

child's symptoms over the previous 4 weeks) and four for the child.[15, 16] A lower score indicates worse asthma control. **Note:** C-ACT is intended for US use.

Lung function tests

Frequent spirometry to guide asthma treatment in children has not been shown to achieve superior outcomes to symptom-based treatment.[17] Current evidence does not support use of home spirometers to guide asthma treatment in children.[18] However, low FEV_1 predicts clinically significant flare-ups, so spirometry should be performed at asthma reviews for children who are old enough to do the test.
The quality and utility of spirometry depends on the skill, clinical expertise and experience of the person doing and interpreting spirometry.

The results of one study in children aged 6–16 years with moderate atopic asthma suggest that asthma treatment guided by airway hyperresponsiveness (measured by bronchial provocation testing) may have a benefit over symptom-guided treatment in improving lung, but this effect was lost after 3–7 years of usual care.[19, 20] Repeated bronchial provocation testing is not feasible in clinical practice.

Measures of airway inflammation

Measures of airway inflammation (e.g. sputum eosinophil count, exhaled nitric oxide measurement) are not recommended in primary care to guide treatment decisions, but are increasingly used in specialist clinics.

Asthma treatment guided by sputum eosinophil count has been shown to reduce the frequency of flare-ups in adults with asthma, but there is insufficient evidence to ascertain its value for children.[21]

Exhaled nitric oxide measurement may be useful in guiding asthma management in some children. In children not taking inhaled corticosteroid, a high nitric oxide level probably predicts a good short-term response to inhaled corticosteroid treatment,[22] but it does not distinguish between asthma and eosinophilic bronchitis and is often high in children with atopy. There is insufficient evidence to ascertain whether a low exhaled nitric oxide level predicts successful withdrawal from inhaled corticosteroids without asthma relapse,[22] or safety of treating asthma without inhaled corticosteroids.

A Cochrane review[23] found that exhaled nitric oxide-guided management was significantly better than other approaches to adjusting medicines for reducing the number of children with flare-ups and the number of children who needed oral corticosteroids, but did not reduce the frequency of flare-ups or the rate of flare-ups requiring hospitalisation, improve lung function or symptoms scores, or reduce inhaled corticosteroid doses. The authors concluded that it could not be recommended for all children but may be beneficial for a subset not yet defined.[23]

Towards personalised asthma care

Emerging understanding of asthma phenotypes and of genetic factors that predict therapeutic response to preventer options is leading to the possibility of personalised, genomics-based treatment for asthma in children.[24] In the near future, individual tailored therapy is may replace the standardised step model based on population data.

Last reviewed version 2.0

Classification of recent asthma symptom control in children

Ongoing review of asthma involves both assessing recent asthma symptom control and assessing risks for poor asthma outcomes such as flare-ups and adverse effects of medicines.

Recent asthma symptom control is assessed according to the frequency of asthma symptoms over the previous 4 weeks.

Table. Definition of levels of recent asthma symptom control in children (regardless of current treatment regimen)

Good control	Partial control	Poor control
All of: • Daytime symptoms† ≤2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • No limitation of activities‡ • No symptoms§ during night or	Any of: • Daytime symptoms† >2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • Any limitation of activities* • Any symptoms during night or	Either of: • Daytime symptoms† >2 days per week (lasting from minutes to hours or recurring, and partially or fully relieved by SABA reliever) • ≥3 features of partial control within the same week

Good control	Partial control	Poor control
when wakes up • Need for SABA reliever[#] ≤2 days per week	when wakes up[††] • Need for SABA reliever[#] >2 days per week	

SABA: short-acting $beta_2$ agonist

† e.g. wheezing or breathing problems

‡ child is fully active; runs and plays without symptoms

§ including no coughing during sleep

not including doses taken prophylactically before exercise. (Record this separately and take into account when assessing management.)

* e.g. wheeze or breathlessness during exercise, vigorous play or laughing

†† e.g. waking with symptoms of wheezing or breathing problems

Notes:

Recent asthma control is based on symptoms over the previous 4 weeks. Each child's risk factors for future asthma outcomes should also be assessed and taken into account in management.

Validated questionnaires can be used for assessing recent symptom control:
Test for Respiratory and Asthma Control in Kids (TRACK) for children < 5 years
Childhood Asthma Control Test (C-ACT) for children aged 4–11 years

Last reviewed version 2.0

Asset ID: 23

Table. Risk factors for life-threatening asthma flare-ups in children

Asthma-related factors

Poor asthma control

Admission to hospital in preceding 12 months

History of intubation for acute asthma

Over-use of short-acting $beta_2$ agonist reliever

Abnormal spirometry findings

Reversible expiratory airflow limitation on spirometry despite treatment

Poor adherence to preventer

Incorrect inhaler technique for preventer

Poor adherence to asthma action plan

Exposure to clinically relevant allergens

Exposure to tobacco smoke

Other clinical factors

Allergies to foods, insects, medicines

Obesity

Family-related factors

Frequent failure to attend consultations/lack of follow-up after an acute flare-up

Significant parental psychological or socioeconomic problems

Parent/carer unequipped to manage asthma emergency

Last reviewed version 2.0

Asset ID: 116

Last reviewed version 2.0

Montelukast for children: efficacy

- Montelukast use has been associated with behavioural and/or neuropsychiatric adverse effects, including suicidality.

▶ Go to: TGA alert

Overview

Montelukast is a leukotriene receptor antagonist preventer. It is registered by the TGA for the treatment of asthma in children aged 2 years and older, and for the symptomatic treatment of allergic rhinitis.[25]

Montelukast can be used as an alternative to inhaled corticosteroids or as an add-on treatment in a child already taking regular inhaled corticosteroids.

However, it is not effective for all children. Overall, only approximately 20–30% of children will respond to montelukast treatment. The effect is thought to depend mainly on the child's genotype.[26, 27, 28] Clinically, it is not possible to predict accurately which children will benefit most from montelukast treatment.

Montelukast as first-line preventer in children aged 2–5 years

Viral-induced wheezing

Overall, regular maintenance montelukast treatment does not reduce the risk of wheezing episodes requiring oral corticosteroid treatment among preschool children who only have wheezing episodes when they have viral upper respiratory tract infections.[29]

However, montelukast may be effective for some children. Some randomised controlled trials have reported a reduction the risk of flare-ups in preschool children with intermittent asthma/wheeze,[30, 31] while others have not.[32]

Persistent asthma or wheezing

A systematic review comparing montelukast with inhaled corticosteroids in preschoolers with asthma or recurrent wheezing requiring daily preventer treatment[33] reported that inhaled corticosteroids appeared to achieve better symptom control and reduce flare-ups (including severe flare-ups requiring treatment with systemic corticosteroids). However, results were inconsistent and meta-analysis was not possible due to heterogeneity of outcomes measured in available clinical trials.[33]

Some preschool children with persistent asthma/wheeze respond to montelukast. A crossover study in preschool children with persistent asthma/wheeze reported that some children showed their best response to montelukast, while most responded better to regular inhaled corticosteroids.[34] Predictors of a better response to inhaled corticosteroids than montelukast were aeroallergen hypersensitivity and blood eosinophilia (eosinophil counts ≥ 300/μL).[34] However, routine blood eosinophil count is not feasible or recommended for this purpose.

Montelukast as first-line preventer children aged 6 years and over

In school-aged children with persistent asthma, inhaled corticosteroids are more effective overall than montelukast in improving lung function and controlling asthma symptoms.[35, 37]

However, symptoms will respond to a treatment trial of montelukast in approximately one-quarter to one-third of children,[35, 38,39] and some may benefit more than from an inhaled corticosteroid.[35] More severe asthma and markers of allergic inflammation may predict a better response to inhaled corticosteroids.[35]

Montelukast as add-on treatment

A systematic review of studies in children over 6 years and adolescents with mild-to-moderate persistent asthma found that the addition of montelukast to inhaled corticosteroids did reduce flare-ups requiring oral corticosteroids or hospital admissions for asthma, compared with the same or an increased dose.[37]

In a study comparing step-up treatments in children with asthma symptoms uncontrolled by low-dose inhaled corticosteroids, the addition of a long-acting beta$_2$ agonist was effective in more children than either montelukast or increasing the dose of inhaled corticosteroid for controlling asthma symptoms and preventing flare-ups requiring systemic corticosteroids.[4] However, some studies in school-aged children with persistent asthma already taking regular inhaled corticosteroids have reported that add-on montelukast reduced the risk of flare-ups[4, 40] and exercise-induced asthma symptoms.[40] Not all children will respond.

In a small study in children with persistent asthma already taking regular inhaled corticosteroids who were homozygous for the Arg16 genotype, montelukast was more effective as an add-on therapy than long-acting beta$_2$ agonist in reducing symptoms, reliever use and days absent from school due to asthma, depending on the child's beta receptor genotype.[28] However, children were given inhaled corticosteroid and long-acting beta$_2$ agonists in separate inhalers, which is which is known to be associated with increased risks.

However, genotyping it is not currently feasible in clinical practice. In practice, a treatment trial of 4–6 weeks can determine which preventer is suitable for controlling a child's asthma symptoms,[35] but longer treatment may be required to evaluate effect on flare-ups,

because flare-ups may be independent of symptom control.

Exercise-induced symptoms

In school-aged children who experience exercise-induced symptoms despite taking regular inhaled corticosteroids, the addition of montelukast is effective in controlling symptoms, but not all children experience a response.[12, 41]

See: *Investigation and management of exercise-induced bronchoconstriction*

Short-term use in the management of flare-ups

Some, but not all studies suggest that a short course of montelukast, introduced at the first signs of an upper respiratory tract infection, may be effective in controlling flare-ups. An Australian study reported that this strategy could achieve a small reduction in symptoms, school absence and medical consultations in preschool and school-aged children with episodic wheeze.[42]

However, the evidence is inconsistent, with some studies showing no benefit.[32,43, 44, 45, 46] The findings of one study suggested that whether or not intermittent montelukast is effective in wheezing children aged 5 years and under depends on genotype.[27]

Montelukast is not TGA-approved or PBS-subsidised for intermittent use.

Note: PBS status as at March 2019: Montelukast is not subsidised by the PBS for adolescents 15 years and over.

Last reviewed version 2.0

Montelukast for children: behavioural and/or neuropsychiatric adverse effects

Montelukast is generally very well tolerated. Behavioural and psychiatric adverse effects were rare in clinical trials.[47, 48] However, post-marketing surveillance reports have identified behavioural and/or neuropsychiatric adverse effects associated with montelukast use in some children.[49]

Behavioural treatment-associated effects are difficult to assess in young children. No factors have been identified to predict which children are at risk.

Reported adverse events include nightmares, sleep disturbance, anxiety, irritability, aggression and depression.[49, 50, 36, 52]

Suicidal ideation has been reported in adolescents and adults taking montelukast.[52] A nested case-control study concluded that children with asthma aged 5–18 years taking leukotriene receptor antagonists were not at increased risk of suicide attempts.[53]

Reported adverse effects are usually mild.[36] The majority occur within 7–14 days of starting montelukast,[49, 36] but some may appear after several months.[52]

Behavioural and/or neuropsychiatric adverse effects typically disappear within 4 days of stopping montelukast treatment.[36] There is no evidence of long term effects.

The TGA recommends that clinicians treating children with montelukast should educate caregivers about these potential adverse effects and should consider providing them with the CMI. Advise them to seek medical advice if they have any concerns.

► Go to: TGA's 2018 safety review of montelukast

Last reviewed version 2.0

Inhaled corticosteroids for children: adverse effects

Local adverse effects

Hoarseness and pharyngeal candidiasis are not commonly reported among preschool children or school-aged children talking inhaled corticosteroids. [54, 1, 55]

Topical effects can be reduced by use of spacer devices (which reduce oropharyngeal deposition), and by mouth-rinsing and spitting after use.[1] Immediate quick mouth-rinsing removes more residual medicine in the mouth than delayed rinsing.[56]

There is limited evidence that inhaled asthma medication can affect dental health.[1, 57] Mouth rinsing might reduce this risk.

Systemic adverse effects

Systemic effects of inhaled corticosteroids in children depend on the dose, but clinically significant adverse effects are uncommon.[1]

The use of spacers and mouth rinsing will not reduce systemic effects, but the use of a spacer may increase efficacy so that a lower dose is required.

Growth

Short-term suppression of linear growth has been demonstrated in children taking inhaled corticosteroids.[58,59] The effect seems to be maximal during the first year of therapy and only one study has reported an effect in subsequent years of treatment.[59] A Cochrane

systematic review concluded that regular use of inhaled corticosteroid at low or medium daily doses is associated with a mean reduction of 0.48 cm per year in linear growth velocity and 0.61 cm less gain in height during 1 year of treatment in children with mild to moderate persistent asthma.[59]

One study of patients who participated in a clinical trial of inhaled corticosteroids as children, reported a reduction in adult height of approximately 1 cm,[58, 60, 61, 62] whereas several studies have reported that children taking inhaled corticosteroids attained normal adult height.[63, 64, 65]

The effect is dose-dependent[61,62] and may be more likely in children who begin inhaled corticosteroid treatment before age 10.[60]

Other factors affect growth in children with asthma. Uncontrolled asthma itself reduces growth and final adult height.[64] One study found that inhaled corticosteroid equivalent to budesonide 400 microg/day affected growth less than low socioeconomic status.[65]

Bone density

Inhaled corticosteroids have not been associated with effects on bone density or fractures in children. [1] However, data from a recent study in Australia suggested asthma itself is associated with increased incidence of fractures in children, independent of medication.[66]

Given that the total dose of corticosteroids (both inhaled corticosteroids and oral corticosteroids) influences bone health, the aim of asthma management is to maintain symptom control using the lowest inhaled corticosteroid dose required, and to avoid repeated courses of oral corticosteroids.

Adrenal suppression

Biochemical testing in a research setting suggests that hypothalamic–pituitary–adrenal axis suppression may occur in up to two-thirds of children treated with inhaled corticosteroids, and may occur at even low doses.[67] The risk is higher among children receiving concomitant intranasal steroids and those with lower body mass index,[67] and is influenced by genetics.[68]

Clinical adrenal insufficiency in children taking inhaled corticosteroids is rare but has been reported, [69, 70, 71] including cases in Australia.[71] Most cases have involved children given more than 500 microg per day fluticasone propionate.[69]

Adrenal suppression is associated with hypoglycaemia, hypotension, weakness, failure to grow, and is potentially fatal. Hypothalamic–pituitary–adrenal axis suppression may not be detected until adrenal crisis is precipitated by physical stress.[72]

Written information (e.g. a steroid alert card) can be prepared for children receiving long-term high-dose inhaled corticosteroids. Parents/carers can be instructed to present the card if the child ever needs to go to the emergency department (for any reason) or be admitted to hospital. A steroid alert card should state that child has asthma and the inhaled corticosteroid dose. A medical alert bracelet could also be considered.

There are no nationally accepted protocols for routine assessment of adrenal function in primary care because it has not yet been possible to identify precisely which children should be tested, to interpret test results reliably, to identify the appropriate interval for retesting, and because a clinical benefit has not been clearly demonstrated.

Regular monitoring of height might help detect adrenal suppression, based on the findings of a study in which a reduction in linear growth velocity occurred before adrenal suppression.[73]

Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)	
	Low	**High**
Beclometasone dipropionate †	100–200	>200 (maximum 400)
Budesonide	200–400	>400 (maximum 800)
Ciclesonide ‡	80–160	>160 (maximum 320)
Fluticasone propionate	100–200	>200 (maximum 500)

† Dose equivalents for *Qvar* (TGA-registered CFC-free formulation of beclometasone dipropionate)

‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

Source

van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma.* The Thoracic

Society of Australia and New Zealand, 2010. Available from: http://www.thoracic.org.au/clinical-documents/area?command=record&id=14

Last reviewed version 2.0

Asset ID: 21

▶ Go to: The Thoracic Society of Australia and New Zealand's *Position Statement: The role of corticosteroids in the management of childhood asthma*

Last reviewed version 2.0

Step-up options in children with asthma that is not controlled by low-dose inhaled corticosteroids

In children whose asthma is inadequately controlled by low-dose inhaled corticosteroids alone (and adherence is good, inhaler technique is correct and diagnosis has been confirmed), treatment options include:

- increasing the inhaled corticosteroid dose
- adding montelukast
- switching to inhaled corticosteroid/long-acting beta$_2$ agonist combination.

Table. Step-up options for children when good asthma control is not achieved with low-dose ICS

Option	TGA-registered indications for add-on therapy	PBS considerations
High-dose ICS	N/A	Subsidised
ICS plus montelukast	2 years and over	2–5 years: not subsidised* 6–14 years: not subsidised unless for exercise-induced bronchoconstriction despite ICS treatment† 15 years and over: not subsidised‡
ICS/long-acting beta$_2$ agonist combination	4 years and over for fluticasone propionate/ salmeterol xinafoate 12 years and over for budesonide/formoterol fumarate dihydrate	Subsidised

- Advise parents about potential adverse psychiatric effects of montelukast

* Montelukast is not subsidised for use in combination with other preventers or for children who require inhaled corticosteroids.

† Montelukast is subsidised for prevention of exercise-induced asthma if asthma is otherwise well controlled while taking optimal-dose inhaled corticosteroids – it is not otherwise subsidised in combination with inhaled corticosteroids (or inhaled corticosteroid/long-acting beta$_2$ agonist combinations).

‡ Montelukast is not subsidised for people aged over 15 years.

Asset ID: 27

In the majority of children with persistent asthma that requires preventive treatment, control can be achieved with one of these options.[1]

Few studies have been conducted in preschool-aged children. The preferred step-up option for children aged 6–12 years is controversial and guidelines differ in their recommendations.[74]

Increasing inhaled corticosteroid dose versus adding a long-acting beta$_2$ agonist

In school-aged children with persistent asthma taking regular inhaled corticosteroid, the addition of a long-acting beta$_2$ agonist does

not reduce the rate of asthma flare-ups requiring systemic steroids compared with the same or higher doses of inhaled corticosteroid.[75, 76] However, the long-acting beta$_2$ agonist–inhaled corticosteroid was superior for improving lung function.[75] Growth is reduced in children treated with higher-dose inhaled corticosteroid, compared with those taking same dose plus a long-acting beta$_2$ agonist.[75]

Adolescents may benefit more from combination inhaled corticosteroid/long-acting beta$_2$ agonist treatment than children under 12 years. In adolescents with persistent asthma that is not controlled by a low dose of inhaled corticosteroids, the combination of a long-acting beta$_2$ agonist and an inhaled corticosteroid is modestly more effective in reducing the risk of flare-ups requiring oral corticosteroids than a higher dose of inhaled corticosteroids.[77]

Adding montelukast versus adding a long-acting beta-2 agonist or increasing inhaled corticosteroid dose

Children aged 1–5 years

In one study in children aged 5 years or less with persistent asthma/wheeze requiring preventer treatment, raised blood eosinophil levels and atopy predicted better short-term response to high-dose inhaled corticosteroid than to montelukast.[34] However, routine eosinophil counts are currently not recommended to guide treatment in children.

In children aged 1–5 years with asthma/wheeze that is not adequately controlled by low-dose inhaled corticosteroid alone, adding montelukast is preferable to increasing the dose of inhaled corticosteroids when the safety profiles of these options are compared.[78] Long-acting beta$_2$ agonists are not recommended for this age group.

- Montelukast use has been associated with behavioural and/or neuropsychiatric adverse effects.

▶ Go to: TGA alert

Note: Montelukast is TGA-approved for children aged 2 years and over.

Children aged 6 years and over

Among children 6 years and over with asthma that is not controlled by low-dose inhaled corticosteroids, the optimal regimen varies between individuals.[6] In one study of children selected for high adherence with maintenance treatment, short-term responses varied between individuals: in some children the best response was achieved by adding a long-acting beta$_2$ agonist, in others by adding montelukast, and in others by increasing the dose of inhaled corticosteroid.[6]

Note: The use of inhaled corticosteroids and long-acting beta$_2$ agonists in separate inhalers is not recommended for either children or adults because of the potential for increased risk due to selective non-adherence to the inhaled corticosteroid.[79]

Overall, the addition of montelukast to an inhaled corticosteroid does not reduce the need for rescue oral corticosteroids or hospital admission, compared with the same or an increased dose of inhaled corticosteroids, in children aged 6 years and over or adolescents with mild-to-moderate asthma.[37]

For children aged 6–14 years with persistent asthma and exercise-induced bronchoconstriction, adding montelukast is more effective in protecting against exercise-induced bronchoconstriction than switching to a combination of inhaled corticosteroid and a long-acting beta$_2$ agonist.[80] The use of montelukast also avoids beta-receptor tolerance associated with long-acting beta$_2$ agonists, so a short-acting beta$_2$ agonist taken after exercise produces a greater bronchodilator response than it does in children taking regular long-acting beta$_2$ agonist.[80]

A treatment trial of montelukast for 4–6 weeks is the best option when effects on exercise-induced symptoms and safety are also considered.[78]

- Montelukast use has been associated with behavioural and/or neuropsychiatric adverse effects.

▶ Go to: TGA alert

See: *Investigation and management of exercise-induced bronchoconstriction*

Genetic influence on effect of long-acting beta$_2$ agonists

Clinical response to long-acting beta$_2$ agonists partly depends on genetics. A beta$_2$receptor genotype (Arg16 polymorphism in the beta$_2$ receptor gene) pre-disposes children with asthma to down-regulation of the beta$_2$ receptor and increased susceptibility to flare-ups during regular treatment with regular long-acting beta$_2$agonists.[28] However, routine genetic testing to tailor asthma therapy is not yet available in clinical practice.

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Inhaled corticosteroid/long-acting beta-2 agonist combinations for children aged 4–11 years

The combination of salmeterol plus fluticasone propionate in a single inhaler is TGA-registered for use in children 4 years and older.

Efficacy

A very large (n=6208) randomised controlled trial in children aged 4–11 years reported that, unlike in adults, the combination of inhaled corticosteroid and long-acting beta$_2$ agonist was not associated with a significant reduction in severe flare-ups, compared with inhaled corticosteroid alone.[2] Combination treatment was not associated with an increase in in symptom-free days or a reduction in reliever use, compared with inhaled corticosteroid alone.[2]

Safety

Clinical response to long-acting beta$_2$ agonists partly depends on genetics. A beta$_2$receptor genotype (Arg16 polymorphism in the beta$_2$ receptor gene) pre-disposes children with asthma to down-regulation of the beta$_2$ receptor and increased susceptibility to flare-ups during regular treatment with regular long-acting beta$_2$agonists.[28, 81] However, routine genetic testing to tailor asthma therapy is not yet available in clinical practice.

Earlier systematic reviews and meta-analyses led to concern about the possibility that the use of long-acting beta-agonists (even in combination with inhaled corticosteroids) might even increase the risk of flare-ups that require treatment with oral steroids or hospital admission, or of severe flare-ups.[1,78, 79] A meta-analysis commissioned by the US Food and Drug Administration found that the use of long-acting beta$_2$ agonists was associated with increased risk of severe asthma-associated adverse events (both overall and among the subset of people using concomitant inhaled corticosteroid and long-acting beta$_2$ agonist), and that this risk was greatest in children aged 4–11 years.[79] However, the increased risk was only seen in studies where inhaled corticosteroid was not provided, or where inhaled corticosteroid and long-acting beta$_2$ agonist were not combined in a single inhaler (i.e. where there was the possibility of selective non-adherence to the inhaled corticosteroid).

The PBAC Post-market review of medicines used to treat asthma in children[11] concluded that there was insufficient evidence to ascertain whether tolerance to long-acting beta$_2$ agonist could explain why it is less effective than montelukast and inhaled corticosteroids in managing exercise-induced asthma symptoms.[11]

A very large randomised controlled trial of children aged 4–11 years, stratified by asthma symptom control and pre-study treatment, found no increased risk of serious adverse outcomes with combination fluticasone propionate and salmeterol in a single inhaler, compared with fluticasone propionate alone.[2] Subsequent to the publication of this and similar studies in adults,[82] regulators in the USA and Australia removed previous 'black box' warnings from combination inhaled corticosteroid–long-acting beta$_2$ agonist products for asthma.[83]

PBS status as at March 2019: All formulations that contain a combination of inhaled corticosteroid plus long-acting beta$_2$ agonist are listed as 'Authority required - streamlined'. Patient using these combinations for asthma must have previously had frequent episodes of asthma while receiving treatment with oral corticosteroids or optimal doses of inhaled corticosteroids.

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References

1. van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma*. The Thoracic Society of Australia and New Zealand, 2010. Available from: https://www.thoracic.org.au/journal-publishing/command/download_file/id/25/filename/The_role_of_corticosteroids_in_the_management_of_childhood_asthma_-_2010.pdf
2. Stempel, D. A., Szefler, S. J., Pedersen, S., *et al*. Safety of adding salmeterol to fluticasone propionate in children with asthma. *N Engl J Med*. 2016; 375: 840-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27579634
3. Chang, T. S., Lemanske, R. F., Jr., Mauger, D. T., *et al*. Childhood asthma clusters and response to therapy in clinical trials. *J Allergy Clin Immunol*. 2014; 133: 363-9. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/24139497/
4. Malka J, Mauger DT, Covar R, *et al*. Eczema and race as combined determinants for differential response to step-up asthma therapy. *J Allergy Clin Immunol*. 2014; 134: 483-5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24835502
5. Rabinovitch, N., Mauger, D. T., Reisdorph, N., *et al*. Predictors of asthma control and lung function responsiveness to step 3 therapy in children with uncontrolled asthma. *J Allergy Clin Immunol*. 2014; 133: 350-6. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/24084071/
6. Lemanske RF, Mauger DT, Sorkness CA, *et al*. Step-up therapy for children with uncontrolled asthma receiving inhaled corticosteroids. *N Engl J Med*. 2010; 362: 975-985. Available from: http://www.nejm.org/doi/full/10.1056/NEJMoa1001278#t=article
7. Papadopoulos, N. G., Philip, G., Giezek, H., *et al*. The efficacy of montelukast during the allergy season in pediatric patients with persistent asthma and seasonal aeroallergen sensitivity. *J Asthma*. 2009; 46: 413-20. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19484680
8. Carroll, W. D., Jones, P. W., Boit, P., *et al*. Childhood evaluation of salmeterol tolerance–a double-blind randomized controlled trial. *Pediatr Allergy Immunol*. 2010; 21: 336-44. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19725893
9. Fogel, R. B., Rosario, N., Aristizabal, G., *et al*. Effect of montelukast or salmeterol added to inhaled fluticasone on exercise-induced

bronchoconstriction in children. *Ann Allergy Asthma Immunol*. 2010; 104: 511-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20568384
10. Adler, A., Uziel, Y., Mei-Zahav, M., Horowitz, I.. Formoterol induces tolerance to the bronchodilating effect of Salbutamol following methacholine-provocation test in asthmatic children. *Pulm Pharmacol Ther*. 2006; 19: 281-5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/16169761
11. Pharmaceutical Benefits Scheme,. *Post-market review. PBS medicines used to treat asthma in children. Report to PBAC. Final Report*. 2017.
12. Grzelewski, T, Stelmach, I. Exercise-induced bronchoconstriction in asthmatic children: a comparative systematic review of the available treatment options. *Drugs*. 2009; 69: 1533-1553. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19678711
13. Murphy KR, Zeiger RS, Kosinski M, *et al*. Test for respiratory and asthma control in kids (TRACK): a caregiver-completed questionnaire for preschool-aged children. *J Allergy Clin Immunol*. 2009; 123: 833-9. Available from: http://www.jacionline.org/article/S0091-6749(09)00212-7/fulltext
14. Zeiger RS, Mellon M, Chipps B, *et al*. Test for Respiratory and Asthma Control in Kids (TRACK): clinically meaningful changes in score. *J Allergy Clin Immunol*. 2011; 128: 983-8. Available from: http://www.jacionline.org/article/S0091-6749(11)01287-5/fulltext
15. Liu AH, Zeiger R, Sorkness C, *et al*. Development and cross-sectional validation of the Childhood Asthma Control Test. *J Allergy Clin Immunol*. 2007; 119: 817-25. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17353040
16. Liu AH, Zeiger RS, Sorkness CA, *et al*. The Childhood Asthma Control Test: retrospective determination and clinical validation of a cut point to identify children with very poorly controlled asthma. *J Allergy Clin Immunol*. 2010; 126: 267-73, 273.e1. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20624640
17. Abramson MJ, Schattner RL, Holton C et al. Spirometry and regular follow-up do not improve quality of life in children or adolescents with asthma: Cluster randomized controlled trials. *Pediatr Pulmonol* 2015; 50: 947-54. (Available from: https://www.ncbi.nlm.nih.gov/pubmed/25200397
18. Deschildre A, Beghin L, Salleron J, *et al*. Home telemonitoring (forced expiratory volume in 1 s) in children with severe asthma does not reduce exacerbations. *Eur Respir J*. 2012; 39: 290-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/21852334
19. Nuijsink M, Hop WC, Sterk PJ et al. Long-term asthma treatment guided by airway hyperresponsiveness in children: a randomised controlled trial. *Eur Respir J* 2007; 30: 457-66. (Available from: https://www.ncbi.nlm.nih.gov/pubmed/17537770
20. Nuijsink M, Vaessen-Verberne AA, Hop WC et al. Long-term follow-up after two years of asthma treatment guided by airway responsiveness in children. *Respir Med* 2013; 107: 981-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23672993
21. Petsky HL, Li A, Chang AB. Tailored interventions based on sputum eosinophils versus clinical symptoms for asthma in children and adults. *Cochrane Database Syst Rev* 2017; 8: Cd005603. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28837221
22. Lehtimaki L, Csonka P, Makinen E et al. Predictive value of exhaled nitric oxide in the management of asthma: a systematic review. *Eur Respir J* 2016; 48: 706-14. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27492830
23. Petsky HL, Kew KM, Chang AB. Exhaled nitric oxide levels to guide treatment for children with asthma. *Cochrane Database Syst*. Rev 2016; Issue 11: CD011439. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27825189/
24. Turner S, Francis B, Vijverberg S et al. Childhood asthma exacerbations and the Arg16 beta2-receptor polymorphism: A meta-analysis stratified by treatment. *J Allergy Clin Immunol* 2016; 138: 107-13.e5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26774659
25. Merck, Sharp and Dohme Australia Pty Ltd. *Product Information: Singulair (montelukast sodium) Tablets*. Therapeutic Goods Administration, Canberra, 2013. Available from: https://www.ebs.tga.gov.au/
26. Bush A. Montelukast in paediatric asthma: where we are now and what still needs to be done? *Paediatr Respir Rev*. 2015; 16: 97-100. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25499571
27. Nwokoro C, Pandya H, Turner S, *et al*. Intermittent montelukast in children aged 10 months to 5 years with wheeze (WAIT trial): a multicentre, randomised, placebo-controlled trial. *Lancet Respir Med*. 2014; 2: 796-803. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25212745
28. Lipworth BJ, Basu K, Donald HP, *et al*. Tailored second-line therapy in asthmatic children with the Arg(16) genotype. *Clin Sci (Lond)*. 2013; 124: 521-528. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23126384
29. Brodlie M, Gupta A, Rodriguez-Martinez CE, *et al*. Leukotriene receptor antagonists as maintenance and intermittent therapy for episodic viral wheeze in children. *Cochrane Database Syst Rev*. 2015; Issue 10: CD008202. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26482324
30. Bisgaard H, Zielen S, Garcia-Garcia ML, *et al*. Montelukast reduces asthma exacerbations in 2- to 5-year-old children with intermittent asthma. *Am J Respir Crit Care Med*. 2005; 171: 315-322. Available from: http://ajrccm.atsjournals.org/content/171/4/315.long
31. Nagao M, Ikeda M, Fukuda N, *et al*. Early control treatment with montelukast in preschool children with asthma: a randomized controlled trial. *Allergol Int*. 2018; 67: 72-78. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28526210
32. Valovirta, E., Boza, M. L., Robertson, C. F., *et al*. Intermittent or daily montelukast versus placebo for episodic asthma in children. *Ann Allergy Asthma Immunol*. 2011; 106: 518-26. Available from: https://www.ncbi.nlm.nih.gov/pubmed/21624752
33. Castro-Rodriguez JA, Rodriguez-Martinez CE, Ducharme FM. Daily inhaled corticosteroids or montelukast for preschoolers with asthma or recurrent wheezing: A systematic review. *Pediatr Pulmonol*. 2018; Epub ahead of print 6 November. Available from: https://www.ncbi.nlm.nih.gov/pubmed/30394700
34. Fitzpatrick AM, Jackson DJ, Mauger DT et al. Individualized therapy for persistent asthma in young children. *J Allergy Clin Immunol*. 2016; 138: 1608-18.e12. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27777180
35. Jartti T. Inhaled corticosteroids or montelukast as the preferred primary long-term treatment for pediatric asthma? *Eur J Pediatr*. 2008; 167: 731-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/18214538
36. Benard, B., Bastien, V., Vinet, B., *et al*. Neuropsychiatric adverse drug reactions in children initiated on montelukast in real-life

practice. *Eur Respir J*. 2017; 50: . Available from: https://www.ncbi.nlm.nih.gov/pubmed/28818882
37. Chauhan BF, Ben Salah R, Ducharme FM. Addition of anti-leukotriene agents to inhaled corticosteroids in children with persistent asthma. *Cochrane Database Syst Rev*. 2013; Issue 10: CD009585. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24089325
38. Maspero, J, Guerra, F, Cuevas, F, *et al*. Efficacy and tolerability of salmeterol/fluticasone propionate versus montelukast in childhood asthma: a prospective, randomized, double-blind, double-dummy, parallel-group study. *Clin Ther*. 2008; 30: 1492-1504.
39. Pedersen S, Maspero J, Gul N, Sharma R. Components of asthma control and treatment response of individual control criteria in children: analysis of the PEACE study. *Pediatr Pulmonol*. 2011; 46: 1182-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/21751432
40. Stelmach I, Ozarek-Hanc A, Zaczeniuk M et al. Do children with stable asthma benefit from addition of montelukast to inhaled corticosteroids: randomized, placebo controlled trial. *Pulm Pharmacol Ther*. 2015; 31: 42-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25640020
41. Fogel RB, Rosario N, Aristizabal G, *et al*. Effect of montelukast or salmeterol added to inhaled fluticasone on exercise-induced bronchoconstriction in children. *Ann Allergy Asthma Immunol*. 2010; 104: 511-517. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20568384
42. Robertson CF, Price D, Henry R, *et al*. Short-course montelukast for intermittent asthma in children: a randomized controlled trial. *Am J Respir Crit Care Med*. 2007; 175: 323-329. Available from: http://ajrccm.atsjournals.org/content/175/4/323.long
43. Watts, K, Chavasse, R J P G. Leukotriene receptor antagonists in addition to usual care for acute asthma in adults and children. *Cochrane Database Syst Rev*. 2012; Issue 5: . Available from: http://cochranelibrary-wiley.com/doi/10.1002/14651858.CD006100.pub2/full
44. Capsomidis, A., Tighe, M.. Archimedes. Question 2. Is oral montelukast beneficial in treating acute asthma exacerbations in children?. *Arch Dis Child*. 2010; 95: 948-50. Available from: http://adc.bmj.com/content/95/11/948.long
45. Schuh, S, Willan, AR, Stephens, D, *et al*. Can montelukast shorten prednisolone therapy in children with mild to moderate acute asthma? A randomized controlled trial. *J Pediatr*. 2009; 155: 795-800. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19656525
46. Bacharier LB, Phillips BR, Zeiger RS, *et al*. Episodic use of an inhaled corticosteroid or leukotriene receptor antagonist in preschool children with moderate-to-severe intermittent wheezing. *J Allergy Clin Immunol*. 2008; 122: 1127-1135. Available from: https://www.ncbi.nlm.nih.gov/pubmed/18973936
47. Philip G, Hustad C, Noonan G, *et al*. Reports of suicidality in clinical trials of montelukast. *J Allergy Clin Immunol*. 2009; 124: 691-6.e6. Available from: http://www.jacionline.org/article/S0091-6749(09)01247-0/fulltext
48. Philip G, Hustad CM, Malice MP, *et al*. Analysis of behavior-related adverse experiences in clinical trials of montelukast. *J Allergy Clin Immunol*. 2009; 124: 699-706.e8. Available from: http://www.jacionline.org/article/S0091-6749(09)01248-2/fulltext
49. Wallerstedt, S. M., Brunlof, G., Sundstrom, A., Eriksson, A. L.. Montelukast and psychiatric disorders in children. *Pharmacoepidemiol Drug Saf*. 2009; 18: 858-64. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19551697
50. Haarman M, van Hunsel F, de Vries T. Adverse drug reactions of montelukast in children and adults. *Pharmacol Res Perspect* 2017; 5: e00341. Available from: http://onlinelibrary.wiley.com/doi/10.1002/prp2.341/full
51. Robertson, CF, Price, D, Henry, R, *et al*. Short-course montelukast for intermittent asthma in children: a randomized controlled trial. *Am J Respir Crit Care Med*. 2007; 175: 323-329. Available from: https://www.ncbi.nlm.nih.gov/pubmed/17110643
52. Aldea Perona, A., Garcia-Saiz, M., Sanz Alvarez, E.. Psychiatric disorders and montelukast in children: a disproportionality analysis of the VigiBase®. *Drug Saf*. 2016; 39: 69-78. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26620206
53. Schumock GT, Stayner LT, Valuck RJ, *et al*. Risk of suicide attempt in asthmatic children and young adults prescribed leukotriene-modifying agents: a nested case-control study. *J Allergy Clin Immunol*. 2012; 130: 368-75. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22698520
54. Brand PL, Baraldi E, Bisgaard H, *et al*. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. *Eur Respir J*. 2008; 32: 1096-1110. Available from: http://erj.ersjournals.com/content/32/4/1096.full
55. Cazeiro C, Silva C, Mayer S et al. Inhaled corticosteroids and respiratory infections in children with asthma: a meta-analysis. *Pediatrics*. 2017; 139. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28235797
56. Yokoyama H, Yamamura Y, Ozeki T, *et al*. Effects of mouth washing procedures on removal of budesonide inhaled by using Turbuhaler. *Yakugaku Zasshi*. 2007; 127: 1245-1249. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17666876
57. Godara N, Godara R, Khullar M. Impact of inhalation therapy on oral health. *Lung India*. 2011; 28: 272-5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/22084541
58. Loke YK, Blanco P, Thavarajah M, Wilson AM. Impact of inhaled corticosteroids on growth in children with asthma: systematic review and meta-analysis. *PloS One*. 2015; 10: e0133428. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26191797
59. Zhang L, Prietsch SO, Ducharme FM. Inhaled corticosteroids in children with persistent asthma: effects on growth. *Cochrane Database Syst Rev*. 2014: Cd009471. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25030198
60. Kelly HW, Sternberg AL, Lescher R, *et al*. Effect of inhaled glucocorticoids in childhood on adult height. *N Engl J Med*. 2012; 367: 904-12. Available from: http://www.nejm.org/doi/full/10.1056/NEJMoa1203229
61. Pruteanu AI, Chauhan BF, Zhang L et al. Inhaled corticosteroids in children with persistent asthma: dose-response effects on growth. *Cochrane Database Syst Rev*. 2014: Cd009878. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25030199
62. De Leonibus C, Attanasi M, Roze Z et al. Influence of inhaled corticosteroids on pubertal growth and final height in asthmatic children. *Pediatr Allergy Immunol*. 2016; 27: 499-506. Available from:https://www.ncbi.nlm.nih.gov/pubmed/26919136
63. Pauwels RA, Pedersen S, Busse WW, *et al*. Early intervention with budesonide in mild persistent asthma: a randomised, double-blind trial. *Lancet*. 2003; 361: 1071-1076. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12672309
64. Pedersen S. Do inhaled corticosteroids inhibit growth in children? *Am J Respir Crit Care Med*. 2001; 164: 521-35. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11520710

65. Agertoft L, Pedersen S. Effect of long-term treatment with inhaled budesonide on adult height in children with asthma. *N Engl J Med*. 2000; 343: 1064-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11027740
66. Degabriele EL, Holloway KL, Pasco JA et al. Associations between asthma status and radiologically confirmed fracture in children: A data-linkage study. *J Paediatr Child Health*. 2018; 54(8): 855-860. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29614205
67. Zöllner EW, Lombard CJ, Galal U, *et al*. Hypothalamic-adrenal-pituitary axis suppression in asthmatic school children. *Pediatrics*. 2012; 130: e1512-19. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23147980
68. Hawcutt DB, Francis B, Carr DF et al. Susceptibility to corticosteroid-induced adrenal suppression: a genome-wide association study. *Lancet Respir Med*. 2018; 6:442-450. Available from: https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(18)30058-4/fulltext
69. Ahmet A, Kim H, Spier S. Adrenal suppression: A practical guide to the screening and management of this under-recognized complication of inhaled corticosteroid therapy. *Allergy Asthma Clin Immunol*. 2011; 7: 13. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3177893/
70. Priftis, K N, Papadimitriou, A, Anthracopoulos, M B, Fretzayas, A, Chrousos, G P. Endocrine-immune interactions in adrenal function of asthmatic children on inhaled corticosteroids. *Neuroimmunomodulation* 2008; 16: 333-339.
71. Macdessi JS, Randell TL, Donaghue KC, *et al*. Adrenal crises in children treated with high-dose inhaled corticosteroids for asthma. *Med J Aust*. 2003; 178: 214-6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12603184
72. Rao Bondugulapati LN, Rees DA. Inhaled corticosteroids and HPA axis suppression: how important is it and how should it be managed? *Clin Endocrinol (Oxf)*. 2016; 85: 165-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27038017
73. Liddell BS, Oberlin JM, Hsu DP. Inhaled corticosteroid related adrenal suppression detected by poor growth and reversed with ciclesonide. *J Asthma*. 2017; 54: 99-104. Available from:https://www.ncbi.nlm.nih.gov/pubmed/27284755
74. Papi, A., Brightling, C., Pedersen, S. E., Reddel, H. K.. Asthma. *Lancet*. 2018; 391: 783-800. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29273246
75. Chauhan BF, Chartrand C, Ni Chroinin M et al. Addition of long-acting beta2-agonists to inhaled corticosteroids for chronic asthma in children. *Cochrane Database Syst Rev* 2015; Volume 11: CD007949. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26594816
76. Castro-Rodriguez, J. A., Rodrigo, G. J., Rodriguez-Martinez, C. E.. Principal findings of systematic reviews for chronic treatment in childhood asthma. *J Asthma*. 2015; 52: 1038-45. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26303207
77. Ducharme FM, Ni Chroinin M, Greenstone I, Lasserson TJ. Addition of long-acting beta2-agonists to inhaled corticosteroids versus same dose inhaled corticosteroids for chronic asthma in adults and children. *Cochrane Database Syst Rev*. 2010; Issue 5: CD005535. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005535.pub2/full
78. van Asperen PP. Long-acting beta agonists for childhood asthma. *Aust Prescr*. 2012; 35: 111-3. Available from: https://www.nps.org.au/australian-prescriber/articles/long-acting-beta2-agonists-for-childhood-asthma
79. McMahon AW, Levenson MS, McEvoy BW, *et al*. Age and risks of FDA-approved long-acting β2-adrenergic receptor agonists. *Pediatrics*. 2011; 128: e1147-1154. Available from: http://pediatrics.aappublications.org/content/128/5/e1147.long
80. Fogel RB, Rosario N, Aristizabal G et al. Effect of montelukast or salmeterol added to inhaled fluticasone on exercise-induced bronchoconstriction in children. *Ann Allergy Asthma Immunol* 2010; 104: 511-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20568384
81. Finkelstein Y, Bournissen FG, Hutson JR, Shannon M. Polymorphism of the ADRB2 gene and response to inhaled beta- agonists in children with asthma: a meta-analysis. *J Asthma* 2009; 46: 900-5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19905915
82. Busse WW, Bateman ED, Caplan AL et al. Combined analysis of asthma safety trials of long-acting beta2-agonists. *N Engl J Med* 2018; 378: 2497-505. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29949492
83. Seymour SM, Lim R, Xia C et al. Inhaled corticosteroids and LABAs - removal of the FDA's boxed warning. *N Engl J Med* 2018; 378: 2461-3. Available from: https://www.nejm.org/doi/10.1056/NEJMp1716858

Stepping down treatment in children aged 6 years and over

Recommendations

If symptoms have been well controlled for at least 6 months in a child taking regular inhaled corticosteroid treatment, consider reducing the dose.

Monitor symptom control and perform spirometry within 4–6 weeks after stepping down.

Do not attempt to step down treatment at the start of the school year or during the child's peak asthma season (if there is a predictable seasonal pattern).

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- van Asperen et al. 2010[1]

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If symptoms have been well controlled for at least 6 months in a child taking regular treatment with a combination of inhaled corticosteroid and long-acting beta$_2$ agonist, consider halving the dose.

If the inhaled corticosteroid dose is already low, replace inhaled corticosteroid plus long-acting beta$_2$ agonist with low-dose inhaled corticosteroid alone.

Monitor symptom control within 4–6 weeks after stepping down.

Do not attempt to step down treatment at the start of the preschool year or during the child's peak asthma season (if there is a predictable seasonal pattern). Take into account previous treatment response, the result of any previous attempts to step down, and changes in the child's environment that could affect exposure to triggers.

How this recommendation was developed

Consensus recommendation following inconclusive literature search

Based on clinical experience and expert opinion after literature review yielded insufficient evidence for an evidence-based recommendation

Key evidence considered:

- Akashi et al. 2016[2]
- Rank et al. 2015[3]
- Rank et al. 2013[4]

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If symptoms are well controlled for at least 6 months on the lowest available inhaled corticosteroid dose, consider stopping treatment.

Monitor symptom control and perform spirometry within 4–6 weeks after stepping down.

Do not attempt to step down treatment at the start of the school year or during the child's peak asthma season (if there is a predictable seasonal pattern).

How this recommendation was developed

Consensus recommendation following inconclusive literature search

Based on clinical experience and expert opinion after literature review yielded insufficient evidence for an evidence-based

recommendation

Key evidence considered:

- Ciółkowski et al. 2014[5]
- Peters et al. 2007[6]
- Rank et al. 2013[7]
- van Asperen et al. 2010[1]

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More information

Stepping down preventer treatment in children

Stepping down can be considered when asthma has been well controlled for 6 months (depending on severity of previous symptoms). This will help identify the minimal dose or regimen needed to maintain control and may minimise the risk of treatment-related adverse effects and help identify the minimal dose or regimen needed to maintain control.

Children who have stable asthma are at increased risk of a flare-up when stepping down treatment, so close monitoring is needed. Stepping down should not be attempted at the beginning of the school year.[4]

Stepping down from regular inhaled corticosteroid

For children already taking the lowest available dose, options are stop preventer treatment entirely, or switch to montelukast. Few studies have compared different options for stepping down.

Children may be at higher risk of a flare-up or loss of asthma control after stopping low-dose inhaled corticosteroid treatment.[8, 7, 5]

Stepping down from regular inhaled corticosteroid plus long-acting beta-2 agonist

Options for stepping down from regular treatment with a combination inhaled corticosteroid and long-acting $beta_2$ agonist are to reduce the inhaled corticosteroid dose or switch to inhaled corticosteroid only (i.e. discontinue the long-acting $beta_2$ agonist).

There is insufficient evidence from randomised trials on which to base recommendations on whether and how to discontinue long-acting $beta_2$ agonist treatment in children once good asthma control has been achieved with the combination of inhaled corticosteroid and long-acting $beta_2$ agonist.[9]

In a study of children aged 4–11 years whose asthma was well controlled while using a combination of inhaled corticosteroid and long-acting $beta_2$-agonist, stepping down to inhaled corticosteroid monotherapy was associated with a higher rate of flare-ups than continuing on combination therapy.[10]

In a study of children aged 5–15 years with well-controlled asthma, halving the inhaled corticosteroid component and discontinuing the long-acting $beta_2$ agonist had equivalent outcomes for asthma symptoms and lung function.[2]

In a study of children with asthma well controlled on twice-daily fluticasone propionate, switching to montelukast was associated with a higher rate of treatment failure and poorer asthma control than halving the fluticasone dose and adding salmeterol.[6]

Stepping down from montelukast

In children taking montelukast, treatment can be stopped abruptly.

Asthma control should be monitored and the child's written asthma action plan updated to ensure parents/carers know how to manage symptoms.

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Inhaled corticosteroids for children: adverse effects

Local adverse effects

Hoarseness and pharyngeal candidiasis are not commonly reported among preschool children or school-aged children talking inhaled corticosteroids. [11, 1, 12]

Topical effects can be reduced by use of spacer devices (which reduce oropharyngeal deposition), and by mouth-rinsing and spitting after use.[1] Immediate quick mouth-rinsing removes more residual medicine in the mouth than delayed rinsing.[13]

There is limited evidence that inhaled asthma medication can affect dental health.[1, 14] Mouth rinsing might reduce this risk.

Systemic adverse effects

Systemic effects of inhaled corticosteroids in children depend on the dose, but clinically significant adverse effects are uncommon.[1]

The use of spacers and mouth rinsing will not reduce systemic effects, but the use of a spacer may increase efficacy so that a lower dose is required.

Growth

Short-term suppression of linear growth has been demonstrated in children taking inhaled corticosteroids.[15,16] The effect seems to be maximal during the first year of therapy and only one study has reported an effect in subsequent years of treatment.[16] A Cochrane systematic review concluded that regular use of inhaled corticosteroid at low or medium daily doses is associated with a mean reduction of 0.48 cm per year in linear growth velocity and 0.61 cm less gain in height during 1 year of treatment in children with mild to moderate persistent asthma.[16]

One study of patients who participated in a clinical trial of inhaled corticosteroids as children, reported a reduction in adult height of approximately 1 cm,[15, 17, 18, 19] whereas several studies have reported that children taking inhaled corticosteroids attained normal adult height.[20, 21, 22]

The effect is dose-dependent[18,19] and may be more likely in children who begin inhaled corticosteroid treatment before age 10.[17]

Other factors affect growth in children with asthma. Uncontrolled asthma itself reduces growth and final adult height.[21] One study found that inhaled corticosteroid equivalent to budesonide 400 microg/day affected growth less than low socioeconomic status.[22]

Bone density

Inhaled corticosteroids have not been associated with effects on bone density or fractures in children. [1] However, data from a recent study in Australia suggested asthma itself is associated with increased incidence of fractures in children, independent of medication.[23]

Given that the total dose of corticosteroids (both inhaled corticosteroids and oral corticosteroids) influences bone health, the aim of asthma management is to maintain symptom control using the lowest inhaled corticosteroid dose required, and to avoid repeated courses of oral corticosteroids.

Adrenal suppression

Biochemical testing in a research setting suggests that hypothalamic–pituitary–adrenal axis suppression may occur in up to two-thirds of children treated with inhaled corticosteroids, and may occur at even low doses.[24] The risk is higher among children receiving concomitant intranasal steroids and those with lower body mass index,[24] and is influenced by genetics.[25]

Clinical adrenal insufficiency in children taking inhaled corticosteroids is rare but has been reported, [26, 27, 28] including cases in Australia.[28] Most cases have involved children given more than 500 microg per day fluticasone propionate.[26]

Adrenal suppression is associated with hypoglycaemia, hypotension, weakness, failure to grow, and is potentially fatal. Hypothalamic–pituitary–adrenal axis suppression may not be detected until adrenal crisis is precipitated by physical stress.[29]

Written information (e.g. a steroid alert card) can be prepared for children receiving long-term high-dose inhaled corticosteroids. Parents/carers can be instructed to present the card if the child ever needs to go to the emergency department (for any reason) or be admitted to hospital. A steroid alert card should state that child has asthma and the inhaled corticosteroid dose. A medical alert bracelet could also be considered.

There are no nationally accepted protocols for routine assessment of adrenal function in primary care because it has not yet been possible to identify precisely which children should be tested, to interpret test results reliably, to identify the appropriate interval for retesting, and because a clinical benefit has not been clearly demonstrated.

Regular monitoring of height might help detect adrenal suppression, based on the findings of a study in which a reduction in linear growth velocity occurred before adrenal suppression.[30]

Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)	
	Low	High
Beclometasone dipropionate †	100–200	>200 (maximum 400)
Budesonide	200–400	>400 (maximum 800)

Inhaled corticosteroid	Daily dose (microg)	
	Low	High
Ciclesonide ‡	80–160	>160 (maximum 320)
Fluticasone propionate	100–200	>200 (maximum 500)

† Dose equivalents for *Qvar* (TGA-registered CFC-free formulation of beclometasone dipropionate)

‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

Source

van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma.* The Thoracic Society of Australia and New Zealand, 2010. Available from: http://www.thoracic.org.au/clinical-documents/area?command=record&id=14

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▶ Go to: The Thoracic Society of Australia and New Zealand's *Position Statement: The role of corticosteroids in the management of childhood asthma*

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Approaches to assessment and monitoring of asthma control in children

Assessment of asthma control in children is based mainly on:

- recent asthma symptom control (assessed by the frequency and severity of symptoms between flare-ups
- the degree to which asthma symptoms affect daily activities such as interference with physical activity or missed school days)
- the frequency of flare-ups
- spirometry in children who are able to perform the test reliably.

Standardised questionnaires

Questionnaire-based instruments have been validated for assessing asthma control in children:

▶ *Test for Respiratory and Asthma Control in Kids (TRACK)* for children less than 5 years old – consists of five questions about frequency of respiratory symptoms (wheeze, cough, shortness of breath), activity limitation, and night-time awakenings in the past 4 weeks, rescue medication use in the past 3 months, and oral corticosteroid use in the previous year.[31, 32] A lower score indicates worse asthma control.

Childhood Asthma Control Test (C-ACT) for children aged 4–11 years – consists of seven items: three for the parent/carer (about the child's symptoms over the previous 4 weeks) and four for the child.[33, 34] A lower score indicates worse asthma control. **Note:** C-ACT is intended for US use.

Lung function tests

Frequent spirometry to guide asthma treatment in children has not been shown to achieve superior outcomes to symptom-based treatment.[35] Current evidence does not support use of home spirometers to guide asthma treatment in children.[36] However, low FEV_1 predicts clinically significant flare-ups, so spirometry should be performed at asthma reviews for children who are old enough to do the test.

The quality and utility of spirometry depends on the skill, clinical expertise and experience of the person doing and interpreting spirometry.

The results of one study in children aged 6–16 years with moderate atopic asthma suggest that asthma treatment guided by airway hyperresponsiveness (measured by bronchial provocation testing) may have a benefit over symptom-guided treatment in improving lung, but this effect was lost after 3–7 years of usual care.[37, 38] Repeated bronchial provocation testing is not feasible in clinical practice.

Measures of airway inflammation

Measures of airway inflammation (e.g. sputum eosinophil count, exhaled nitric oxide measurement) are not recommended in primary care to guide treatment decisions, but are increasingly used in specialist clinics.

Asthma treatment guided by sputum eosinophil count has been shown to reduce the frequency of flare-ups in adults with asthma, but there is insufficient evidence to ascertain its value for children.[39]

Exhaled nitric oxide measurement may be useful in guiding asthma management in some children. In children not taking inhaled corticosteroid, a high nitric oxide level probably predicts a good short-term response to inhaled corticosteroid treatment,[40] but it does not distinguish between asthma and eosinophilic bronchitis and is often high in children with atopy. There is insufficient evidence to ascertain whether a low exhaled nitric oxide level predicts successful withdrawal from inhaled corticosteroids without asthma relapse,[40] or safety of treating asthma without inhaled corticosteroids.

A Cochrane review[41] found that exhaled nitric oxide-guided management was significantly better than other approaches to adjusting medicines for reducing the number of children with flare-ups and the number of children who needed oral corticosteroids, but did not reduce the frequency of flare-ups or the rate of flare-ups requiring hospitalisation, improve lung function or symptoms scores, or reduce inhaled corticosteroid doses. The authors concluded that it could not be recommended for all children but may be beneficial for a subset not yet defined.[41]

Towards personalised asthma care

Emerging understanding of asthma phenotypes and of genetic factors that predict therapeutic response to preventer options is leading to the possibility of personalised, genomics-based treatment for asthma in children.[42] In the near future, individual tailored therapy is may replace the standardised step model based on population data.

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Classification of recent asthma symptom control in children

Ongoing review of asthma involves both assessing recent asthma symptom control and assessing risks for poor asthma outcomes such as flare-ups and adverse effects of medicines.

Recent asthma symptom control is assessed according to the frequency of asthma symptoms over the previous 4 weeks.

Table. Definition of levels of recent asthma symptom control in children (regardless of current treatment regimen)

Good control	Partial control	Poor control
All of: • Daytime symptoms† ≤2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • No limitation of activities‡ • No symptoms§ during night or when wakes up • Need for SABA reliever# ≤2 days per week	Any of: • Daytime symptoms† >2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • Any limitation of activities* • Any symptoms during night or when wakes up†† • Need for SABA reliever# >2 days per week	Either of: • Daytime symptoms† >2 days per week (lasting from minutes to hours or recurring, and partially or fully relieved by SABA reliever) • ≥3 features of partial control within the same week

SABA: short-acting $beta_2$ agonist

† e.g. wheezing or breathing problems

‡ child is fully active; runs and plays without symptoms

§ including no coughing during sleep

not including doses taken prophylactically before exercise. (Record this separately and take into account when assessing management.)

* e.g. wheeze or breathlessness during exercise, vigorous play or laughing

†† e.g. waking with symptoms of wheezing or breathing problems

Notes:

Recent asthma control is based on symptoms over the previous 4 weeks. Each child's risk factors for future asthma outcomes should

also be assessed and taken into account in management.

Validated questionnaires can be used for assessing recent symptom control:
Test for Respiratory and Asthma Control in Kids (TRACK) for children < 5 years
Childhood Asthma Control Test (C-ACT) for children aged 4–11 years

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Table. Risk factors for life-threatening asthma flare-ups in children

Asthma-related factors

Poor asthma control

Admission to hospital in preceding 12 months

History of intubation for acute asthma

Over-use of short-acting beta$_2$ agonist reliever

Abnormal spirometry findings

Reversible expiratory airflow limitation on spirometry despite treatment

Poor adherence to preventer

Incorrect inhaler technique for preventer

Poor adherence to asthma action plan

Exposure to clinically relevant allergens

Exposure to tobacco smoke

Other clinical factors

Allergies to foods, insects, medicines

Obesity

Family-related factors

Frequent failure to attend consultations/lack of follow-up after an acute flare-up

Significant parental psychological or socioeconomic problems

Parent/carer unequipped to manage asthma emergency

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References

1. van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma.* The Thoracic Society of Australia and New Zealand, 2010. Available from: https://www.thoracic.org.au/journal-publishing/command/download_file/id/25/filename/The_role_of_corticosteroids_in_the_management_of_childhood_asthma_-_2010.pdf
2. Akashi K, Mezawa H, Tabata Y, *et al*. Optimal step-down approach for pediatric asthma controlled by salmeterol/fluticasone: A randomized, controlled trial (OSCAR study). *Allergol Int*. 2016; 65: 306-11. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27155753
3. Rank, M. A., Johnson, R., Branda, M., *et al*. Long-term outcomes after stepping down asthma controller medications: a claims-based, time-to-event analysis. *Chest*. 2015; 148: 630-639. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4556120/
4. Rank, M. A., Branda, M. E., McWilliams, D. B., *et al*. Outcomes of stepping down asthma medications in a guideline-based pediatric asthma management program. *Ann Allergy Asthma Immunol*. 2013; 110: 354-358.e2. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23622006
5. Ciolkowski, J., Mazurek, H., Stasiowska, B.. Evaluation of step-down therapy from an inhaled steroid to montelukast in childhood asthma. *Allergol Immunopathol (Madr)*. 2014; 42: 282-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23684855
6. Peters SP, Anthonisen N, Castro M, *et al*. Randomized comparison of strategies for reducing treatment in mild persistent asthma. *N Engl J Med*. 2007; 356: 2027-39. Available from: https://www.ncbi.nlm.nih.gov/pubmed/17507702
7. Rank MA, Hagan JB, Park MA, *et al*. The risk of asthma exacerbation after stopping low-dose inhaled corticosteroids: a systematic review and meta-analysis of randomized controlled trials. *J Allergy Clin Immunol*. 2013; 131: 724-9. Available from:

http://www.ncbi.nlm.nih.gov/pubmed/23321206
8. Kwong KY, Morphew T, Huynh P et al. Loss of asthma control in inner city children with asthma after withdraw of asthma controller medication. *J Asthma* 2009; 46: 1001-5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19995137
9. Kew, K. M., Beggs, S., Ahmad, S.. Stopping long-acting beta2-agonists (LABA) for children with asthma well controlled on LABA and inhaled corticosteroids. *Cochrane Database Syst Rev*. 2015; Issue 5: CD011316. Available from: [https://www.ncbi.nlm.nih.gov /pubmed/25997166 Full text at: http://cochranelibrary-wiley.com/doi/10.1002/14651858.CD011316.pub2/full](https: //www.ncbi.nlm.nih.gov/pubmed/25997166 Full text at: http://cochranelibrary-wiley.com/doi/10.1002 /14651858.CD011316.pub2/full)
10. Stempel, D. A., Szefler, S. J., Pedersen, S., *et al*. Safety of adding salmeterol to fluticasone propionate in children with asthma. *N Engl J Med*. 2016; 375: 840-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27579634
11. Brand PL, Baraldi E, Bisgaard H, *et al*. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. *Eur Respir J*. 2008; 32: 1096-1110. Available from: http://erj.ersjournals.com/content/32/4/1096.full
12. Cazeiro C, Silva C, Mayer S et al. Inhaled corticosteroids and respiratory infections in children with asthma: a meta-analysis. *Pediatrics*. 2017; 139. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28235797
13. Yokoyama H, Yamamura Y, Ozeki T, *et al*. Effects of mouth washing procedures on removal of budesonide inhaled by using Turbuhaler. *Yakugaku Zasshi*. 2007; 127: 1245-1249. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17666876
14. Godara N, Godara R, Khullar M. Impact of inhalation therapy on oral health. *Lung India*. 2011; 28: 272-5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/22084541
15. Loke YK, Blanco P, Thavarajah M, Wilson AM. Impact of inhaled corticosteroids on growth in children with asthma: systematic review and meta-analysis. *PloS One*. 2015; 10: e0133428. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26191797
16. Zhang L, Prietsch SO, Ducharme FM. Inhaled corticosteroids in children with persistent asthma: effects on growth. *Cochrane Database Syst Rev*. 2014: Cd009471. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25030198
17. Kelly HW, Sternberg AL, Lescher R, *et al*. Effect of inhaled glucocorticoids in childhood on adult height. *N Engl J Med*. 2012; 367: 904-12. Available from: http://www.nejm.org/doi/full/10.1056/NEJMoa1203229
18. Pruteanu AI, Chauhan BF, Zhang L et al. Inhaled corticosteroids in children with persistent asthma: dose-response effects on growth. *Cochrane Database Syst Rev*. 2014: Cd009878. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25030199
19. De Leonibus C, Attanasi M, Roze Z et al. Influence of inhaled corticosteroids on pubertal growth and final height in asthmatic children. *Pediatr Allergy Immunol*. 2016; 27: 499-506. Available from:https://www.ncbi.nlm.nih.gov/pubmed/26919136
20. Pauwels RA, Pedersen S, Busse WW, *et al*. Early intervention with budesonide in mild persistent asthma: a randomised, double-blind trial. *Lancet*. 2003; 361: 1071-1076. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12672309
21. Pedersen S. Do inhaled corticosteroids inhibit growth in children? *Am J Respir Crit Care Med*. 2001; 164: 521-35. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11520710
22. Agertoft L, Pedersen S. Effect of long-term treatment with inhaled budesonide on adult height in children with asthma. *N Engl J Med*. 2000; 343: 1064-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11027740
23. Degabriele EL, Holloway KL, Pasco JA et al. Associations between asthma status and radiologically confirmed fracture in children: A data-linkage study. *J Paediatr Child Health*. 2018; 54(8): 855-860. Available from: https://www.ncbi.nlm.nih.gov/pubmed /29614205
24. Zöllner EW, Lombard CJ, Galal U, *et al*. Hypothalamic-adrenal-pituitary axis suppression in asthmatic school children. *Pediatrics*. 2012; 130: e1512-19. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23147980
25. Hawcutt DB, Francis B, Carr DF et al. Susceptibility to corticosteroid-induced adrenal suppression: a genome-wide association study. *Lancet Respir Med*. 2018; 6:442-450. Available from: https://www.thelancet.com/journals/lanres/article /PIIS2213-2600(18)30058-4/fulltext
26. Ahmet A, Kim H, Spier S. Adrenal suppression: A practical guide to the screening and management of this under-recognized complication of inhaled corticosteroid therapy. *Allergy Asthma Clin Immunol*. 2011; 7: 13. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3177893/
27. Priftis, K N, Papadimitriou, A, Anthracopoulos, M B, Fretzayas, A, Chrousos, G P. Endocrine-immune interactions in adrenal function of asthmatic children on inhaled corticosteroids. *Neuroimmunomodulation* 2008; 16: 333-339.
28. Macdessi JS, Randell TL, Donaghue KC, *et al*. Adrenal crises in children treated with high-dose inhaled corticosteroids for asthma. *Med J Aust*. 2003; 178: 214-6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12603184
29. Rao Bondugulapati LN, Rees DA. Inhaled corticosteroids and HPA axis suppression: how important is it and how should it be managed? *Clin Endocrinol (Oxf)*. 2016; 85: 165-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27038017
30. Liddell BS, Oberlin JM, Hsu DP. Inhaled corticosteroid related adrenal suppression detected by poor growth and reversed with ciclesonide. *J Asthma*. 2017; 54: 99-104. Available from:https://www.ncbi.nlm.nih.gov/pubmed/27284755
31. Murphy KR, Zeiger RS, Kosinski M, *et al*. Test for respiratory and asthma control in kids (TRACK): a caregiver-completed questionnaire for preschool-aged children. *J Allergy Clin Immunol*. 2009; 123: 833-9. Available from: http://www.jacionline.org /article/S0091-6749(09)00212-7/fulltext
32. Zeiger RS, Mellon M, Chipps B, *et al*. Test for Respiratory and Asthma Control in Kids (TRACK): clinically meaningful changes in score. *J Allergy Clin Immunol*. 2011; 128: 983-8. Available from: http://www.jacionline.org/article/S0091-6749(11)01287-5/fulltext
33. Liu AH, Zeiger R, Sorkness C, *et al*. Development and cross-sectional validation of the Childhood Asthma Control Test. *J Allergy Clin Immunol*. 2007; 119: 817-25. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17353040
34. Liu AH, Zeiger RS, Sorkness CA, *et al*. The Childhood Asthma Control Test: retrospective determination and clinical validation of a cut point to identify children with very poorly controlled asthma. *J Allergy Clin Immunol*. 2010; 126: 267-73, 273.e1. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20624640
35. Abramson MJ, Schattner RL, Holton C et al. Spirometry and regular follow-up do not improve quality of life in children or

adolescents with asthma: Cluster randomized controlled trials. *Pediatr Pulmonol* 2015; 50: 947-54. (Available from: https://www.ncbi.nlm.nih.gov/pubmed/25200397
36. Deschildre A, Beghin L, Salleron J, *et al*. Home telemonitoring (forced expiratory volume in 1 s) in children with severe asthma does not reduce exacerbations. *Eur Respir J*. 2012; 39: 290-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/21852334
37. Nuijsink M, Hop WC, Sterk PJ et al. Long-term asthma treatment guided by airway hyperresponsiveness in children: a randomised controlled trial. *Eur Respir J* 2007; 30: 457-66. (Available from: https://www.ncbi.nlm.nih.gov/pubmed/17537770
38. Nuijsink M, Vaessen-Verberne AA, Hop WC et al. Long-term follow-up after two years of asthma treatment guided by airway responsiveness in children. *Respir Med* 2013; 107: 981-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23672993
39. Petsky HL, Li A, Chang AB. Tailored interventions based on sputum eosinophils versus clinical symptoms for asthma in children and adults. *Cochrane Database Syst Rev* 2017; 8: Cd005603. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28837221
40. Lehtimaki L, Csonka P, Makinen E et al. Predictive value of exhaled nitric oxide in the management of asthma: a systematic review. *Eur Respir J* 2016; 48: 706-14. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27492830
41. Petsky HL, Kew KM, Chang AB. Exhaled nitric oxide levels to guide treatment for children with asthma. *Cochrane Database Syst*. Rev 2016; Issue 11: CD011439. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27825189/
42. Turner S, Francis B, Vijverberg S et al. Childhood asthma exacerbations and the Arg16 beta2-receptor polymorphism: A meta-analysis stratified by treatment. *J Allergy Clin Immunol* 2016; 138: 107-13.e5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26774659

Managing flare-ups in children aged 6 years and over

See also: Managing acute asthma in adults and children

Recommendations

Ensure all children with asthma have a short-acting inhaled bronchodilator (reliever) inhaler (and spacer, if needed) with them at all times. Educate parents/carers how and when to give reliever.

Note: The recommended dose for non-emergency bronchodilator in children aged 6–11 years is salbutamol 2–4 puffs (100 microg per puff) as needed, 1 puff at a time, via pressurised metered-dose inhaler plus spacer, and repeated 4 hours later, if needed.

- **Advise parents/carers to get medical advice if reliever is needed again within 4 hours.**
- **Do not prescribe oral salbutamol. Inhalation is the recommended route for delivering relievers for all children and adults.**

Table. Non-emergency use of bronchodilators (relievers) in children aged 6–11 years

Option	Dose	Mode of delivery
Salbutamol 100 microg per actuation (puff)	**2–4 puffs as needed (one at a time)** **Repeat if needed**	**Pressurised metered-dose inhaler plus spacer**
Terbutaline 500 microg/actuation	**1–2 actuations** **Repeat if needed**	**Dry-powder inhaler†**

Note: This table lists usual doses to be administered by parents/carers in the community to manage symptoms as needed. Higher during may be given during acute asthma, including emergencies.

† If able to use this type of inhaler correctly

- **Do not prescribe oral salbutamol.**

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How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

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Consider prescribing a short course of prednisolone for a child with acute asthma if beta$_2$ agonist reliever is needed approximately every 4 hours over a period of 24 hours.

Note: the recommended dose is 1 mg/kg (maximum 50 mg) orally each morning for 3 days.

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- van Asperen et al. 2010[1]

Last reviewed version 2.0

If oral corticosteroids are needed to manage severe acute flare-ups, reassess regular medicine regimen (including adherence and inhaler technique) and consider specialist referral.

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- van Asperen et al. 2010[1]

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Do not start long-term oral corticosteroids except on the advice of a paediatric specialist (respiratory physician or paediatrician).

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- van Asperen et al. 2010[1]

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For all children using a regular preventer (montelukast, inhaled corticosteroid, or combination of inhaled corticosteroid plus long-acting beta$_2$ agonist) explain to children and parents that the child should keep taking it during asthma flare-ups, including acute asthma episodes that require treatment in an emergency department.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

Do not routinely prescribe antibiotics for children with upper respiratory tract infections who experience acute wheeze or asthma associated with viral respiratory infections.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Normansell et al. 2018[2]
- Johnston et al. 2016[3]
- Fonseca-Aten et al. 2006[4]

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More information

Short-acting beta-2 agonist relievers for children: 6 years and over

Inhaled short-acting beta$_2$ agonists is the major class of bronchodilators used for relief of symptoms in asthma.[5]

Children with well-controlled asthma need little or no reliever (on no more than 2 days per week).

Increased use of short-acting beta$_2$ agonists for relief of asthma symptoms, especially daily use, indicates deterioration of asthma control.[6, 7]

Dispensing of 3 or more canisters in a year (average 1.6 puffs per day) is associated with increased risk of flare-ups.[8] Dispensing 12 or more canisters in a year (average 6.6 puffs per day) is associated with increased risk of asthma death.[2]

Table. Definition of levels of recent asthma symptom control in children (regardless of current treatment regimen)

Good control	Partial control	Poor control
All of: • Daytime symptoms† ≤2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • No limitation of activities‡ • No symptoms§ during night or when wakes up • Need for SABA reliever# ≤2 days per week	Any of: • Daytime symptoms† >2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • Any limitation of activities* • Any symptoms during night or when wakes up†† • Need for SABA reliever# >2 days per week	Either of: • Daytime symptoms† >2 days per week (lasting from minutes to hours or recurring, and partially or fully relieved by SABA reliever) • ≥3 features of partial control within the same week

SABA: short-acting beta$_2$ agonist

† e.g. wheezing or breathing problems

‡ child is fully active; runs and plays without symptoms

§ including no coughing during sleep

not including doses taken prophylactically before exercise. (Record this separately and take into account when assessing management.)

* e.g. wheeze or breathlessness during exercise, vigorous play or laughing

†† e.g. waking with symptoms of wheezing or breathing problems

Notes:

Recent asthma control is based on symptoms over the previous 4 weeks. Each child's risk factors for future asthma outcomes should also be assessed and taken into account in management.

Validated questionnaires can be used for assessing recent symptom control:
Test for Respiratory and Asthma Control in Kids (TRACK) for children < 5 years
Childhood Asthma Control Test (C-ACT) for children aged 4–11 years

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Asset ID: 23

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Parent/carer-initiated oral corticosteroids for wheezing and asthma flare-ups

▶ See also: Managing acute asthma in clinical settings

- Oral corticosteroids are associated with adverse effects on behaviour and bone health. Frequent courses may affect the hypothalamus–pituitary–adrenal axis.

Children aged 1–5 years

Short courses of oral corticosteroids initiated by parents/carers in response to children's wheezing, or at the first sign of a cold, are not effective in managing symptoms in preschool children.[9, 10, 11]

There is inconsistent evidence for the benefits of systemic corticosteroids in preschool children with acute viral-induced wheezing presenting to acute care services.[11, 12, 13] Current evidence does not strongly support their use in this age group.[14]

The Thoracic Society of Australia and New Zealand position statement on the use of corticosteroids in children[1] recommends that oral corticosteroid treatment in preschool children, particularly those with intermittent viral-induced wheezing, should be limited to children with wheeze severe enough to need admission to hospital.

Children aged 6 years and over

A Cochrane systematic review found that there was insufficient evidence supporting the use of parent-initiated courses of oral corticosteroids in school-aged children,[15] although some clinical trials have reported benefits.

In a clinical trial in children aged 6–14 years with a history of recurrent episodes of acute asthma, short courses of oral prednisolone (1 mg/kg a day), initiated by parents in response to an asthma flare-ups, reduced asthma symptoms and the number of missed school days.[16] Another quasi-experimental study found that home initiation of corticosteroids reduced the rate of emergency department visits among school-aged children with moderate-to-severe persistent asthma, compared with rates pre-intervention.[17]

The Thoracic Society of Australia and New Zealand position statement on the use of corticosteroids in children[1] recommends a short course of systemic corticosteroid therapy for children with moderate-to-severe acute asthma or when there is an incomplete response to beta-agonists, and does not recommend against parent/carer-initiated courses.

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Back-to-school asthma care

Each year during February, a few days after the school year starts, there is an annual increase in asthma flare-ups among children with asthma.

Asthma flare-ups in children, including those resulting in emergency department presentations and hospitalisations, surge during the first month of the school year. [18, 19, 20, 22] There are smaller increases at the beginning of the other school terms.[23] These flare-ups may be due to changes in exposure to virus, allergens, pollution and/or stress during the early days after school return.[24]

Primary care health professionals can help parents/carers prepare for back-to-school flare-ups by:

- recommending a full asthma review at the end of the school holidays to check asthma control, adherence to preventer and inhaler technique
- ensuring that each child has an up-to-date written asthma action plan and the child and/or parents/carers understand how to follow it
- reminding parents/carers to get their child back into their asthma routine before the school year starts, including taking preventer medications every day, if prescribed

▶ Go to: National Asthma Council Australia's Back to school checklist for kids with asthma

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Increasing the inhaled corticosteroid dose to control flare-ups in children

In children taking regular inhaled corticosteroid-containing preventers, there is conflicting evidence for whether, and by how much, the dose should be increased when symptoms worsen or at the onset of an acute flare-up.

Overall, current evidence from highly controlled randomised controlled trials does not support increasing the dose of inhaled corticosteroid as part of a self-initiated action plan to manage flare-ups in children younger than 12 years.[25]

There is some evidence that high doses of inhaled steroids used pre-emptively might be effective in preventing severe acute asthma in children aged under 5 years, based on studies in children not taking regular inhaled corticosteroids.[26] However, very high pre-emptive doses affect children's growth[27] and are not recommended.

Recent randomised controlled trials reported a lack of effect with a range of dose increases:

- A five-fold increase in the inhaled corticosteroid dose at early signs of worsening asthma did not reduce the rate of severe acute asthma in children aged 5–11 years with well-controlled asthma while taking maintenance inhaled corticosteroid treatment (with high adherence).[28] This strategy was associated with a small reduction in linear growth.[28]
- Dose increases of four or eight times usual inhaled corticosteroid maintenance dose at the onset of an acute flare-up in children aged 2–17 years did not reduce requirement for oral corticosteroids, compared with doubling the dose.[29]

A Cochrane systematic review[25] in children and adults reported that increasing the inhaled corticosteroid dose did not prevent severe flare-ups, regardless of how soon the increase was initiated after the onset of symptoms or the magnitude of the dose increase

(doubling versus quadrupling). The results did not differ between children under 15 and adults or older adolescents.[25] However, there were too few studies in children to make firm conclusions.

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Oral corticosteroids for children: adverse effects

Oral corticosteroids may have adverse psychiatric effects in children, including aggression and hyperactivity.[30] Effects in the general population include euphoria, hypomania, depression, disturbances of mood, cognition, sleep and behaviour.[31]

A short course of oral corticosteroid therapy (less than 2 weeks) is associated with little risk of long-term suppression of the hypothalamus–pituitary–adrenal axis.[1] However, risk can accumulate if frequent courses (four or more per year) are given.[1]

Recurrent courses of oral corticosteroids may also affect bone mineral density, especially in boys.[1,32]

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Thunderstorm asthma

Certain types of thunderstorms in spring or early summer in regions with high grass pollen concentrations in the air can cause life-threatening allergic asthma flare-ups in individuals sensitised to rye grass, even if they have not had asthma before.[33, 34, 35, 36, 37]

Sensitisation to rye grass allergen is almost universal in patients who have reported flare-ups consistent with thunderstorm asthma in Australia.

People with allergic rhinitis and allergy to ryegrass pollen (i.e. most people with springtime allergic rhinitis symptoms) are at risk of thunderstorm asthma if they live in, or are travelling to, a region with seasonal high grass pollen levels – even if they have never had asthma symptoms before. This includes people with undiagnosed asthma, no previous asthma, known asthma.[33, 34] Lack of inhaled corticosteroid preventer treatment has been identified as a risk factor.[33]

Epidemics of thunderstorm asthma can occur when such a storm travels across a region and triggers asthma in many susceptible individuals. Epidemic thunderstorm asthma events are uncommon, but when they occur can they make a high demand on ambulance and health services.[38, 37, 39]

Data from thunderstorm asthma epidemics suggest that the risk of asthma flare-ups being triggered by a thunderstorm is highest in adults who are sensitised to grass pollen and have seasonal allergic rhinitis (with or without known asthma).[33]

The worst outcomes are seen in people with poorly controlled asthma.[38] Treatment with an inhaled corticosteroid asthma preventer was significantly protective in a well-conducted Australian case-control study.[34]

There is insufficient evidence to determine whether intranasal corticosteroids help protect against thunderstorm asthma. Intranasal corticosteroids reduce symptoms of allergic rhinitis and limited indirect evidence suggests they may protect against asthma flare-ups in people not taking inhaled corticosteroids.[40]

The effectiveness of specific allergen immunotherapy in protecting against thunderstorm asthma has not been evaluated in randomised clinical trials, but data from a small Australian open-label study suggest that short-term treatment with five-grass sublingual immunotherapy may have been protective in individuals.[41]

▶ Go to: National Asthma Council Australia's *Epidemic thunderstorm asthma* information paper
Go to: ASCIA's *Pollen calendar*
Go to: *Vic Emergency's Thunderstorm asthma forecast (Victoria only)*

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Administration of inhaled medicines in children: 6 years and over

Parents, carers and children need training to use inhaler devices correctly, including inhaler technique, and care and cleaning of inhalers and spacers.

School-aged children (depending on the child's age, ability, and with individualised training) can learn to use a range of inhaler types, including manually actuated pressurised metered-dose inhalers with spacers, breath-actuated pressurised metered-dose inhalers (e.g. Autohaler), and dry-powder inhalers (e.g. Accuhaler, Turbuhaler).[42, 43, 44, 45, 46]

Table. Types of inhaler devices for delivering asthma and COPD medicines

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/75

A pressurised metered-dose inhaler and spacer is an appropriate first choice for most children.[44]

School-aged children are unlikely to use their inhaler device correctly without careful training and repeated checking.[47]

▶ Go to: National Asthma Council Australia's *How to use a puffer and spacer for kids* video
Go to: National Asthma Council Australia's information paper for health professionals on *Inhaler technique for people with asthma or COPD*

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Preparation of new spacers before first use

Spacers are made of plastic, antistatic polymer/polycarbonate polyurethane, or cardboard.

Plastic spacers (e.g. Breath-A-Tech, Volumatic)

Electrostatic surface charge on new spacers made of plastic (e.g. *Breath-A-Tech*, *Volumatic*) reduces the proportion of medicine available for delivery to the airway. This charge can be reduced by washing the plastic spacer in dishwashing liquid and allowing it to air dry or drip-dry without rinsing or wiping.[48]

Alternatively, priming the spacer by actuating the device several times into the spacer also overcomes the charge, but this wastes medicine. The optimal number of actuations for priming is not known and the findings of in vitro studies vary widely. One study (using older, CFC-based formulations of asthma medicines) reported that up to 40 actuations fired into a new plastic spacer overcame the effect of the electrostatic charge.[49] Others have concluded that the electrostatic charge on plastic spacers does not reduce in vivo efficacy of bronchodilator therapy in children with asthma.[50] The number of actuations necessary may be known when the results of recent studies become available.

When a new plastic spacer must be used immediately (e.g. for a person with asthma symptoms), patients, parents and carers should follow the manufacturer's priming instructions. In hospitals and emergency departments, a new spacer that has not been pre-treated by washing can be primed using multiple (at least 10) puffs of salbutamol. (This is an arbitrary number of actuations in the absence of evidence that would enable a precise guideline.)

Non-plastic spacers

Disposable cardboard spacers (e.g. DispozABLE, LiteAire) and polyurethane/antistatic polymer spacers (e.g. *Able A2A*, *AeroChamber Plus*, *La Petite E-Chamber*, *La Grande E-Chamber*) do not require preparation before first use.[48]

Note: The term 'priming' is also used for the preparation process that is necessary for new pressurised metered-dose inhalers that have not been used for more than a week. This involves first actuating the inhaler into the air (away from the patient). Users should follow the manufacturer's instructions for the particular brand of inhaler, which specify the number of actuations required.

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Correct use of inhaler devices

Checking and correcting inhaler technique is essential to effective asthma management.

Most patients with asthma or COPD do not use their inhalers properly,[51, 52,53, 53, 54] and most have not had their technique checked or corrected by a health professional.

Incorrect inhaler technique when using maintenance treatments increases the risk of severe flare-ups and hospitalisation for people with asthma or COPD.[51, 52, 55, 56, 57, 58]

Poor asthma symptom control is often due to incorrect inhaler technique.[59, 60]

Incorrect inhaler technique when using inhaled corticosteroids increases the risk of local side effects like dysphonia and oral thrush.

The steps for using an inhaler device correctly differ between brands. Checklists of correct steps for each inhaler type and how-to videos are available from the National Asthma Council website.

▶ Go to: National Asthma Council Australia's *Using your inhaler* webpage for information, patient resources and videos on inhaler technique
Go to: National Asthma Council Australia's information paper for health professionals on *Inhaler technique for people with asthma or COPD*
Go to: NPS MedicineWise information on *Inhaler devices for respiratory medicines*

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References

1. van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma.* The Thoracic Society of Australia and New Zealand, 2010. Available from: https://www.thoracic.org.au/journal-publishing/command/download_file/id/25/filename/The_role_of_corticosteroids_in_the_management_of_childhood_asthma_-_2010.pdf

2. Normansell, R., Sayer, B., Waterson, S., *et al*. Antibiotics for exacerbations of asthma. *Cochrane Database Syst Rev*. 2018; 6: CD002741. Available from: http://cochranelibrary-wiley.com/doi/10.1002/14651858.CD002741.pub2/full
3. Johnston, S. L., Szigeti, M., Cross, M., *et al*. Azithromycin for acute exacerbations of asthma : the AZALEA randomized clinical trial. *JAMA Intern Med*. 2016; 176: 1630-1637. Available from: https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2553295
4. Fonseca-Aten, M, Okada, P J, Bowlware, K L, *et al*. Effect of clarithromycin on cytokines and chemokines in children with an acute exacerbation of recurrent wheezing: a double-blind, randomized, placebo-controlled trial. *Ann Allergy Asthma Immunol*. 2006; 97: 457-463.
5. Walters EH, Walters JA, Gibson PG, Jones P. Inhaled short acting beta2-agonist use in chronic asthma: regular versus as needed treatment. *Cochrane Database Syst Rev*. 2003; Issue 1: CD001285. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001285/full
6. Global Initiative for Asthma (GINA). *Global strategy for asthma management and prevention*. GINA, 2012. Available from: http://www.ginasthma.org
7. British Thoracic Society (BTS) Scottish Intercollegiate Guidelines Network (SIGN). *British Guideline on the Management of Asthma. Quick Reference Guide*. Revised May 2011. BTS, SIGN, Edinburgh, 2008.
8. Stanford, R. H., Shah, M. B., D'Souza, A. O., *et al*. Short-acting beta-agonist use and its ability to predict future asthma-related outcomes. *Ann Allergy Asthma Immunol*. 2012; 109: 403-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23176877
9. Beigelman A, King TS, Mauger D, *et al*. Do oral corticosteroids reduce the severity of acute lower respiratory tract illnesses in preschool children with recurrent wheezing?. *J Allergy Clin Immunol*. 2013; 131: 1518-1525. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23498594
10. Oommen A, Lambert PC, Grigg J. Efficacy of a short course of parent-initiated oral prednisolone for viral wheeze in children aged 1-5 years: randomised controlled trial. *Lancet*. 2003; 362: 1433-1438. Available from: http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(03)14685-5/fulltext
11. Panickar J, Lakhanpaul M, Lambert PC, *et al*. Oral prednisolone for preschool children with acute virus-induced wheezing. *N Engl J Med*. 2009; 360: 329-328. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19164186
12. Foster SJ, Cooper MN, Oosterhof S, Borland ML. Oral prednisolone in preschool children with virus-associated wheeze: a prospective, randomised, double-blind, placebo-controlled trial. *Lancet Respir Med*. 2018; 6: 97-106. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29373235
13. Therapeutic guidelines [Electronic book]: Therapeutic Guidelines Limited; 2018 [cited 2018 April].
14. Castro-Rodriguez JA, Beckhaus AA, Forno E. Efficacy of oral corticosteroids in the treatment of acute wheezing episodes in asthmatic preschoolers: Systematic review with meta-analysis. *Pediatric pulmonology* 2016; 51: 868-76. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27074244
15. Ganaie MB, Munavvar M, Gordon M et al. Patient- and parent-initiated oral steroids for asthma exacerbations. *Cochrane Database Syst Rev* 2016; 12: Cd012195. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27943237
16. Vuillermin P, Robertson CF, Carlin JB, *et al*. Parent initiated prednisolone for acute asthma in children of school age: randomised controlled crossover trial. *BMJ*. 2010; 340: c843. Available from: http://www.bmj.com/content/340/bmj.c843.long
17. Sarzynski LM, Turner T, Stukus DR, Allen E. Home supply of emergency oral steroids and reduction in asthma healthcare utilization. *Pediatr Pulmonol* 2017; 52: 1546-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29034999
18. Johnston NW, Johnston SL, Duncan JM et al. The September epidemic of asthma exacerbations in children: a search for etiology. *J Allergy Clin Immunol* 2005; 115: 132-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/15637559
19. Sears MR, Johnston NW. Understanding the September asthma epidemic. *J Allergy Clin Immunol* 2007; 120: 526-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/17658590
20. Eggo RM, Scott JG, Galvani AP, Meyers LA. Respiratory virus transmission dynamics determine timing of asthma exacerbation peaks: Evidence from a population-level model. *Proc Natl Acad Sci U S A* 2016; 113: 2194-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26858436
21. Ahmet, A, Kim, H, Spier, S. Adrenal suppression: A practical guide to the screening and management of this under-recognized complication of inhaled corticosteroid therapy. *Allergy Asthma Clin Immunol*. 2011; 7: 13.
22. Australian Institute of Health and Welfare. *Asthma hospitalisations in Australia 2010-11*. Australian Institute of Health and Welfare, Canberra, 2013. Available from: http://www.aihw.gov.au/publication-detail/?id=60129544541
23. Australian Centre for Asthma Monitoring. *Asthma in Australia 2011: with a focus chapter on chronic obstructive pulmonary disease*. Asthma series no. 4. Cat. no ACM 22. Australian Institute of Health and Welfare, Canberra, 2011. Available from: http://www.aihw.gov.au/publication-detail/?id=10737420159
24. Tovey ER, Rawlinson WD. A modern miasma hypothesis and back-to-school asthma exacerbations. *Med Hypotheses* 2011; 76: 113-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20869177
25. Kew KM, Quinn M, Quon BS, Ducharme FM. Increased versus stable doses of inhaled corticosteroids for exacerbations of chronic asthma in adults and children. *Cochrane Database Syst Rev* 2016; Issue 6: CD007524. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27272563
26. Kaiser SV, Huynh T, Bacharier LB et al. Preventing exacerbations in preschoolers with recurrent wheeze: a meta-analysis. *Pediatrics* 2016; 137: Available from: https://www.ncbi.nlm.nih.gov/pubmed/27230765
27. Ducharme FM, Lemire C, Noya FJ, *et al*. Preemptive use of high-dose fluticasone for virus-induced wheezing in young children. *N Engl J Med*. 2009; 360: 339-353. Available from: http://www.nejm.org/doi/full/10.1056/NEJMoa0808907#t=article
28. Jackson DJ, Bacharier LB, Mauger DT et al. Quintupling Inhaled Glucocorticoids to Prevent Childhood Asthma Exacerbations. *N Engl J Med* 2018; 378: 891-901. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29504498
29. Yousef, E., Hossain, J., Mannan, S., *et al*. Early intervention with high-dose inhaled corticosteroids for control of acute asthma

exacerbations at home and improved outcomes: a randomized controlled trial. *Allergy Asthma Proc*. 2012; 33: 508-13. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23394509
30. Stuart, F. A., Segal, T. Y., Keady, S.. Adverse psychological effects of corticosteroids in children and adolescents. *Arch Dis Child*. 2005; 90: 500-6. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1720409/
31. Australian Medicines Handbook. Last modified July 2018: *Australian Medicines Handbook Pty Ltd*. 2018
32. Kelly, H. W., Van Natta, M. L., Covar, R. A., *et al*. Effect of long-term corticosteroid use on bone mineral density in children: a prospective longitudinal assessment in the childhood Asthma Management Program (CAMP) study. *Pediatrics*. 2008; 122: e53-61. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/18595975/
33. Davies J, Queensland University of Technology. Literature review on thunderstorm asthma and its implications for public health advice. Final report. Melbourne: *Victorian State Government Department of Health and Human Services*; 2017. Available from: https://www2.health.vic.gov.au/about/publications/researchandreports/thunderstorm-asthma-literature-review-may-2107/
34. Girgis ST, Marks GB, Downs SH et al. Thunderstorm-associated asthma in an inland town in south-eastern Australia. Who is at risk? *Eur Respir J* 2000; 16: 3-8.
35. Marks GB, Colquhoun JR, Girgis ST, *et al*. Thunderstorm outflows preceding epidemics of asthma during spring and summer. *Thorax*. 2001; 56: 468-71.
36. D'Amato G, Vitale C, D'Amato M et al. Thunderstorm-related asthma: what happens and why. *Clin Exp Allergy* 2016; 46: 390-6.
37. Victoria State Government Department of Health and Human Services. *The November 2016 Victorian epidemic thunderstorm asthma event: an assessment of the health impacts. The Chief Health Officer's Report, 27 April 2017*. Melbourne: Victorian Government; 2017.
38. Thien F, Beggs PJ, Csutoros D et al. The Melbourne epidemic thunderstorm asthma event 2016: an investigation of environmental triggers, effect on health services, and patient risk factors. *Lancet Planet Health* 2018; 2: e255-e63. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29880157/
39. Andrew E, Nehme Z, Bernard S et al. Stormy weather: a retrospective analysis of demand for emergency medical services during epidemic thunderstorm asthma. *BMJ* 2017; 359: j5636. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29237604/
40. Lohia S, Schlosser RJ, Soler ZM. Impact of intranasal corticosteroids on asthma outcomes in allergic rhinitis: a meta-analysis. *Allergy*. 2013; 68: 569-79. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23590215/
41. O'Hehir RE, Varese NP, Deckert K et al. Epidemic thunderstorm asthma protection with five-grass pollen tablet sublingual immunotherapy: a clinical trial. *Am J Respir Crit Care Med* 2018; 198: 126-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29461859/
42. Gillette, C., Rockich-Winston, N., Kuhn, J. A., *et al*. Inhaler technique in children with asthma: a systematic review. *Acad Pediatr*. 2016; 16: 605-15. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27130811
43. Capanoglu, M., Dibek Misirlioglu, E., Toyran, M., *et al*. Evaluation of inhaler technique, adherence to therapy and their effect on disease control among children with asthma using metered dose or dry powder inhalers. *J Asthma*. 2015; 52: 838-45. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26037396
44. Ram, F S F, Brocklebank, D D M, White, J, *et al*. Pressurised metered dose inhalers versus all other hand-held inhaler devices to deliver beta-2 agonist bronchodilators for non-acute asthma. *Cochrane Database Syst Rev*. 2002; Issue 2: .
45. Nikander, K, Turpeinen, M, Pelkonen, A S, *et al*. True adherence with the Turbuhaler in young children with asthma. *Arch Dis Child*. 2011; 96: 168-173.
46. Pedersen, S., Mortensen, S.. Use of different inhalation devices in children. *Lung*. 1990; 168 Suppl: 653-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/2117175
47. Sleath, B, Ayala, G X, Gillette, C, *et al*. Provider demonstration and assessment of child device technique during pediatric asthma visits. *Pediatrics*. 2011; 127: 642-648.
48. Brand PL, Baraldi E, Bisgaard H, *et al*. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. *Eur Respir J*. 2008; 32: 1096-1110. Available from: http://erj.ersjournals.com/content/32/4/1096.full
49. Berg E. In vitro properties of pressurized metered dose inhalers with and without spacer devices. *J Aerosol Med*. 1995; 8 Suppl 3: S3-10; discussion S11. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10157897
50. Dompeling E, Oudesluys-Murphy AM, Janssens HM, *et al*. Randomised controlled study of clinical efficacy of spacer therapy in asthma with regard to electrostatic charge. *Arch Dis Child*. 2001; 84: 178-182. Available from: http://adc.bmj.com/content/84/2/178.full
51. The Inhaler Error Steering Committee,, Price, D., Bosnic-Anticevich, S., *et al*. Inhaler competence in asthma: common errors, barriers to use and recommended solutions. *Respir Med*. 2013; 107: 37-46. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23098685
52. Bjermer, L.. The importance of continuity in inhaler device choice for asthma and chronic obstructive pulmonary disease. *Respiration; international review of thoracic diseases*. 2014; 88: 346-52. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25195762
53. Basheti, I A, Armour, C L, Bosnic-Anticevich, S Z, Reddel, H K. Evaluation of a novel educational strategy, including inhaler-based reminder labels, to improve asthma inhaler technique. *Patient Educ Couns*. 2008; 72: 26-33. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18314294
54. Bosnic-Anticevich, S. Z., Sinha, H., So, S., Reddel, H. K.. Metered-dose inhaler technique: the effect of two educational interventions delivered in community pharmacy over time. *The Journal of asthma : official journal of the Association for the Care of Asthma*. 2010; 47: 251-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20394511
55. Melani AS, Bonavia M, Cilenti V, *et al*. Inhaler mishandling remains common in real life and is associated with reduced disease control. *Respir Med*. 2011; 105: 930-8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21367593
56. Levy ML, Dekhuijzen PN, Barnes PJ, *et al*. Inhaler technique: facts and fantasies. A view from the Aerosol Drug Management Improvement Team (ADMIT). *NPJ Prim Care Respir Med*. 2016; 26: 16017. Available from: https://www.ncbi.nlm.nih.gov/pubmed

/27098045
57. Haughney, J., Price, D., Barnes, N. C., *et al*. Choosing inhaler devices for people with asthma: current knowledge and outstanding research needs. *Respiratory medicine*. 2010; 104: 1237-45. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20472415
58. Giraud, V., Roche, N.. Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability. *The European respiratory journal*. 2002; 19: 246-51. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11866004
59. Harnett, C. M., Hunt, E. B., Bowen, B. R., *et al*. A study to assess inhaler technique and its potential impact on asthma control in patients attending an asthma clinic. *J Asthma*. 2014; 51: 440-5.
60. Hardwell, A., Barber, V., Hargadon, T., *et al*. Technique training does not improve the ability of most patients to use pressurised metered-dose inhalers (pMDIs). *Prim Care Respir J*. 2011; 20: 92-6. Available from: http://www.nature.com/articles/pcrj201088

Managing difficult-to-treat and severe asthma in children aged 6 years and over

Recommendations

If asthma symptoms remain uncontrolled (persisting symptoms or flare-ups) despite maximal regular preventer treatment:

- **assess adherence**
- **check inhaler technique**
- **review the diagnosis**
- **check that the dose and regimen is appropriate**
- **assess comorbidities (e.g. allergic rhinitis)**
- **check whether the child is exposed to environmental triggers (e.g. allergens, cigarette smoke).**

Table. Reviewing and adjusting preventer treatment for children aged 6–11 years

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/26

Figure. Stepped approach to adjusting asthma medication in children aged 6-11 years

Please view and print this figure separately: http://www.asthmahandbook.org.au/figure/show/120

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Chung et al. 2014[1]
- Bush et al. 2011[2]
- Bush et al. 2010[3]

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If good asthma control is still not achieved after eliminating common reasons for treatment failure, offer referral to a paediatric respiratory physician or paediatrician.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

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Regular treatment with a theophylline is not recommended routinely for children.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

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Identify children with uncontrolled asthma who might benefit from monoclonal antibody therapy and offer referral for specialist assessment (after checking and correcting common causes of uncontrolled asthma such as incorrect inhaler technique and suboptimal adherence).

Notes:
Omalizumab is indicated as add-on treatment for uncontrolled severe allergic asthma in children ≥6 years.
Before becoming eligible for PBS subsidy for monoclonal antibody therapy treatment, patients must have been treated by the same specialist (paediatric respiratory physician, clinical immunologist, allergist or a paediatrician or general physician experienced in the management of patients with severe asthma, in consultation with a respiratory physician), for at least 6 months. Stringent criteria for starting and continuing therapy apply.

▶ **Go to: National Asthma Council Australia's information paper for health professionals on** *Monoclonal antibody therapy for severe asthma*

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- National Asthma Council Australia 2018[4]

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More information

Definitions of severe and difficult-to-treat asthma

Although most people's asthma can be effectively treated with currently available medicines, a substantial subset of people have uncontrolled asthma (as indicated by persisting symptoms, low lung function and/or flare-ups) despite treatment. These patients are described as having difficult-to-treat asthma.

Some patients with difficult-to-treat asthma have severe asthma. Asthma severity is classified retrospectively according to the level of treatment needed to achieve or maintain good asthma control, rather than by the intensity or frequency of symptoms.[5] International guidelines have been published for the assessment and management of patients with severe asthma.[6] 'Severe asthma' (also called severe refractory asthma' or 'severe treatment-resistant asthma') is defined as asthma for which good control is not achieved despite the highest level of recommended treatment, or asthma for which control can be maintained only with the highest level of recommended treatment.[6] It is estimated that 5-10% of patients with asthma have severe asthma.[6]

Not all patients with difficult-to-treat asthma have severe asthma. 'Difficult-to-treat asthma' includes asthma that is uncontrolled due to adherence issues, inappropriate or incorrect use of medicines, environmental triggers or comorbidities. Patients whose asthma control improves rapidly with correction of such problems are not considered to have severe asthma.[6]

Treatment-resistant asthma or severe refractory asthma can only be diagnosed after confirming the diagnosis, confirming good adherence to high-dose inhaled corticosteroid and correct inhaler technique, excluding alternative or overlapping diagnoses, identifying and minimising exposure to preventable triggers including allergens, irritants and medicines that cause bronchoconstriction, managing comorbidities, and closely monitoring for at least 6 months.[7, 6]

Omalizumab is a treatment option for some adults, adolescents and children with severe asthma.

The definition of severe asthma proposed by the World Health Organization (WHO) Consultation on Severe Asthma for global use is 'uncontrolled asthma which can result in risk of frequent severe exacerbations (or death) and/or adverse reactions to medications and/or chronic morbidity (including impaired lung function or reduced lung growth in children)'.[8] The WHO definition of severe asthma includes a category called 'severe untreated asthma', a term recommended only for use in countries that lack access to standard asthma medications such as inhaled corticosteroids.

Patients with severe symptoms due to untreated asthma may be found, after starting regular treatment, to have mild asthma (i.e. asthma that is easily controlled with low-dose inhaled corticosteroids).[5]

▶ Go to: European Respiratory Society and American Thoracic Society guidelines on *definition, evaluation and treatment of severe asthma*

Common reasons for poor response to preventer treatment

Apparent lack of response to asthma treatment is commonly due to one or more of the following:[3]

- poor adherence (which may be due to lack of perceived need for the medication, concern about potential or actual side-effects, cost

of medicines, a busy lifestyle, misunderstanding of the purpose and effects of asthma medicines, or inability to follow the medical instructions)
- poor inhaler technique
- mishandling devices (e.g. failure to clean spacer, allowing mouthpiece of dry-powder inhalers to become blocked)
- incorrect dose or frequency
- empty inhaler
- expired medicines
- continued exposure to smoke or allergen triggers.

Failure to identify these causes before adjusting medicines could result in over-medication with preventers.

▶ See: *Management challenges*

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Classification of recent asthma symptom control in children

Ongoing review of asthma involves both assessing recent asthma symptom control and assessing risks for poor asthma outcomes such as flare-ups and adverse effects of medicines.

Recent asthma symptom control is assessed according to the frequency of asthma symptoms over the previous 4 weeks.

Table. Definition of levels of recent asthma symptom control in children (regardless of current treatment regimen)

Good control	Partial control	Poor control
All of: • Daytime symptoms† ≤2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • No limitation of activities‡ • No symptoms§ during night or when wakes up • Need for SABA reliever# ≤2 days per week	Any of: • Daytime symptoms† >2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • Any limitation of activities* • Any symptoms during night or when wakes up†† • Need for SABA reliever# >2 days per week	Either of: • Daytime symptoms† >2 days per week (lasting from minutes to hours or recurring, and partially or fully relieved by SABA reliever) • ≥3 features of partial control within the same week

SABA: short-acting beta$_2$ agonist

† e.g. wheezing or breathing problems

‡ child is fully active; runs and plays without symptoms

§ including no coughing during sleep

not including doses taken prophylactically before exercise. (Record this separately and take into account when assessing management.)

* e.g. wheeze or breathlessness during exercise, vigorous play or laughing

†† e.g. waking with symptoms of wheezing or breathing problems

Notes:

Recent asthma control is based on symptoms over the previous 4 weeks. Each child's risk factors for future asthma outcomes should also be assessed and taken into account in management.

Validated questionnaires can be used for assessing recent symptom control:
Test for Respiratory and Asthma Control in Kids (TRACK) for children < 5 years
Childhood Asthma Control Test (C-ACT) for children aged 4–11 years

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Asset ID: 23

Table. Risk factors for life-threatening asthma flare-ups in children
Asthma-related factors

Poor asthma control

Admission to hospital in preceding 12 months

History of intubation for acute asthma

Over-use of short-acting beta$_2$ agonist reliever

Abnormal spirometry findings

Reversible expiratory airflow limitation on spirometry despite treatment

Poor adherence to preventer

Incorrect inhaler technique for preventer

Poor adherence to asthma action plan

Exposure to clinically relevant allergens

Exposure to tobacco smoke

Other clinical factors

Allergies to foods, insects, medicines

Obesity

Family-related factors

Frequent failure to attend consultations/lack of follow-up after an acute flare-up

Significant parental psychological or socioeconomic problems

Parent/carer unequipped to manage asthma emergency

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Asset ID: 116

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Step-up options in children with asthma that is not controlled by low-dose inhaled corticosteroids

In children whose asthma is inadequately controlled by low-dose inhaled corticosteroids alone (and adherence is good, inhaler technique is correct and diagnosis has been confirmed), treatment options include:

- increasing the inhaled corticosteroid dose
- adding montelukast
- switching to inhaled corticosteroid/long-acting beta$_2$ agonist combination.

Table. Step-up options for children when good asthma control is not achieved with low-dose ICS

Option	TGA-registered indications for add-on therapy	PBS considerations
High-dose ICS	N/A	Subsidised
ICS plus montelukast	2 years and over	2–5 years: not subsidised* 6–14 years: not subsidised unless for exercise-induced bronchoconstriction despite ICS treatment† 15 years and over: not subsidised‡
ICS/long-acting beta$_2$ agonist combination	4 years and over for fluticasone propionate/ salmeterol xinafoate 12 years and over for budesonide/formoterol fumarate dihydrate	Subsidised

- Advise parents about potential adverse psychiatric effects of montelukast

* Montelukast is not subsidised for use in combination with other preventers or for children who require inhaled corticosteroids.

† Montelukast is subsidised for prevention of exercise-induced asthma if asthma is otherwise well controlled while taking optimal-dose inhaled corticosteroids – it is not otherwise subsidised in combination with inhaled corticosteroids (or inhaled corticosteroid/long-acting beta$_2$ agonist combinations).

‡ Montelukast is not subsidised for people aged over 15 years.

Asset ID: 27

In the majority of children with persistent asthma that requires preventive treatment, control can be achieved with one of these options.[9]

Few studies have been conducted in preschool-aged children. The preferred step-up option for children aged 6–12 years is controversial and guidelines differ in their recommendations.[10]

Increasing inhaled corticosteroid dose versus adding a long-acting beta$_2$ agonist

In school-aged children with persistent asthma taking regular inhaled corticosteroid, the addition of a long-acting beta$_2$ agonist does not reduce the rate of asthma flare-ups requiring systemic steroids compared with the same or higher doses of inhaled corticosteroid.[11, 12] However, the long-acting beta$_2$ agonist–inhaled corticosteroid was superior for improving lung function.[11] Growth is reduced in children treated with higher-dose inhaled corticosteroid, compared with those taking same dose plus a long-acting beta$_2$ agonist.[11]

Adolescents may benefit more from combination inhaled corticosteroid/long-acting beta$_2$ agonist treatment than children under 12 years. In adolescents with persistent asthma that is not controlled by a low dose of inhaled corticosteroids, the combination of a long-acting beta$_2$ agonist and an inhaled corticosteroid is modestly more effective in reducing the risk of flare-ups requiring oral corticosteroids than a higher dose of inhaled corticosteroids.[13]

Adding montelukast versus adding a long-acting beta-2 agonist or increasing inhaled corticosteroid dose

Children aged 1–5 years

In one study in children aged 5 years or less with persistent asthma/wheeze requiring preventer treatment, raised blood eosinophil levels and atopy predicted better short-term response to high-dose inhaled corticosteroid than to montelukast.[14] However, routine eosinophil counts are currently not recommended to guide treatment in children.

In children aged 1–5 years with asthma/wheeze that is not adequately controlled by low-dose inhaled corticosteroid alone, adding montelukast is preferable to increasing the dose of inhaled corticosteroids when the safety profiles of these options are compared.[15] Long-acting beta$_2$ agonists are not recommended for this age group.

- Montelukast use has been associated with behavioural and/or neuropsychiatric adverse effects.

▶ Go to: TGA alert

Note: Montelukast is TGA-approved for children aged 2 years and over.

Children aged 6 years and over

Among children 6 years and over with asthma that is not controlled by low-dose inhaled corticosteroids, the optimal regimen varies between individuals.[16] In one study of children selected for high adherence with maintenance treatment, short-term responses varied between individuals: in some children the best response was achieved by adding a long-acting beta$_2$ agonist, in others by adding montelukast, and in others by increasing the dose of inhaled corticosteroid.[16]

Note: The use of inhaled corticosteroids and long-acting beta$_2$ agonists in separate inhalers is not recommended for either children or adults because of the potential for increased risk due to selective non-adherence to the inhaled corticosteroid.[17]

Overall, the addition of montelukast to an inhaled corticosteroid does not reduce the need for rescue oral corticosteroids or hospital admission, compared with the same or an increased dose of inhaled corticosteroids, in children aged 6 years and over or adolescents with mild-to-moderate asthma.[18]

For children aged 6–14 years with persistent asthma and exercise-induced bronchoconstriction, adding montelukast is more effective in protecting against exercise-induced bronchoconstriction than switching to a combination of inhaled corticosteroid and a long-acting beta$_2$ agonist.[19] The use of montelukast also avoids beta-receptor tolerance associated with long-acting beta$_2$ agonists, so a short-acting beta$_2$ agonist taken after exercise produces a greater bronchodilator response than it does in children taking regular long-acting beta$_2$ agonist.[19]

A treatment trial of montelukast for 4–6 weeks is the best option when effects on exercise-induced symptoms and safety are also considered.[15]

- Montelukast use has been associated with behavioural and/or neuropsychiatric adverse effects.

▶ Go to: TGA alert

See: *Investigation and management of exercise-induced bronchoconstriction*

Genetic influence on effect of long-acting beta$_2$ agonists

Clinical response to long-acting beta$_2$ agonists partly depends on genetics. A beta$_2$receptor genotype (Arg16 polymorphism in the beta$_2$ receptor gene) pre-disposes children with asthma to down-regulation of the beta$_2$ receptor and increased susceptibility to flare-ups during regular treatment with regular long-acting beta$_2$agonists.[20] However, routine genetic testing to tailor asthma therapy is not

yet available in clinical practice.

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Tiotropium for children aged 6 years and over

Tiotropium (5 microg administered via mist inhaler as two puffs once daily) is approved by TGA for use in children aged 6 years and older with moderate-to-severe asthma.

Tiotropium is subsidised by then PBS for children aged 6–17 years when used in combination with maintenance ICS+LABA treatment, for patients with severe asthma treated by, or in consultation with, a specialist (respiratory physician, paediatric respiratory physician, clinical immunologist, allergist, paediatrician or general physician experienced in severe asthma management), with frequent moderate exacerbations or ≥ one documented severe exacerbation that required systemic corticosteroids in the previous 12 months despite maintenance treatment with a medium-to-high dose of inhaled corticosteroid in combination with a long-acting beta2 agonist, and correct inhaler technique has been assessed, demonstrated and documented (see PBS for details).

▶ Go to: *PBS listings*

Children aged 6–11

A systematic review of three randomised controlled trials reported that, in children aged 6–11 years with moderate-to-severe symptomatic asthma, tiotropium improved lung function, improved symptoms, and reduced the rate of flare-ups.[21] Tiotropium was generally well tolerated.[21]

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Specific allergen immunotherapy (desensitisation)

- Specific allergen immunotherapy should not be started unless the patient has stable asthma, including spirometry-demonstrated forced expiratory volume in 1 second (FEV_1) greater than 80% predicted for subcutaneous immunotherapy and greater than 70% predicted for sublingual immunotherapy.[22, 23] For patients with unstable asthma (e.g. frequent symptoms, marked variability in airflow measured by spirometry or peak flow monitor), the risks of treatment should be considered. These patients will need specialist supervision during treatment.

Options available in Australia

Two forms of specific allergen immunotherapy are available:

- sublingual immunotherapy
- subcutaneous immunotherapy.

Both forms of specific allergen immunotherapy require 3–5 years of treatment. Specific allergy immunotherapy can be repeated.

Although some specific allergen therapies can be prescribed by primary care health professionals, it is recommended that they are initiated under the care of an allergy specialist (allergist or clinical immunologist), where possible.

Commercial allergen preparations for immunotherapy are available in Australia for aeroallergens including house dust mite, pollens (e.g. grass, tree and weed pollens), animal dander and moulds.

▶ Go to: ASCIA's *Allergen Immunotherapy* fact sheet for patients
Go to: ASCIA's *Allergen immunotherapy e-training for health professionals*

Overview of efficacy

There is strong evidence that allergen immunotherapy is effective in the treatment of seasonal and perennial allergic rhinitis.[24, 25, 26] There is less evidence supporting specific allergen immunotherapy in children than in adults.[25] Specific allergen immunotherapy in children with seasonal allergic rhinoconjunctivitis might prevent development of asthma.[27, 28, 29]

Single-allergen specific allergen immunotherapy is effective in patients sensitised to one allergen and those sensitised to multiple allergens.[30, 31, 32] In selected cases more than one allergen may be administered as separate extracts. There is weak evidence for the efficacy of allergen mixes.[33]

A systematic review of studies directly comparing subcutaneous immunotherapy and sublingual immunotherapy in the treatment of allergic rhinoconjunctivitis and asthma found:[34]

- low-grade evidence that subcutaneous immunotherapy is more effective than sublingual immunotherapy for reducing asthma symptoms and for reducing a combined measure of rhinitis symptoms and medication use
- moderate-grade evidence that subcutaneous immunotherapy is more effective than sublingual immunotherapy for reducing nasal and/or eye symptoms.

Sublingual immunotherapy is associated with a lower rate of severe adverse effects (anaphylaxis and death) than subcutaneous

immunotherapy, based on indirect comparison.[35, 36, 37]

Sublingual immunotherapy

Sublingual immunotherapy (self-administered at home) is effective for the treatment of allergic rhinitis in adults and children.[38, 39] The greatest benefits have been demonstrated in those with allergies to temperate grass pollens or house dust mite.[39] Therapeutic Goods Administration (TGA)-approved indications for commercially available preparations vary according to age group.

The extract must be held under the tongue without swallowing for 2 minutes (liquid extracts) or 1 minute (tablets).

Sublingual immunotherapy is generally well tolerated.[38] Local adverse effects are common in children receiving sublingual immunotherapy.[35] Systemic adverse reactions, such as anaphylaxis, are very rare.[35] The majority of adverse events occur soon after beginning treatment.[39]

TGA-approved indications

Asthma: Acarizax (house dust mite) is indicated for adults 18–65 years with house dust mite allergic asthma that is not well controlled by inhaled corticosteroids and is associated with mild-to-severe house dust mite allergic rhinitis.[40] It is contraindicated in patients with FEV_1 <70% predicted after adequate treatment, and for patients who have experienced a severe flare-up within the previous 3 months.[40]

Allergic rhinitis: Several commercial preparations of aeroallergens for sublingual immunotherapy in patients with allergic rhinitis are used in Australia, including:

- *Acarizax* (house dust mite) – indicated for adults 18–65 years with persistent moderate to severe house dust mite allergic rhinitis despite symptomatic treatment.[40]
- *Actair* (house dust mite) – indicated for the treatment of house dust mite allergic rhinitis with or without conjunctivitis in adults and adolescents over 12 years diagnosed with house dust mite allergy.[41]
- *Grazax* (Timothy grass *[Phleum pratense]* pollen extract) – indicated for adults, adolescents and children older than 5 years with allergic rhinitis induced by Timothy grass[42]
- *Oralair* tablets (mix of grass pollens) – indicated for adults and children over 5 years with grass pollen allergic rhinitis.[43]

Various single allergens and/or multiple allergen mixes are available for use as advised by the treating allergist, available as liquid extracts. Age restrictions vary between products.

Note: PBS status as at October 2016: Treatment with sublingual immunotherapy specific allergen preparations is not subsidised by the PBS.

Subcutaneous immunotherapy

Subcutaneous immunotherapy involves injections in which the dose is gradually increased at regular intervals (usually weekly), or until a therapeutic/maintenance dose is reached. This can take approximately 3–6 months.[44] Treatment is then continued for a further 3–5 years.

Subcutaneous immunotherapy is generally not suitable for younger children (e.g. less than 7 years) because they may not be able to tolerate frequent injections.

Several commercial preparations of aeroallergens for subcutaneous immunotherapy are available in Australia, including various single allergens and/or multiple allergen mixes for use as advised by the treating allergist. Age restrictions vary between products.

Subcutaneous immunotherapy is effective for the treatment of allergic rhinitis and asthma, particularly when single-allergen immunotherapy regimens are used.[36] There is strong evidence that it reduces asthma symptoms, asthma medication usage, rhinitis/rhinoconjunctivitis symptoms, conjunctivitis symptoms, and rhinitis/rhinoconjunctivitis disease-specific quality of life, in comparison to placebo or usual care.[36] There is also moderate evidence that subcutaneous immunotherapy reduces rhinitis/rhinoconjunctivitis medication usage.[36]

Subcutaneous immunotherapy is associated with local adverse effects (e.g. injection-site swelling) and, less frequently, serious systemic adverse effects.[35, 39] The most common systemic reactions are respiratory symtoms. There have been few reports of anaphylaxis.[35]

Note: PBS status as at March 2019: Treatment with subcutaneous specific allergen immunotherapy preparations is not subsidised by the PBS.

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Oral corticosteroids for children: adverse effects

Oral corticosteroids may have adverse psychiatric effects in children, including aggression and hyperactivity.[45] Effects in the general population include euphoria, hypomania, depression, disturbances of mood, cognition, sleep and behaviour.[46]

A short course of oral corticosteroid therapy (less than 2 weeks) is associated with little risk of long-term suppression of the hypothalamus–pituitary–adrenal axis.[9] However, risk can accumulate if frequent courses (four or more per year) are given.[9]

Recurrent courses of oral corticosteroids may also affect bone mineral density, especially in boys.[9,47]

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Correct use of inhaler devices

Checking and correcting inhaler technique is essential to effective asthma management.

Most patients with asthma or COPD do not use their inhalers properly,[48, 49,50, 50, 51] and most have not had their technique checked or corrected by a health professional.

Incorrect inhaler technique when using maintenance treatments increases the risk of severe flare-ups and hospitalisation for people with asthma or COPD.[48, 49, 52, 53, 54, 55]

Poor asthma symptom control is often due to incorrect inhaler technique.[56, 57]

Incorrect inhaler technique when using inhaled corticosteroids increases the risk of local side effects like dysphonia and oral thrush.

The steps for using an inhaler device correctly differ between brands. Checklists of correct steps for each inhaler type and how-to videos are available from the National Asthma Council website.

▶ Go to: National Asthma Council Australia's *Using your inhaler* webpage for information, patient resources and videos on inhaler technique
Go to: National Asthma Council Australia's information paper for health professionals on *Inhaler technique for people with asthma or COPD*
Go to: NPS MedicineWise information on *Inhaler devices for respiratory medicines*

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References

1. Chung, K F, Wenzel, S E, Brozek, J L, *et al*. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J*. 2014; 43: 343-73. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24337046
2. Bush, A, Pedersen, S, Hedlin, G, *et al*. Pharmacological treatment of severe, therapy-resistant asthma in children: what can we learn from where?. *Eur Respir J*. 2011; 38: 947-958. Available from: http://erj.ersjournals.com/content/38/4/947.long
3. Bush A, Saglani S. Management of severe asthma in children. *Lancet*. 2010; 376: 814-25. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20816548
4. National Asthma Council Australia,. *Monoclonal antibody therapy for severe asthma. An information paper for health professionals.*. NACA, Melbourne, 2018.
5. Reddel HK, Taylor DR, Bateman ED, *et al*. An official American Thoracic Society/European Respiratory Society statement: asthma control and exacerbations: standardizing endpoints for clinical asthma trials and clinical practice. *Am J Respir Crit Care Med*. 2009; 180: 59-99. Available from: http://ajrccm.atsjournals.org/content/180/1/59.long
6. Chung, K. F., Wenzel, S. E., Brozek, J. L., *et al*. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *The European respiratory journal*. 2014; 43: 343-73. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24337046
7. Bel EH, Sousa A, Fleming L, *et al*. Diagnosis and definition of severe refractory asthma: an international consensus statement from the Innovative Medicine Initiative (IMI). *Thorax*. 2011; 66: 910-917. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21106547
8. Bousquet J, Mantzouranis E, Cruz AA, *et al*. Uniform definition of asthma severity, control, and exacerbations: document presented for the World Health Organization Consultation on Severe Asthma. *J Allergy Clin Immunol*. 2010; 126: 926-38. Available from: http://www.jacionline.org/article/S0091-6749(10)01126-7/fulltext
9. van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma*. The Thoracic Society of Australia and New Zealand, 2010. Available from: https://www.thoracic.org.au/journal-publishing/command/download_file/id/25/filename/The_role_of_corticosteroids_in_the_management_of_childhood_asthma_-_2010.pdf
10. Papi, A., Brightling, C., Pedersen, S. E., Reddel, H. K.. Asthma. *Lancet*. 2018; 391: 783-800. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29273246
11. Chauhan BF, Chartrand C, Ni Chroinin M et al. Addition of long-acting beta2-agonists to inhaled corticosteroids for chronic asthma in children. *Cochrane Database Syst Rev* 2015; Volume 11: CD007949. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26594816

12. Castro-Rodriguez, J. A., Rodrigo, G. J., Rodriguez-Martinez, C. E.. Principal findings of systematic reviews for chronic treatment in childhood asthma. *J Asthma*. 2015; 52: 1038-45. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26303207
13. Ducharme FM, Ni Chroinin M, Greenstone I, Lasserson TJ. Addition of long-acting beta2-agonists to inhaled corticosteroids versus same dose inhaled corticosteroids for chronic asthma in adults and children. *Cochrane Database Syst Rev*. 2010; Issue 5: CD005535. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005535.pub2/full
14. Fitzpatrick AM, Jackson DJ, Mauger DT et al. Individualized therapy for persistent asthma in young children. *J Allergy Clin Immunol*. 2016; 138: 1608-18.e12. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27777180
15. van Asperen PP. Long-acting beta agonists for childhood asthma. *Aust Prescr*. 2012; 35: 111-3. Available from: https://www.nps.org.au/australian-prescriber/articles/long-acting-beta2-agonists-for-childhood-asthma
16. Lemanske RF, Mauger DT, Sorkness CA, *et al*. Step-up therapy for children with uncontrolled asthma receiving inhaled corticosteroids. *N Engl J Med*. 2010; 362: 975-985. Available from: http://www.nejm.org/doi/full/10.1056/NEJMoa1001278#t=article
17. McMahon AW, Levenson MS, McEvoy BW, *et al*. Age and risks of FDA-approved long-acting β2-adrenergic receptor agonists. *Pediatrics*. 2011; 128: e1147-1154. Available from: http://pediatrics.aappublications.org/content/128/5/e1147.long
18. Chauhan BF, Ben Salah R, Ducharme FM. Addition of anti-leukotriene agents to inhaled corticosteroids in children with persistent asthma. *Cochrane Database Syst Rev*. 2013; Issue 10: CD009585. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24089325
19. Fogel RB, Rosario N, Aristizabal G et al. Effect of montelukast or salmeterol added to inhaled fluticasone on exercise-induced bronchoconstriction in children. *Ann Allergy Asthma Immunol* 2010; 104: 511-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20568384
20. Lipworth BJ, Basu K, Donald HP, *et al*. Tailored second-line therapy in asthmatic children with the Arg(16) genotype. *Clin Sci (Lond)*. 2013; 124: 521-528. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23126384
21. Rodrigo GJ, Neffen H. Efficacy and safety of tiotropium in school-age children with moderate-to-severe symptomatic asthma: A systematic review. *Pediatr Allergy Immunol* 2017; 28: 573-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28692145
22. Ciolkowski, J., Mazurek, H., Stasiowska, B.. Evaluation of step-down therapy from an inhaled steroid to montelukast in childhood asthma. *Allergol Immunopathol (Madr)*. 2014; 42: 282-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23684855
23. Nagao M, Ikeda M, Fukuda N, *et al*. Early control treatment with montelukast in preschool children with asthma: a randomized controlled trial. *Allergol Int*. 2018; 67: 72-78. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28526210
24. Kew KM, Beggs S, Ahmad S. Stopping long-acting beta2-agonists (LABA) for children with asthma well controlled on LABA and inhaled corticosteroids. *Cochrane Database Syst Rev*. 2015; Issue 5: CD011316. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25997166
25. Kew, KM; Quinn, M; Quon, B. S; Ducharme, FM;. Increased versus stable doses of inhaled corticosteroids for exacerbations of chronic asthma in adults and children. *Cochrane Database Syst Rev*. 2016; Issue 6: CD007524: . Available from: https://www.ncbi.nlm.nih.gov/pubmed/27272563
26. Basheti, IA; Obeidat, NM; Reddel, HK;. Effect of novel inhaler technique reminder labels on the retention of inhaler technique skills in asthma: a single-blind randomized controlled trial.. *NPJ Prim Care Respir Med*. 2017; 27: 9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28184045
27. Rank, M. A., Johnson, R., Branda, M., *et al*. Long-term outcomes after stepping down asthma controller medications: a claims-based, time-to-event analysis. *Chest*. 2015; 148: 630-639. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4556120/
28. Jacobsen, L., Niggemann, B., Dreborg, S., *et al*. Specific immunotherapy has long-term preventive effect of seasonal and perennial asthma: 10-year follow-up on the PAT study. *Allergy*. 2007; 62: 943-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/17620073
29. Pike, K. C., Akhbari, M., Kneale, D., Harris, K. M.. Interventions for autumn exacerbations of asthma in children. *Cochrane Database Syst Rev*. 2018; Issue 3: Cd012393. Available from: http://cochranelibrary-wiley.com/doi/10.1002/14651858.CD012393.pub2/full
30. Mann, RD; Pearce, GL; Dunn, N; Shakir, S. Sedation with "non-sedating" antihistamines: four prescription-event monitoring studies in general practice. *BMJ (Clinical research ed)*. 2000; 320: 1184-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/10784544
31. Ducharme, F. M., Noya, F. J., Allen-Ramey, F. C., *et al*. Clinical effectiveness of inhaled corticosteroids versus montelukast in children with asthma: prescription patterns and patient adherence as key factors. *Curr Med Res Opin*. 2012; 28: 111-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/22077107
32. Garcia Garcia, ML, Wahn, U, Gilles, L, *et al*. Montelukast, compared with fluticasone, for control of asthma among 6- to 14-year-old patients with mild asthma: The MOSAIC Study. *Pediatrics*. 2005; 116: 360-369. Available from: https://www.ncbi.nlm.nih.gov/pubmed/16061590
33. Fonseca-Aten, M, Okada, P J, Bowlware, K L, *et al*. Effect of clarithromycin on cytokines and chemokines in children with an acute exacerbation of recurrent wheezing: a double-blind, randomized, placebo-controlled trial. *Ann Allergy Asthma Immunol*. 2006; 97: 457-463.
34. Philip, G, Hustad, C, Noonan, G, *et al*. Reports of suicidality in clinical trials of montelukast. *J Allergy Clin Immunol*. 2009; 124: 691-696. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19815114
35. Brożek JL, Bousquet J, Baena-Cagnani CE, *et al*. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 Revision. *J Allergy Clin Immunol*. 2010; 126: 466-476. Available from: http://www.jacionline.org/article/S0091-6749(10)01057-2/fulltext
36. Philip, G., Hustad, C. M., Malice, M. P., *et al*. Analysis of behavior-related adverse experiences in clinical trials of montelukast. *J Allergy Clin Immunol*. 2009; 124: 699-706. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19815116
37. Ali, M. M., O'Brien, C. E., Cleves, M. A., Martin, B. C.. Exploring the possible association between montelukast and neuropsychiatric events among children with asthma: a matched nested case-control study. *Pharmacoepidemiol Drug Saf*. 2015; 24: 435-45. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25683909
38. Therapeutic Goods Administration,. Montelukast – neuropsychiatric risks. *Aust Prescr*. 2013; 36: 168-171. Available from:

https://www.nps.org.au/australian-prescriber/articles/medicines-safety-update-2-58#article
39. Schumock, G T, Stayner, L T, Valuck, R J, *et al*. Risk of suicide attempt in asthmatic children and young adults prescribed leukotriene-modifying agents: a nested case-control study. *J Allergy Clin Immunol*. 2012; 130: 368-375. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22698520
40. Seqirus. *Product Information: Acarizax (standardised allergen extract from the house dust mites*. Therapeutic Goods Administration, Canberra, 2016. Available from: https://www.ebs.tga.gov.au/
41. Stallergenes. *Product Information: Actair Initiation Sublingual Tablets 100 IR & 300 IR and Actair Continuation Treatment Sublingual Tablets 300 IR (mixture of*. Therapeutic Goods Administration, Canberra, 2016. Available from: https://www.ebs.tga.gov.au/
42. Seqirus. *Product Information: Grazax*. Therapeutic Goods Administration, Canberra, 2017. Available from: https://www.ebs.tga.gov.au
43. Stallergenes. *Product Information: Oralair (allergen pollen extract of five grasses)*. Therapeutic Goods Administration, Canberra, 2016. Available from: https://www.ebs.tga.gov.au/
44. Australasian Society of Clinical Immunology and Allergy (ASCIA). *Allergen Immunotherapy*. ASCIA, Sydney, 2013. Available from: http://www.allergy.org.au/patients/allergy-treatment/immunotherapy
45. Stuart, F. A., Segal, T. Y., Keady, S.. Adverse psychological effects of corticosteroids in children and adolescents. *Arch Dis Child*. 2005; 90: 500-6. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1720409/
46. Australian Medicines Handbook. Last modified July 2018: *Australian Medicines Handbook Pty Ltd*. 2018
47. Kelly, H. W., Van Natta, M. L., Covar, R. A., *et al*. Effect of long-term corticosteroid use on bone mineral density in children: a prospective longitudinal assessment in the childhood Asthma Management Program (CAMP) study. *Pediatrics*. 2008; 122: e53-61. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/18595975/
48. The Inhaler Error Steering Committee,, Price, D., Bosnic-Anticevich, S., *et al*. Inhaler competence in asthma: common errors, barriers to use and recommended solutions. *Respir Med*. 2013; 107: 37-46. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23098685
49. Bjermer, L.. The importance of continuity in inhaler device choice for asthma and chronic obstructive pulmonary disease. *Respiration; international review of thoracic diseases*. 2014; 88: 346-52. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25195762
50. Basheti, I A, Armour, C L, Bosnic-Anticevich, S Z, Reddel, H K. Evaluation of a novel educational strategy, including inhaler-based reminder labels, to improve asthma inhaler technique. *Patient Educ Couns*. 2008; 72: 26-33. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18314294
51. Bosnic-Anticevich, S. Z., Sinha, H., So, S., Reddel, H. K.. Metered-dose inhaler technique: the effect of two educational interventions delivered in community pharmacy over time. *The Journal of asthma : official journal of the Association for the Care of Asthma*. 2010; 47: 251-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20394511
52. Melani AS, Bonavia M, Cilenti V, *et al*. Inhaler mishandling remains common in real life and is associated with reduced disease control. *Respir Med*. 2011; 105: 930-8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21367593
53. Levy ML, Dekhuijzen PN, Barnes PJ, *et al*. Inhaler technique: facts and fantasies. A view from the Aerosol Drug Management Improvement Team (ADMIT). *NPJ Prim Care Respir Med*. 2016; 26: 16017. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27098045
54. Haughney, J., Price, D., Barnes, N. C., *et al*. Choosing inhaler devices for people with asthma: current knowledge and outstanding research needs. *Respiratory medicine*. 2010; 104: 1237-45. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20472415
55. Giraud, V., Roche, N.. Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability. *The European respiratory journal*. 2002; 19: 246-51. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11866004
56. Harnett, C. M., Hunt, E. B., Bowen, B. R., *et al*. A study to assess inhaler technique and its potential impact on asthma control in patients attending an asthma clinic. *J Asthma*. 2014; 51: 440-5.
57. Hardwell, A., Barber, V., Hargadon, T., *et al*. Technique training does not improve the ability of most patients to use pressurised metered-dose inhalers (pMDIs). *Prim Care Respir J*. 2011; 20: 92-6. Available from: http://www.nature.com/articles/pcrj201088

Administering inhaled medicines correctly in children

Recommendations

Check the child's inhaler technique at each asthma consultation or when dispensing inhaled asthma medicines:

- **Have the child or parent demonstrate how the child uses the inhaler, while checking against a checklist of steps for that type of inhaler.**
- **Demonstrate correct technique using a placebo device and correct any specific errors identified.**
- **Have the child or parent repeat the demonstration to check they can now use the device correctly. If necessary, repeat instruction until the patient has all steps correct.**
- **Provide the checklist as a reminder, and write down or highlight any steps that were done incorrectly (e.g. on a sticker attached to their inhaler).**

Note: Watch the child/parent use the inhaler – don't just ask if they think they know how to use it properly.

Checklists of steps, and videos demonstrating correct technique, for various types of inhalers are available on National Asthma Council Australia's website.

▶ **Go to: National Asthma Council Australia's *How to use a puffer and spacer for kids* video**
Go to: National Asthma Council Australia's *Using your inhaler* webpage for information, patient resources and videos on inhaler technique
Go to: National Asthma Council Australia's information paper for health professionals on *Inhaler technique for people with asthma or COPD*

How this recommendation was developed

Evidence-based recommendation

Based on literature search and formulated by multidisciplinary working group

Key evidence considered:

- The Inhaler Error Steering Committee 2013[1]
- Basheti *et al.* 2008[2]
- Basheti *et al.* 2017[3]
- Crane *et al.* 2014[4]
- Giraud *et al.* 2011[5]
- Lavorini *et al.* 2014[6]
- Newman *et al.* 2014[7]
- Hesso *et al.* 2016[8]

Last reviewed version 2.0

For children too young to use a mouthpiece (most children under 4 years), deliver inhaled medicines via a pressurised metered-dose inhaler and small-volume spacer with tightly fitting facemask.

Note: The child's face should be washed after using inhaled corticosteroids.

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- Brand *et al.* 2008[9]

Last reviewed version 2.0

For children who are able to cooperate and understand how to seal their lips tightly around a spacer mouthpiece (usually those aged 4 years and over), deliver inhaled medicines via a pressurised metered-dose inhaler and small-volume spacer with a mouthpiece.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

For children using spacers made of plastic (e.g. Breath-A-Tech, Volumatic), advise parents to wash the spacer before first use to reduce electrostatic charge. This should be done by disassembling if necessary, washing in warm water and dishwashing detergent, then allowing to air dry without rinsing or wiping before carefully reassembling.

If a new plastic spacer must be used immediately, it can be primed by firing multiple (at least 10) puffs of medicine into the spacer. (This is an arbitrary number of actuations in the absence of evidence that would enable a precise guideline.) Patients should follow the manufacturer's instructions.

Notes:
Priming or washing spacers to reduce electrostatic charge before using for the first time is only necessary for plastic spacers (e.g. *Breath-A-Tech, Volumatic***). Priming or washing is not necessary for polyurethane/antistatic polymer spacers (e.g.** *Able A2A*, *AeroChamber Plus*, *La Petite E-Chamber, La Grande E-Chamber***) or disposable cardboard spacers (e.g.** *DispozABLE*, *LiteAire***).**

Table. Types of spacers

Name	Material	Cleaning necessary	Priming necessary before first use*
Able A2A	**Antistatic polymer**	**Yes**	**No**
AeroChamber Plus	**Polycarbonate polyurethane**	**Yes**	**No**
Breath-A-Tech	**Plastic**	**Yes**	**Yes**
DispozABLE	**Cardboard**	**No**	**No**
La Grande E-Chamber	**Polycarbonate polyurethane**	**Yes**	**No**
LiteAire	**Cardboard**	**No**	**No**
La Petite E-Chamber	**Polycarbonate polyurethane**	**Yes**	**No**
Volumatic	**Plastic**	**Yes**	**Yes**

Washing: disassemble (if necessary), wash in warm water and dishwashing detergent, then allow to air dry without rinsing or wiping. Reassemble carefully.

Priming plastic spacers: wash and allow to dry (as above) before first use, to reduce static charge. If an unwashed plastic spacer needs to be used immediately, fire multiple (at least 10) actuations of medicine into the spacer, following manufacturer's instructions. (This is an arbitrary number of actuations in the absence of evidence that would enable a precise guideline.)

Last reviewed version 2.0

Asset ID: 98

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Berg 1995[10]
- Brand et al. 2008[9]
- Dompeling et al. 2001[11]
- National Asthma Council Australia 2018[12]

Last reviewed version 2.0

For children using standard plastic spacers (e.g. *Breath-A-Tech*, *Volumatic*) **or polyurethane/antistatic polymer spacers (e.g.** *Able A2A*, *AeroChamber Plus*, *La Petite E-Chamber*, *La Grande E-Chamber*), **advise patients and parents to clean the spacer monthly (but not more often) and after the resolution of any respiratory tract infection.**

To clean a spacer:

- **dismantle as per manufacturer's instructions, if necessary**
- **wash parts in warm water with liquid dishwashing detergent**
- **allow to air dry without rinsing**
- **reassemble carefully, if necessary.**

Notes:
Do not dry spacers with a cloth or paper towel. Wiping can increase the electrostatic charge on the inside of the spacer, which can reduce the available dose.
Spacers become cloudy after use – this is normal and does not affect their use.

Table. Types of spacers

Name	Material	Cleaning necessary	Priming necessary before first use*
Able A2A	**Antistatic polymer**	**Yes**	**No**
AeroChamber Plus	**Polycarbonate polyurethane**	**Yes**	**No**
Breath-A-Tech	**Plastic**	**Yes**	**Yes**
DispozABLE	**Cardboard**	**No**	**No**
La Grande E-Chamber	**Polycarbonate polyurethane**	**Yes**	**No**
LiteAire	**Cardboard**	**No**	**No**
La Petite E-Chamber	**Polycarbonate polyurethane**	**Yes**	**No**
Volumatic	**Plastic**	**Yes**	**Yes**

Washing: disassemble (if necessary), wash in warm water and dishwashing detergent, then allow to air dry without rinsing or wiping. Reassemble carefully.

Priming plastic spacers: wash and allow to dry (as above) before first use, to reduce static charge. If an unwashed plastic spacer needs to be used immediately, fire multiple (at least 10) actuations of medicine into the spacer, following manufacturer's instructions. (This is an arbitrary number of actuations in the absence of evidence that would enable a precise guideline.)

Last reviewed version 2.0

Asset ID: 98

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the

following source(s):

- Berg 1995[10]
- Brand et al. 2008[9]
- Dompeling et al. 2001[11]
- National Asthma Council Australia 2018[12]

Last reviewed version 2.0

When giving multiple puffs via a spacer, shake the inhaler, then fire one puff into the spacer and ask the child to take 4–6 breaths in and out of spacer after each puff.

Shake the inhaler again, and repeat.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

For children taking inhaled corticosteroids, recommend:

- **rinsing the mouth with water and spitting after inhaling the last dose, to minimise the amount of medicine deposited in the oropharynx**
- **using a spacer (if using a manually-actuated pressurised metered-dose inhaler).**

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- van Asperen et al. 2010[13]

Last reviewed version 2.0

Consider using a nebuliser only if a child cannot be taught to inhale medicine from a spacer.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

More information

Administration of inhaled medicines in children: 6 years and over

Parents, carers and children need training to use inhaler devices correctly, including inhaler technique, and care and cleaning of inhalers and spacers.

School-aged children (depending on the child's age, ability, and with individualised training) can learn to use a range of inhaler types, including manually actuated pressurised metered-dose inhalers with spacers, breath-actuated pressurised metered-dose inhalers (e.g. Autohaler), and dry-powder inhalers (e.g. Accuhaler, Turbuhaler).[14, 15, 16, 17, 18]

Table. Types of inhaler devices for delivering asthma and COPD medicines

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/75

A pressurised metered-dose inhaler and spacer is an appropriate first choice for most children.[16]

School-aged children are unlikely to use their inhaler device correctly without careful training and repeated checking.[19]

▶ Go to: National Asthma Council Australia's *How to use a puffer and spacer for kids* video
Go to: National Asthma Council Australia's information paper for health professionals on *Inhaler technique for people with asthma or COPD*

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Correct use of inhaler devices

Checking and correcting inhaler technique is essential to effective asthma management.

Most patients with asthma or COPD do not use their inhalers properly,[1, 20,2, 2, 21] and most have not had their technique checked or corrected by a health professional.

Incorrect inhaler technique when using maintenance treatments increases the risk of severe flare-ups and hospitalisation for people with asthma or COPD.[1, 20, 22, 23, 24, 25]

Poor asthma symptom control is often due to incorrect inhaler technique.[26, 27]

Incorrect inhaler technique when using inhaled corticosteroids increases the risk of local side effects like dysphonia and oral thrush.

The steps for using an inhaler device correctly differ between brands. Checklists of correct steps for each inhaler type and how-to videos are available from the National Asthma Council website.

▶ Go to: National Asthma Council Australia's *Using your inhaler* webpage for information, patient resources and videos on inhaler technique
Go to: National Asthma Council Australia's information paper for health professionals on *Inhaler technique for people with asthma or COPD*
Go to: NPS MedicineWise information on *Inhaler devices for respiratory medicines*

Last reviewed version 2.0

References

1. The Inhaler Error Steering Committee,, Price, D., Bosnic-Anticevich, S., *et al*. Inhaler competence in asthma: common errors, barriers to use and recommended solutions. *Respir Med*. 2013; 107: 37-46. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23098685
2. Basheti, I A, Armour, C L, Bosnic-Anticevich, S Z, Reddel, H K. Evaluation of a novel educational strategy, including inhaler-based reminder labels, to improve asthma inhaler technique. *Patient Educ Couns*. 2008; 72: 26-33. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18314294
3. Basheti, IA; Obeidat, NM; Reddel, HK;. Effect of novel inhaler technique reminder labels on the retention of inhaler technique skills in asthma: a single-blind randomized controlled trial.. *NPJ Prim Care Respir Med*. 2017; 27: 9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28184045
4. Crane, M. A., Jenkins, C. R., Goeman, D. P., Douglass, J. A.. Inhaler device technique can be improved in older adults through tailored education: findings from a randomised controlled trial. *NPJ Prim Care Respir Med*. 2014; 24: 14034. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25188403
5. Giraud, V., Allaert, F. A., Roche, N.. Inhaler technique and asthma: feasability and acceptability of training by pharmacists. *Respir Med*. 2011; 105: 1815-22. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21802271
6. Lavorini, F.. Inhaled drug delivery in the hands of the patient. *Journal of aerosol medicine and pulmonary drug delivery*. 2014; 27: 414-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25238005
7. Newman, S.. Improving inhaler technique, adherence to therapy and the precision of dosing: major challenges for pulmonary drug delivery. *Expert opinion on drug delivery*. 2014; 11: 365-78. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24386924
8. Hesso, I., Gebara, S. N., Kayyali, R.. Impact of community pharmacists in COPD management: Inhalation technique and medication adherence. *Respir Med*. 2016; 118: 22-30. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27578467
9. Brand PL, Baraldi E, Bisgaard H, *et al*. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. *Eur Respir J*. 2008; 32: 1096-1110. Available from: http://erj.ersjournals.com/content/32/4/1096.full
10. Berg E. In vitro properties of pressurized metered dose inhalers with and without spacer devices. *J Aerosol Med*. 1995; 8 Suppl 3: S3-10; discussion S11. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10157897
11. Dompeling E, Oudesluys-Murphy AM, Janssens HM, *et al*. Randomised controlled study of clinical efficacy of spacer therapy in asthma with regard to electrostatic charge. *Arch Dis Child*. 2001; 84: 178-182. Available from: http://adc.bmj.com/content/84/2/178.full
12. National Asthma Council Australia,. *Inhaler technique in adults with asthma or COPD. An information paper for health professionals*. NACA, Melbourne, 2018. Available from: https://www.nationalasthma.org.au/living-with-asthma/resources/health-professionals/information-paper/hp-inhaler-technique-for-people-with-asthma-or-copd

13. van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma*. The Thoracic Society of Australia and New Zealand, 2010. Available from: https://www.thoracic.org.au/journal-publishing/command/download_file/id/25/filename/The_role_of_corticosteroids_in_the_management_of_childhood_asthma_-_2010.pdf
14. Gillette, C., Rockich-Winston, N., Kuhn, J. A., *et al*. Inhaler technique in children with asthma: a systematic review. *Acad Pediatr*. 2016; 16: 605-15. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27130811
15. Capanoglu, M., Dibek Misirlioglu, E., Toyran, M., *et al*. Evaluation of inhaler technique, adherence to therapy and their effect on disease control among children with asthma using metered dose or dry powder inhalers. *J Asthma*. 2015; 52: 838-45. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26037396
16. Ram, F S F, Brocklebank, D D M, White, J, *et al*. Pressurised metered dose inhalers versus all other hand-held inhaler devices to deliver beta-2 agonist bronchodilators for non-acute asthma. *Cochrane Database Syst Rev*. 2002; Issue 2: .
17. Nikander, K, Turpeinen, M, Pelkonen, A S, *et al*. True adherence with the Turbuhaler in young children with asthma. *Arch Dis Child*. 2011; 96: 168-173.
18. Pedersen, S., Mortensen, S.. Use of different inhalation devices in children. *Lung*. 1990; 168 Suppl: 653-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/2117175
19. Sleath, B, Ayala, G X, Gillette, C, *et al*. Provider demonstration and assessment of child device technique during pediatric asthma visits. *Pediatrics*. 2011; 127: 642-648.
20. Bjermer, L.. The importance of continuity in inhaler device choice for asthma and chronic obstructive pulmonary disease. *Respiration; international review of thoracic diseases*. 2014; 88: 346-52. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25195762
21. Bosnic-Anticevich, S. Z., Sinha, H., So, S., Reddel, H. K.. Metered-dose inhaler technique: the effect of two educational interventions delivered in community pharmacy over time. *The Journal of asthma : official journal of the Association for the Care of Asthma*. 2010; 47: 251-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20394511
22. Melani AS, Bonavia M, Cilenti V, *et al*. Inhaler mishandling remains common in real life and is associated with reduced disease control. *Respir Med*. 2011; 105: 930-8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21367593
23. Levy ML, Dekhuijzen PN, Barnes PJ, *et al*. Inhaler technique: facts and fantasies. A view from the Aerosol Drug Management Improvement Team (ADMIT). *NPJ Prim Care Respir Med*. 2016; 26: 16017. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27098045
24. Haughney, J., Price, D., Barnes, N. C., *et al*. Choosing inhaler devices for people with asthma: current knowledge and outstanding research needs. *Respiratory medicine*. 2010; 104: 1237-45. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20472415
25. Giraud, V., Roche, N.. Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability. *The European respiratory journal*. 2002; 19: 246-51. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11866004
26. Harnett, C. M., Hunt, E. B., Bowen, B. R., *et al*. A study to assess inhaler technique and its potential impact on asthma control in patients attending an asthma clinic. *J Asthma*. 2014; 51: 440-5.
27. Hardwell, A., Barber, V., Hargadon, T., *et al*. Technique training does not improve the ability of most patients to use pressurised metered-dose inhalers (pMDIs). *Prim Care Respir J*. 2011; 20: 92-6. Available from: http://www.nature.com/articles/pcrj201088

Planning and conducting routine asthma review for children

Recommendations

As a general guide, review each child's asthma:

- **every 3–6 months when asthma is stable and well controlled**
- **4 weeks after increasing the dose or number of medicines to regain control of partially or poorly controlled asthma**
- **4–6 weeks after reducing dose of preventer or stepping down treatment**
- **within 4 weeks after a visit to the emergency department or a hospital stay due to acute asthma (in addition to early post-acute reassessment within 3 days of discharge).**

Table. Definition of levels of recent asthma symptom control in children (regardless of current treatment regimen)

Good control	Partial control	Poor control
All of: • Daytime symptoms† ≤2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • No limitation of activities‡ • No symptoms§ during night or when wakes up • Need for SABA reliever# ≤2 days per week	**Any of:** • Daytime symptoms† >2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • Any limitation of activities* • Any symptoms during night or when wakes up†† • Need for SABA reliever# >2 days per week	**Either of:** • Daytime symptoms† >2 days per week (lasting from minutes to hours or recurring, and partially or fully relieved by SABA reliever) • ≥3 features of partial control within the same week

SABA: short-acting beta$_2$ agonist

† e.g. wheezing or breathing problems

‡ child is fully active; runs and plays without symptoms

§ including no coughing during sleep

 # not including doses taken prophylactically before exercise. (Record this separately and take into account when assessing management.)

*** e.g. wheeze or breathlessness during exercise, vigorous play or laughing**

†† e.g. waking with symptoms of wheezing or breathing problems

Notes:

Recent asthma control is based on symptoms over the previous 4 weeks. Each child's risk factors for future asthma outcomes should also be assessed and taken into account in management.

Validated questionnaires can be used for assessing recent symptom control:
Test for Respiratory and Asthma Control in Kids (TRACK) for children < 5 years
Childhood Asthma Control Test (C-ACT) for children aged 4–11 years

Last reviewed version 2.0

Asset ID: 23

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

Arrange more frequent follow-up for children with any of the following risk factors:

- **confirmed food allergy**
- **poor asthma control**
- **admission to hospital in preceding 12 months**
- **a history of intubation for acute asthma**
- **over-use of short-acting beta$_2$ agonist reliever**
- **frequent failure to attend consultations**
- **abnormal spirometry findings**
- **reversible expiratory airflow limitation on spirometry despite treatment**
- **poor adherence to preventer**
- **poor inhaler technique for preventer**
- **poor adherence to asthma action plan**
- **significant parental psychological or socioeconomic problems**
- **carer unequipped to manage asthma emergency**
- **exposure to clinically relevant allergens**
- **exposure to tobacco smoke**
- **obesity.**

- **food allergy is risk factor for life-threatening asthma flare-ups**

Notes:
Normal spirometry includes FEV$_1$/FVC greater than lower limit of normal for age and FEV1 % predicted ≥80%.
Reversible expiratory airflow limitation in children is defined as an increase in FEV$_1$ ≥12% from baseline 10–15 minutes after administration of bronchodilator.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- NSW Child Death Review Team 2017[1]
- Consultative Council on Obstetric and Paediatric Mortality and Morbidity[2]
- GINA 2018[3]
- Quezada et al. 2016[4]

Last reviewed version 2.0

At each asthma review, assess:

- **recent asthma symptom control based on reported symptoms, limitation of daily activity and need for reliever medicine**
- **whether the child has any risk factors for poor asthma outcomes in future (e.g. persistent symptoms, over-use of short-acting beta$_2$ agonist reliever, severe asthma, poor adherence, exposure to tobacco smoke, obesity, severe allergies such as food allergies or history of anaphylaxis, previous severe life-threatening acute asthma or hospital admission for asthma, history of sudden severe unpredictable asthma flare-ups, or significant psychosocial factors including socioeconomic deprivation)**
- **lung function using spirometry (for children old enough to perform the test)**
- **adherence to treatment**
- **inhaler technique**
- **whether the written asthma action plan is up to date**
- **modifiable environmental factors including exposure to tobacco smoke or significant airborne allergens**
- **whether parents or child have any concerns about the treatment (e.g. cost, potential side effects).**

Notes:
Assessments can be made by asking the same questions at each visit, or using validated questionnaires.
If children are referred to a lung function laboratory for spirometry for the purpose of monitoring asthma treatment, they should keep taking their

preventer as usual. Inhaled corticosteroid–long-acting beta$_2$ agonist preventers should not be withheld before the test. (If referred for diagnostic spirometry, preventer should be withheld to ensure the test is accurate.)

Table. Definition of levels of recent asthma symptom control in children (regardless of current treatment regimen)

Good control	Partial control	Poor control
All of: • Daytime symptoms† ≤2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • No limitation of activities‡ • No symptoms§ during night or when wakes up • Need for SABA reliever# ≤2 days per week	Any of: • Daytime symptoms† >2 days per week (lasting only a few minutes and rapidly relieved by rapid-acting bronchodilator) • Any limitation of activities* • Any symptoms during night or when wakes up†† • Need for SABA reliever# >2 days per week	Either of: • Daytime symptoms† >2 days per week (lasting from minutes to hours or recurring, and partially or fully relieved by SABA reliever) • ≥3 features of partial control within the same week

SABA: short-acting beta$_2$ agonist

† e.g. wheezing or breathing problems

‡ child is fully active; runs and plays without symptoms

§ including no coughing during sleep

not including doses taken prophylactically before exercise. (Record this separately and take into account when assessing management.)

* e.g. wheeze or breathlessness during exercise, vigorous play or laughing

†† e.g. waking with symptoms of wheezing or breathing problems

Notes:

Recent asthma control is based on symptoms over the previous 4 weeks. Each child's risk factors for future asthma outcomes should also be assessed and taken into account in management.

Validated questionnaires can be used for assessing recent symptom control:
Test for Respiratory and Asthma Control in Kids (TRACK) for children < 5 years
Childhood Asthma Control Test (C-ACT) for children aged 4–11 years

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Table. Sample questions for reviewing asthma in children

Recent symptom control

How often does child wheeze or become short of breath?

Does child wake during the night due to wheezing or shortness of breath? (How many times per month?)

How often does child need to take reliever inhaler? (How many days per week? How many times per day? How many puffs?)*

How many weeks does child's reliever inhaler last?

Has child missed time from childcare, school and or sport due to asthma?

Validated questionnaires are available for assessing recent symptom control:

- Test for Respiratory and Asthma Control in Kids (TRACK) for children < 5 years
- Childhood Asthma Control Test (C-ACT) for children aged 4–11 years

Adherence to preventer treatment (if prescribed)

Does child take a preventer inhaler? (What dose is on the label? How many puffs per day have you been told to use?)

Many children miss some doses. In the last four weeks:

- **how many days a week would your child have taken the preventer medication? None at all? One? Two? (etc).**
- **how many times a day would your child take it? Morning only? Evening only? Morning and evening? (or other)**
- **each time, how many puffs would they take? One? Two? (etc).**

Do you find it easier to remember to give it in the mornings or evenings?

How often does child need new script for preventer medicine? (Note: number of doses per unit varies between brands)

Flare-ups

Has child had a flare-up since last visit?

What triggered it? (e.g. cold symptoms, allergies, stopping preventer)

How was the flare-up treated?

Has child since last visit/ever needed to take oral corticosteroids? (How often and how much?)

Has child ever been hospitalised for asthma or a wheezing episode?

When was the child's last flare-up (and last flare-up before that one)? How were these flare-ups treated?

How many times has child visited GP/hospital emergency room for asthma symptoms in the last [specify time period, e.g. year/month/2 weeks]?

Allergies

Does child have allergic rhinitis (hay fever)?

Is child using other medicines for respiratory symptoms (e.g. oral or intranasal antihistamines, intranasal corticosteroids)?

Does the child have allergies (e.g. to foods or insect bites) or need an adrenaline injector (e.g. *Epipen*) for emergencies?

Does the child get skin rashes caused by allergies?

Inhaler technique

Can you show me how you use the inhaler?

When did you last wash the spacer? (How do you wash it?)

***Note: The use of more than 3 canisters per year (equivalent to use every day) is associated with doubling of the risk of severe flare-ups.[1]**

1: Stanford RH, Shah MB, D'Souza AO et al. Short-acting beta-agonist use and its ability to predict future asthma-related outcomes. Ann Allergy Asthma Immunol 2012; 109: 403-7. (Abstract available from: https://www.ncbi.nlm.nih.gov/pubmed/23176877).

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How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

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Validated checklists or questionnaires can be used to assess recent asthma symptom control at each visit, e.g:

- *Test for Respiratory and Asthma Control in Kids (TRACK)* **– suitable for children under 5 years**
- *Childhood Asthma Control Test (C-ACT)* **– suitable for children aged 4–11 years**

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

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Pharmacists should record the number of times a non-prescription short-acting beta$_2$ agonist is dispensed for a child and ask parents how long puffer usually lasts, so that over-use can be identified and addressed (e.g. by counselling parents about risk of over-use of relievers, assessing asthma control and advising parents to visit their GP if poor control is identified, or alerting the child's GP).

- **Dispensing of 3 or more canisters in a year (average 1.6 puffs per day) is associated with increased risk of exacerbations. Dispensing 12 or more canisters in a year (average 6.6 puffs per day) is associated with increased risk of asthma death.**

Notes:
Recent asthma symptom control can be assessed using validated checklists or questionnaires.
Recording short-acting beta$_2$ reliever dispensing is a regulatory requirement in some states.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Stanford et al. 2012[5]
- Suissa et al. 2000[6]

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For children taking inhaled corticosteroids long term, monitor linear growth. At least annually, measure height and weight, accurately measured and plotted on a percentile chart.

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- van Asperen et al. 2010[7]

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If treatment with high-dose inhaled corticosteroids is needed for 6 months or longer to control asthma or wheezing symptoms, or frequent courses of oral corticosteroids are needed:

- **refer to a paediatric specialist (e.g. paediatric respiratory physician or paediatrician) for assessment, including screening for adrenal suppression**
- **provide specific written advice (steroid alert card) for other health professionals such as emergency services (e.g. that if child shows reduced consciousness, consider the possibility of adrenal insufficiency, check serum biochemistry, blood glucose level and serum cortisol urgently, and consider whether intramuscular hydrocortisone is indicated)**
- **warn parents that adrenal suppression is a possible side effect and advise them what to do if the child develops symptoms consistent with adrenal insufficiency, such as lethargy, vomiting, abdominal pain or seizures (e.g. go to the emergency department without delay, tell staff that the child is using regular high-dose medicine for asthma, and hand them the child's steroid alert card)**
- **advise parents to consider having the child wear a medical alert bracelet.**

Note:
Morning cortisol level is the standard screening test for adrenal suppression. If abnormal, it is followed up with a low-dose adrenocorticotropic hormone stimulation test. Referral to an endocrinologist is indicated if adrenal suppression is suspected or detected.

Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)

	Low	High
Beclometasone dipropionate †	**100–200**	**>200 (maximum 400)**
Budesonide	**200–400**	**>400 (maximum 800)**
Ciclesonide ‡	**80–160**	**>160 (maximum 320)**
Fluticasone propionate	**100–200**	**>200 (maximum 500)**

† Dose equivalents for *Qvar* **(TGA-registered CFC-free formulation of beclometasone dipropionate)**

‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

Source

van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma***. The Thoracic Society of Australia and New Zealand, 2010. Available from: http://www.thoracic.org.au/clinical-documents/area?command=record&id=14**

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How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available), with particular reference to the following source(s):

- Issa-El-Khoury et al. 2015[8]
- van Asperen et al 2010[7]
- Zöllner et al. 2012[9]
- Schwartz et al. 2012[10]
- Ahmet et al. 2011[11]
- Priftis et al. 2009[12]
- Macdessi et al. 2003[13]

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More information

Inhaled corticosteroids for children: adverse effects

Local adverse effects

Hoarseness and pharyngeal candidiasis are not commonly reported among preschool children or school-aged children talking inhaled corticosteroids. [14, 7, 15]

Topical effects can be reduced by use of spacer devices (which reduce oropharyngeal deposition), and by mouth-rinsing and spitting after use.[7] Immediate quick mouth-rinsing removes more residual medicine in the mouth than delayed rinsing.[16]

There is limited evidence that inhaled asthma medication can affect dental health.[7, 17] Mouth rinsing might reduce this risk.

Systemic adverse effects

Systemic effects of inhaled corticosteroids in children depend on the dose, but clinically significant adverse effects are uncommon.[7]

The use of spacers and mouth rinsing will not reduce systemic effects, but the use of a spacer may increase efficacy so that a lower dose is required.

Growth

Short-term suppression of linear growth has been demonstrated in children taking inhaled corticosteroids.[18,19] The effect seems to be

maximal during the first year of therapy and only one study has reported an effect in subsequent years of treatment.[19] A Cochrane systematic review concluded that regular use of inhaled corticosteroid at low or medium daily doses is associated with a mean reduction of 0.48 cm per year in linear growth velocity and 0.61 cm less gain in height during 1 year of treatment in children with mild to moderate persistent asthma.[19]

One study of patients who participated in a clinical trial of inhaled corticosteroids as children, reported a reduction in adult height of approximately 1 cm,[18, 20, 21, 22] whereas several studies have reported that children taking inhaled corticosteroids attained normal adult height.[23, 24, 25]

The effect is dose-dependent[21,22] and may be more likely in children who begin inhaled corticosteroid treatment before age 10.[20]

Other factors affect growth in children with asthma. Uncontrolled asthma itself reduces growth and final adult height.[24] One study found that inhaled corticosteroid equivalent to budesonide 400 microg/day affected growth less than low socioeconomic status.[25]

Bone density

Inhaled corticosteroids have not been associated with effects on bone density or fractures in children. [7] However, data from a recent study in Australia suggested asthma itself is associated with increased incidence of fractures in children, independent of medication.[26]

Given that the total dose of corticosteroids (both inhaled corticosteroids and oral corticosteroids) influences bone health, the aim of asthma management is to maintain symptom control using the lowest inhaled corticosteroid dose required, and to avoid repeated courses of oral corticosteroids.

Adrenal suppression

Biochemical testing in a research setting suggests that hypothalamic–pituitary–adrenal axis suppression may occur in up to two-thirds of children treated with inhaled corticosteroids, and may occur at even low doses.[9] The risk is higher among children receiving concomitant intranasal steroids and those with lower body mass index,[9] and is influenced by genetics.[27]

Clinical adrenal insufficiency in children taking inhaled corticosteroids is rare but has been reported, [11, 12, 28] including cases in Australia.[28] Most cases have involved children given more than 500 microg per day fluticasone propionate.[11]

Adrenal suppression is associated with hypoglycaemia, hypotension, weakness, failure to grow, and is potentially fatal. Hypothalamic–pituitary–adrenal axis suppression may not be detected until adrenal crisis is precipitated by physical stress.[29]

Written information (e.g. a steroid alert card) can be prepared for children receiving long-term high-dose inhaled corticosteroids. Parents/carers can be instructed to present the card if the child ever needs to go to the emergency department (for any reason) or be admitted to hospital. A steroid alert card should state that child has asthma and the inhaled corticosteroid dose. A medical alert bracelet could also be considered.

There are no nationally accepted protocols for routine assessment of adrenal function in primary care because it has not yet been possible to identify precisely which children should be tested, to interpret test results reliably, to identify the appropriate interval for retesting, and because a clinical benefit has not been clearly demonstrated.

Regular monitoring of height might help detect adrenal suppression, based on the findings of a study in which a reduction in linear growth velocity occurred before adrenal suppression.[30]

Table. Definitions of ICS dose levels in children

Inhaled corticosteroid	Daily dose (microg)	
	Low	**High**
Beclometasone dipropionate †	100–200	>200 (maximum 400)
Budesonide	200–400	>400 (maximum 800)
Ciclesonide ‡	80–160	>160 (maximum 320)
Fluticasone propionate	100–200	>200 (maximum 500)

† Dose equivalents for *Qvar* (TGA-registered CFC-free formulation of beclometasone dipropionate)

‡ Ciclesonide is registered by the TGA for use in children aged 6 and over

Source

van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma.* The Thoracic Society of Australia and New Zealand, 2010. Available from: http://www.thoracic.org.au/clinical-documents/area?command=record&id=14

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▶ Go to: The Thoracic Society of Australia and New Zealand's *Position Statement: The role of corticosteroids in the management of childhood asthma*

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Approaches to assessment and monitoring of asthma control in children

Assessment of asthma control in children is based mainly on:

- recent asthma symptom control (assessed by the frequency and severity of symptoms between flare-ups
- the degree to which asthma symptoms affect daily activities such as interference with physical activity or missed school days)
- the frequency of flare-ups
- spirometry in children who are able to perform the test reliably.

Standardised questionnaires

Questionnaire-based instruments have been validated for assessing asthma control in children:

▶ *Test for Respiratory and Asthma Control in Kids (TRACK)* for children less than 5 years old – consists of five questions about frequency of respiratory symptoms (wheeze, cough, shortness of breath), activity limitation, and night-time awakenings in the past 4 weeks, rescue medication use in the past 3 months, and oral corticosteroid use in the previous year.[31, 32] A lower score indicates worse asthma control.

Childhood Asthma Control Test (C-ACT) for children aged 4–11 years – consists of seven items: three for the parent/carer (about the child's symptoms over the previous 4 weeks) and four for the child.[33, 34] A lower score indicates worse asthma control. **Note:** C-ACT is intended for US use.

Lung function tests

Frequent spirometry to guide asthma treatment in children has not been shown to achieve superior outcomes to symptom-based treatment.[35] Current evidence does not support use of home spirometers to guide asthma treatment in children.[36] However, low FEV_1 predicts clinically significant flare-ups, so spirometry should be performed at asthma reviews for children who are old enough to do the test.
The quality and utility of spirometry depends on the skill, clinical expertise and experience of the person doing and interpreting spirometry.

The results of one study in children aged 6–16 years with moderate atopic asthma suggest that asthma treatment guided by airway hyperresponsiveness (measured by bronchial provocation testing) may have a benefit over symptom-guided treatment in improving lung, but this effect was lost after 3–7 years of usual care.[37, 38] Repeated bronchial provocation testing is not feasible in clinical practice.

Measures of airway inflammation

Measures of airway inflammation (e.g. sputum eosinophil count, exhaled nitric oxide measurement) are not recommended in primary care to guide treatment decisions, but are increasingly used in specialist clinics.

Asthma treatment guided by sputum eosinophil count has been shown to reduce the frequency of flare-ups in adults with asthma, but there is insufficient evidence to ascertain its value for children.[39]

Exhaled nitric oxide measurement may be useful in guiding asthma management in some children. In children not taking inhaled corticosteroid, a high nitric oxide level probably predicts a good short-term response to inhaled corticosteroid treatment,[40] but it does not distinguish between asthma and eosinophilic bronchitis and is often high in children with atopy. There is insufficient evidence to ascertain whether a low exhaled nitric oxide level predicts successful withdrawal from inhaled corticosteroids without asthma relapse,[40] or safety of treating asthma without inhaled corticosteroids.

A Cochrane review[41] found that exhaled nitric oxide-guided management was significantly better than other approaches to adjusting medicines for reducing the number of children with flare-ups and the number of children who needed oral corticosteroids, but did not reduce the frequency of flare-ups or the rate of flare-ups requiring hospitalisation, improve lung function or symptoms scores, or reduce inhaled corticosteroid doses. The authors concluded that it could not be recommended for all children but may be beneficial for a subset not yet defined.[41]

Towards personalised asthma care

Emerging understanding of asthma phenotypes and of genetic factors that predict therapeutic response to preventer options is leading to the possibility of personalised, genomics-based treatment for asthma in children.[42] In the near future, individual tailored therapy is may replace the standardised step model based on population data.

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Asthma triggers in children: respiratory tract infections

Viral respiratory infections, such as the common cold, are a frequent cause of wheezing and asthma flare-ups in children, especially in preschool children.

The findings of observational cohort studies and limited randomised controlled trials show that influenza vaccination reduces the number, frequency and duration of asthma flare-ups in children, and lower the rate of emergency department visits and hospitalisation for asthma.[43]

Although bacterial respiratory infections may also trigger wheezing, antibiotics are not routinely indicated for asthma flare-ups or wheezing, and should only be given if they would otherwise be indicated.

▶ See: Preventive care

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Asthma triggers in children: environmental allergens

There is insufficient evidence on which to base recommendations for the reduction of exposure to environmental allergens in the treatment of wheezing in preschool children.[14]

▶ See: *Allergies and asthma*
See: *Asthma triggers*

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Asthma triggers in children: tobacco smoke

There is consistent, high-quality evidence that exposure to environmental tobacco smoke can both cause and worsen wheezing in preschool children.[14, 44]

The Introduction of environmental tobacco controls has led to significant reduction in asthma hospitalisations among children.

▶ See: *Smoking and asthma*
See: *Asthma triggers*

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Written asthma action plans for children

Every child with asthma should have their own written asthma action plan.

A systematic review found that the use of written asthma action plans significantly reduces the rate of visits to acute care facilities, the number of school days missed and night-time waking, and improves symptoms.[45]

For children and adolescents, written asthma action plans that are based on symptoms appear to be more effective than action plans based on peak expiratory flow monitoring.[45]

A written asthma action plan should include all the following:

- a list of the child's usual medicines (names of medicines, doses, when to take each dose) – including treatment for related conditions such as allergic rhinitis
- clear instructions on what to do in all the following situations:
  - when asthma is getting worse (e.g. when needing more reliever than usual, waking up with asthma, more symptoms than usual, asthma is interfering with usual activities)
  - when asthma symptoms get substantially worse (e.g. when needing reliever again within 3 hours, experiencing increasing difficulty breathing, waking often at night with asthma symptoms)
  - during an asthma emergency.
- instructions on when and how to get medical care (including contact telephone numbers)
- the name and contact details of the child's emergency contact person (e.g. parent)
- the name of the person writing the action plan, and the date it was issued.

Table. Checklist for reviewing a written asthma action plan

- Ask if the person (or parent) knows where their written asthma action plan is.
- Ask if they have used their written asthma action plan because of worsening asthma.
- Ask if the person (or parent) has had any problems using their written asthma action plan, or has any comments about whether they find it suitable and effective.
- Check that the medication recommendations are appropriate to the person's current treatment.
- Check that all action points are appropriate to the person's level of recent asthma symptom control.
- Check that the person (or parent) understands and is satisfied with the action points.
- If the written asthma action plan has been used because of worsening asthma more than once in the past 12 months: review the person's usual asthma treatment, adherence, inhaler technique, and exposure to avoidable trigger factors.
- Check that the contact details for medical care and acute care are up to date.

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Templates for written asthma action plans

Templates are available from National Asthma Council Australia:

- National Asthma Council Australia colour-coded plan, available as a printed handout that folds to wallet size and as the *Asthma Buddy* mobile site
- Asthma Cycle of Care asthma action plan
- A plan designed for patients using budesonide/formoterol combination as maintenance and reliever therapy
- Remote Indigenous Australian Asthma Action Plan
- Every Day Asthma Action Plan (designed for remote Indigenous Australians who do not use written English – may also be useful for others for whom written English is inappropriate)
- Children's written asthma action plans.

Some written asthma action plans are available in community languages.

Software for developing electronic pictorial asthma action plans[46, 47] is available online.

▶ Go to: National Asthma Council Australia's *Asthma Action Plan Library*

Download: Imperial College London's *Electronic Asthma Action Plan*

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Asthma education programs for parents/carers and children

Asthma education for children and/or caregivers reduces the risk of emergency department visit for asthma, compared with usual care.[48]

However, the most effective components of education have not been clearly identified.[48, 49] There have been relatively few Australian controlled trials assessing education programs.[49]

There is not enough evidence to tell whether asthma education programs in the child's home are more effective in helping control asthma than asthma education provided somewhere else or standard care,[49] or to identify which types of education is more effective.

All age groups

A systematic review[50] found that asthma education programs were associated with moderate improvement in lung function and with a small reduction in school absence, restriction of physical activity, and emergency department visits. The greatest effects were in children with more severe asthma.[50]

Another systematic review found that educational programmes for the self-management of asthma in children and adolescents improved lung function, reduced the number of school days missed and the number of days with restricted activity, reduced the rate of visits to an emergency department, and possibly reduced the number of disturbed nights.[51]

0-5 years

There is little evidence about the effects of education for parents of preschool-aged children with asthma or wheezing. Most studies have investigated the effects of asthma management education for older children and their parents.[14] Limited evidence suggests that:

- education for parents of preschool children (e.g. written information and review by a health professional, small-group teaching by

nurses or education in the family's home) may help improve asthma control[14]
- education programs are more likely to be effective if they involve multiple sessions, each longer than 20 minutes' duration.[14]

Opportunistic asthma education

In addition to the types of structured or formal asthma education evaluated in research trials, all health professionals who work with children with asthma and their parents/carers can provide asthma education whenever the opportunity occurs.

Table. Childhood asthma education checklist

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/30

Resources

Education resources are available from the National Asthma Council Australia, Asthma Australia, and the Asthma Foundation in your state or territory.

▶ Go to: *National Asthma Council Australia*
Go to: *Asthma Australia*

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Correct use of inhaler devices

Checking and correcting inhaler technique is essential to effective asthma management.

Most patients with asthma or COPD do not use their inhalers properly,[52, 53,54, 54, 55] and most have not had their technique checked or corrected by a health professional.

Incorrect inhaler technique when using maintenance treatments increases the risk of severe flare-ups and hospitalisation for people with asthma or COPD.[52, 53, 56, 57, 58, 59]

Poor asthma symptom control is often due to incorrect inhaler technique.[60, 61]

Incorrect inhaler technique when using inhaled corticosteroids increases the risk of local side effects like dysphonia and oral thrush.

The steps for using an inhaler device correctly differ between brands. Checklists of correct steps for each inhaler type and how-to videos are available from the National Asthma Council website.

▶ Go to: National Asthma Council Australia's *Using your inhaler* webpage for information, patient resources and videos on inhaler technique
Go to: National Asthma Council Australia's information paper for health professionals on *Inhaler technique for people with asthma or COPD*
Go to: NPS MedicineWise information on *Inhaler devices for respiratory medicines*

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Common reasons for poor response to preventer treatment

Apparent lack of response to asthma treatment is commonly due to one or more of the following:[62]

- poor adherence (which may be due to lack of perceived need for the medication, concern about potential or actual side-effects, cost of medicines, a busy lifestyle, misunderstanding of the purpose and effects of asthma medicines, or inability to follow the medical instructions)
- poor inhaler technique
- mishandling devices (e.g. failure to clean spacer, allowing mouthpiece of dry-powder inhalers to become blocked)
- incorrect dose or frequency
- empty inhaler
- expired medicines
- continued exposure to smoke or allergen triggers.

Failure to identify these causes before adjusting medicines could result in over-medication with preventers.

▶ See: *Management challenges*

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References

1. NSW Child Death Review Team,. *NSW Child Death Review Team annual report 2016–17*. NSW Ombudsman, Sydney, 2017.
2. The Consultative Council on Obstetric and Paediatric Mortality and Morbidity,. *Victoria's mothers, babies and children 2014 and 2015*. Victoria State Government Health and Human Services, Melbourne, 2017.
3. Global Initiative for Asthma (GINA). *Global strategy for asthma management and prevention*. 2018. Available from: https://ginasthma.org/
4. Quezada, W., Kwak, E. S., Reibman, J., *et al*. Predictors of asthma exacerbation among patients with poorly controlled asthma despite inhaled corticosteroid treatment. *Ann Allergy Asthma Immunol*. 2016; 116: 112-7. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/26712474/
5. Stanford, R. H., Shah, M. B., D'Souza, A. O., *et al*. Short-acting beta-agonist use and its ability to predict future asthma-related outcomes. *Ann Allergy Asthma Immunol*. 2012; 109: 403-7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23176877
6. Suissa, S, Ernst, P, Benayoun, S, *et al*. Low-dose inhaled corticosteroids and the prevention of death from asthma. *N Engl J Med*. 2000; 343: 332-336.
7. van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma*. The Thoracic Society of Australia and New Zealand, 2010. Available from: https://www.thoracic.org.au/journal-publishing/command/download_file/id/25/filename/The_role_of_corticosteroids_in_the_management_of_childhood_asthma_-_2010.pdf
8. Issa-El-Khoury K, Kim H, Chan ES, *et al*. CSACI position statement: systemic effect of inhaled corticosteroids on adrenal suppression in the management of pediatric asthma. *Allergy Asthma Clin Immunol*. 2015; 11: 9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25802532/
9. Zöllner EW, Lombard CJ, Galal U, *et al*. Hypothalamic-adrenal-pituitary axis suppression in asthmatic school children. *Pediatrics*. 2012; 130: e1512-19. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23147980
10. Schwartz, R. H., Neacsu, O., Ascher, D. P., Alpan, O.. Moderate dose inhaled corticosteroid-induced symptomatic adrenal suppression: case report and review of the literature. *Clin Pediatr (Phila)*. 2012; 51: 1184-90. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23043135
11. Ahmet A, Kim H, Spier S. Adrenal suppression: A practical guide to the screening and management of this under-recognized complication of inhaled corticosteroid therapy. *Allergy Asthma Clin Immunol*. 2011; 7: 13. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3177893/
12. Priftis, K N, Papadimitriou, A, Anthracopoulos, M B, Fretzayas, A, Chrousos, G P. Endocrine-immune interactions in adrenal function of asthmatic children on inhaled corticosteroids. *Neuroimmunomodulation* 2008; 16: 333-339.
13. Macdessi, J S, van Asperen, P P, Randell, T L, *et al*. Adrenal crises in children treated with high-dose inhaled corticosteroids for asthma. *Med J Aust*. 2003; 178: 214-216.
14. Brand PL, Baraldi E, Bisgaard H, *et al*. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. *Eur Respir J*. 2008; 32: 1096-1110. Available from: http://erj.ersjournals.com/content/32/4/1096.full
15. Cazeiro C, Silva C, Mayer S et al. Inhaled corticosteroids and respiratory infections in children with asthma: a meta-analysis. *Pediatrics*. 2017; 139. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28235797
16. Yokoyama H, Yamamura Y, Ozeki T, *et al*. Effects of mouth washing procedures on removal of budesonide inhaled by using Turbuhaler. *Yakugaku Zasshi*. 2007; 127: 1245-1249. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17666876
17. Godara N, Godara R, Khullar M. Impact of inhalation therapy on oral health. *Lung India*. 2011; 28: 272-5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/22084541
18. Loke YK, Blanco P, Thavarajah M, Wilson AM. Impact of inhaled corticosteroids on growth in children with asthma: systematic review and meta-analysis. *PloS One*. 2015; 10: e0133428. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26191797
19. Zhang L, Prietsch SO, Ducharme FM. Inhaled corticosteroids in children with persistent asthma: effects on growth. *Cochrane Database Syst Rev*. 2014: Cd009471. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25030198
20. Kelly HW, Sternberg AL, Lescher R, *et al*. Effect of inhaled glucocorticoids in childhood on adult height. *N Engl J Med*. 2012; 367: 904-12. Available from: http://www.nejm.org/doi/full/10.1056/NEJMoa1203229
21. Pruteanu AI, Chauhan BF, Zhang L et al. Inhaled corticosteroids in children with persistent asthma: dose-response effects on growth. *Cochrane Database Syst Rev*. 2014: Cd009878. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25030199
22. De Leonibus C, Attanasi M, Roze Z et al. Influence of inhaled corticosteroids on pubertal growth and final height in asthmatic children. *Pediatr Allergy Immunol*. 2016; 27: 499-506. Available from:https://www.ncbi.nlm.nih.gov/pubmed/26919136
23. Pauwels RA, Pedersen S, Busse WW, *et al*. Early intervention with budesonide in mild persistent asthma: a randomised, double-blind trial. *Lancet*. 2003; 361: 1071-1076. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12672309
24. Pedersen S. Do inhaled corticosteroids inhibit growth in children? *Am J Respir Crit Care Med*. 2001; 164: 521-35. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11520710
25. Agertoft L, Pedersen S. Effect of long-term treatment with inhaled budesonide on adult height in children with asthma. *N Engl J Med*. 2000; 343: 1064-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11027740
26. Degabriele EL, Holloway KL, Pasco JA et al. Associations between asthma status and radiologically confirmed fracture in children: A data-linkage study. *J Paediatr Child Health*. 2018; 54(8): 855-860. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29614205
27. Hawcutt DB, Francis B, Carr DF et al. Susceptibility to corticosteroid-induced adrenal suppression: a genome-wide association study. *Lancet Respir Med*. 2018; 6:442-450. Available from: https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(18)30058-4/fulltext
28. Macdessi JS, Randell TL, Donaghue KC, *et al*. Adrenal crises in children treated with high-dose inhaled corticosteroids for asthma. *Med J Aust*. 2003; 178: 214-6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12603184
29. Rao Bondugulapati LN, Rees DA. Inhaled corticosteroids and HPA axis suppression: how important is it and how should it be managed? *Clin Endocrinol (Oxf)*. 2016; 85: 165-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27038017

30. Liddell BS, Oberlin JM, Hsu DP. Inhaled corticosteroid related adrenal suppression detected by poor growth and reversed with ciclesonide. *J Asthma*. 2017; 54: 99-104. Available from:https://www.ncbi.nlm.nih.gov/pubmed/27284755
31. Murphy KR, Zeiger RS, Kosinski M, *et al*. Test for respiratory and asthma control in kids (TRACK): a caregiver-completed questionnaire for preschool-aged children. *J Allergy Clin Immunol*. 2009; 123: 833-9. Available from: http://www.jacionline.org/article/S0091-6749(09)00212-7/fulltext
32. Zeiger RS, Mellon M, Chipps B, *et al*. Test for Respiratory and Asthma Control in Kids (TRACK): clinically meaningful changes in score. *J Allergy Clin Immunol*. 2011; 128: 983-8. Available from: http://www.jacionline.org/article/S0091-6749(11)01287-5/fulltext
33. Liu AH, Zeiger R, Sorkness C, *et al*. Development and cross-sectional validation of the Childhood Asthma Control Test. *J Allergy Clin Immunol*. 2007; 119: 817-25. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17353040
34. Liu AH, Zeiger RS, Sorkness CA, *et al*. The Childhood Asthma Control Test: retrospective determination and clinical validation of a cut point to identify children with very poorly controlled asthma. *J Allergy Clin Immunol*. 2010; 126: 267-73, 273.e1. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20624640
35. Abramson MJ, Schattner RL, Holton C et al. Spirometry and regular follow-up do not improve quality of life in children or adolescents with asthma: Cluster randomized controlled trials. *Pediatr Pulmonol* 2015; 50: 947-54. (Available from: https://www.ncbi.nlm.nih.gov/pubmed/25200397
36. Deschildre A, Beghin L, Salleron J, *et al*. Home telemonitoring (forced expiratory volume in 1 s) in children with severe asthma does not reduce exacerbations. *Eur Respir J*. 2012; 39: 290-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/21852334
37. Nuijsink M, Hop WC, Sterk PJ et al. Long-term asthma treatment guided by airway hyperresponsiveness in children: a randomised controlled trial. *Eur Respir J* 2007; 30: 457-66. (Available from: https://www.ncbi.nlm.nih.gov/pubmed/17537770
38. Nuijsink M, Vaessen-Verberne AA, Hop WC et al. Long-term follow-up after two years of asthma treatment guided by airway responsiveness in children. *Respir Med* 2013; 107: 981-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23672993
39. Petsky HL, Li A, Chang AB. Tailored interventions based on sputum eosinophils versus clinical symptoms for asthma in children and adults. *Cochrane Database Syst Rev* 2017; 8: Cd005603. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28837221
40. Lehtimaki L, Csonka P, Makinen E et al. Predictive value of exhaled nitric oxide in the management of asthma: a systematic review. *Eur Respir J* 2016; 48: 706-14. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27492830
41. Petsky HL, Kew KM, Chang AB. Exhaled nitric oxide levels to guide treatment for children with asthma. *Cochrane Database Syst*. Rev 2016; Issue 11: CD011439. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27825189/
42. Turner S, Francis B, Vijverberg S et al. Childhood asthma exacerbations and the Arg16 beta2-receptor polymorphism: A meta-analysis stratified by treatment. *J Allergy Clin Immunol* 2016; 138: 107-13.e5. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26774659
43. Vasileiou, E., Sheikh, A., Butler, C., *et al*. Effectiveness of influenza vaccines in asthma: a systematic review and meta-analysis. *Clin Infect Dis*. 2017; 65: 1388-1395. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28591866 Full text at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5850022
44. Burke H, Leonardi-Bee J, Hashim A, *et al*. Prenatal and passive smoke exposure and incidence of asthma and wheeze: systematic review and meta-analysis. *Pediatrics*. 2012; 129: 735-744. Available from: http://pediatrics.aappublications.org/content/129/4/735.long
45. Zemek RL, Bhogal S, Ducharme FM. Systematic Review of Randomized Controlled Trials Examining Written Action Plans in Children - What Is the Plan?. *Arch Pediatr Adolesc Med*. 2008; 162: 157-63. Available from: http://archpedi.jamanetwork.com/article.aspx?articleid=379087#tab1
46. Roberts NJ, Mohamed Z, Wong PS, *et al*. The development and comprehensibility of a pictorial asthma action plan. *Patient Educ Couns*. 2009; 74: 12-18. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18789626
47. Roberts NJ, Evans G, Blenkhorn P, Partridge M. Development of an electronic pictorial asthma action plan and its use in primary care. *Patient Educ Couns*. 2010; 80: 141-146. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19879092
48. Coffman JM, Cabana MD, Halpin HA, Yelin EH. Effects of asthma education on children's use of acute care services: a meta-analysis. *Pediatrics*. 2008; 121: 575-86. Available from: http://pediatrics.aappublications.org/content/121/3/575.long
49. Welsh EJ, Hasan M, Li P. Home-based educational interventions for children with asthma. *Cochrane Database Syst Rev*. 2011; Issue 10: CD008469. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008469.pub2/full
50. Wolf F, Guevara JP, Grum CM, *et al*. Educational interventions for asthma in children. *Cochrane Database Syst Rev*. 2002; Issue 4: CD000326. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000326/full
51. Guevara JP, Wolf FM, Grum CM, Clark NM. Effects of educational interventions for self management of asthma in children and adolescents: systematic review and meta-analysis. *BMJ*. 2003; 326: 1308-1309. Available from: http://www.bmj.com/content/326/7402/1308
52. The Inhaler Error Steering Committee,, Price, D., Bosnic-Anticevich, S., *et al*. Inhaler competence in asthma: common errors, barriers to use and recommended solutions. *Respir Med*. 2013; 107: 37-46. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23098685
53. Bjermer, L.. The importance of continuity in inhaler device choice for asthma and chronic obstructive pulmonary disease. *Respiration; international review of thoracic diseases*. 2014; 88: 346-52. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25195762
54. Basheti, I A, Armour, C L, Bosnic-Anticevich, S Z, Reddel, H K. Evaluation of a novel educational strategy, including inhaler-based reminder labels, to improve asthma inhaler technique. *Patient Educ Couns*. 2008; 72: 26-33. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18314294
55. Bosnic-Anticevich, S. Z., Sinha, H., So, S., Reddel, H. K.. Metered-dose inhaler technique: the effect of two educational interventions delivered in community pharmacy over time. *The Journal of asthma : official journal of the Association for the Care of Asthma*. 2010; 47:

251-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20394511
56. Melani AS, Bonavia M, Cilenti V, *et al*. Inhaler mishandling remains common in real life and is associated with reduced disease control. *Respir Med*. 2011; 105: 930-8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21367593
57. Levy ML, Dekhuijzen PN, Barnes PJ, *et al*. Inhaler technique: facts and fantasies. A view from the Aerosol Drug Management Improvement Team (ADMIT). *NPJ Prim Care Respir Med*. 2016; 26: 16017. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27098045
58. Haughney, J., Price, D., Barnes, N. C., *et al*. Choosing inhaler devices for people with asthma: current knowledge and outstanding research needs. *Respiratory medicine*. 2010; 104: 1237-45. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20472415
59. Giraud, V., Roche, N.. Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability. *The European respiratory journal*. 2002; 19: 246-51. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11866004
60. Harnett, C. M., Hunt, E. B., Bowen, B. R., *et al*. A study to assess inhaler technique and its potential impact on asthma control in patients attending an asthma clinic. *J Asthma*. 2014; 51: 440-5.
61. Hardwell, A., Barber, V., Hargadon, T., *et al*. Technique training does not improve the ability of most patients to use pressurised metered-dose inhalers (pMDIs). *Prim Care Respir J*. 2011; 20: 92-6. Available from: http://www.nature.com/articles/pcrj201088
62. Bush A, Saglani S. Management of severe asthma in children. *Lancet*. 2010; 376: 814-25. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20816548

Managing triggers in children

Recommendations

Advise parents/carers to ensure that children are not exposed to tobacco smoke and to ensure that the home and car are smoke-free zones. Explain that smoking outdoors near children still exposes children to smoke.

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

All health professionals should advise parents and household members about smoking cessation options and support them to quit smoking.

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- RACGP 2014[1]

Last reviewed version 2.0

Identify aeroallergens to which the child is sensitised and reduce exposure to allergic triggers, where avoidance is feasible and has been shown to be effective and cost-effective.

Table. Summary of asthma triggers

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/52

▶ **See:** Considering allergen avoidance where feasible

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

More information

Back-to-school asthma care

Each year during February, a few days after the school year starts, there is an annual increase in asthma flare-ups among children with asthma.

Asthma flare-ups in children, including those resulting in emergency department presentations and hospitalisations, surge during the first month of the school year. [2, 3, 4, 6] There are smaller increases at the beginning of the other school terms.[7] These flare-ups may be due to changes in exposure to virus, allergens, pollution and/or stress during the early days after school return.[8]

Primary care health professionals can help parents/carers prepare for back-to-school flare-ups by:

- recommending a full asthma review at the end of the school holidays to check asthma control, adherence to preventer and inhaler technique
- ensuring that each child has an up-to-date written asthma action plan and the child and/or parents/carers understand how to follow it
- reminding parents/carers to get their child back into their asthma routine before the school year starts, including taking preventer medications every day, if prescribed

▶ Go to: National Asthma Council Australia's Back to school checklist for kids with asthma

Last reviewed version 2.0

Thunderstorm asthma

Certain types of thunderstorms in spring or early summer in regions with high grass pollen concentrations in the air can cause life-threatening allergic asthma flare-ups in individuals sensitised to rye grass, even if they have not had asthma before.[9, 10, 11, 12, 13]

Sensitisation to rye grass allergen is almost universal in patients who have reported flare-ups consistent with thunderstorm asthma in Australia.

People with allergic rhinitis and allergy to ryegrass pollen (i.e. most people with springtime allergic rhinitis symptoms) are at risk of thunderstorm asthma if they live in, or are travelling to, a region with seasonal high grass pollen levels – even if they have never had asthma symptoms before. This includes people with undiagnosed asthma, no previous asthma, known asthma.[9, 10] Lack of inhaled corticosteroid preventer treatment has been identified as a risk factor.[9]

Epidemics of thunderstorm asthma can occur when such a storm travels across a region and triggers asthma in many susceptible individuals. Epidemic thunderstorm asthma events are uncommon, but when they occur can they make a high demand on ambulance and health services.[14, 13, 15]

Data from thunderstorm asthma epidemics suggest that the risk of asthma flare-ups being triggered by a thunderstorm is highest in adults who are sensitised to grass pollen and have seasonal allergic rhinitis (with or without known asthma).[9]

The worst outcomes are seen in people with poorly controlled asthma.[14] Treatment with an inhaled corticosteroid asthma preventer was significantly protective in a well-conducted Australian case-control study.[10]

There is insufficient evidence to determine whether intranasal corticosteroids help protect against thunderstorm asthma. Intranasal corticosteroids reduce symptoms of allergic rhinitis and limited indirect evidence suggests they may protect against asthma flare-ups in people not taking inhaled corticosteroids.[16]

The effectiveness of specific allergen immunotherapy in protecting against thunderstorm asthma has not been evaluated in randomised clinical trials, but data from a small Australian open-label study suggest that short-term treatment with five-grass sublingual immunotherapy may have been protective in individuals.[17]

▶ Go to: National Asthma Council Australia's *Epidemic thunderstorm asthma* information paper
Go to: ASCIA's *Pollen calendar*
Go to: *Vic Emergency's Thunderstorm asthma forecast (Victoria only)*

Last reviewed version 2.0

Asthma triggers in children: respiratory tract infections

Viral respiratory infections, such as the common cold, are a frequent cause of wheezing and asthma flare-ups in children, especially in preschool children.

The findings of observational cohort studies and limited randomised controlled trials show that influenza vaccination reduces the number, frequency and duration of asthma flare-ups in children, and lower the rate of emergency department visits and hospitalisation for asthma.[18]

Although bacterial respiratory infections may also trigger wheezing, antibiotics are not routinely indicated for asthma flare-ups or wheezing, and should only be given if they would otherwise be indicated.

▶ See: Preventive care

Last reviewed version 2.0

Asthma triggers in children: environmental allergens

There is insufficient evidence on which to base recommendations for the reduction of exposure to environmental allergens in the

treatment of wheezing in preschool children.[19]

▶ See: *Allergies and asthma*
See: *Asthma triggers*

Last reviewed version 2.0

Asthma triggers in children: tobacco smoke

There is consistent, high-quality evidence that exposure to environmental tobacco smoke can both cause and worsen wheezing in preschool children.[19, 20]

The Introduction of environmental tobacco controls has led to significant reduction in asthma hospitalisations among children.

▶ See: *Smoking and asthma*
See: *Asthma triggers*

Last reviewed version 2.0

References

1. Royal Australian College of General Practitioners,. *Supporting smoking cessation. A guide for health professionals*. RACGP, 2014. Available from: https://www.racgp.org.au/your-practice/guidelines/smoking-cessation/
2. Johnston NW, Johnston SL, Duncan JM et al. The September epidemic of asthma exacerbations in children: a search for etiology. *J Allergy Clin Immunol* 2005; 115: 132-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/15637559
3. Sears MR, Johnston NW. Understanding the September asthma epidemic. *J Allergy Clin Immunol* 2007; 120: 526-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/17658590
4. Eggo RM, Scott JG, Galvani AP, Meyers LA. Respiratory virus transmission dynamics determine timing of asthma exacerbation peaks: Evidence from a population-level model. *Proc Natl Acad Sci U S A* 2016; 113: 2194-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26858436
5. Ahmet, A, Kim, H, Spier, S. Adrenal suppression: A practical guide to the screening and management of this under-recognized complication of inhaled corticosteroid therapy. *Allergy Asthma Clin Immunol*. 2011; 7: 13.
6. Australian Institute of Health and Welfare. *Asthma hospitalisations in Australia 2010-11*. Australian Institute of Health and Welfare, Canberra, 2013. Available from: http://www.aihw.gov.au/publication-detail/?id=60129544541
7. Australian Centre for Asthma Monitoring. *Asthma in Australia 2011: with a focus chapter on chronic obstructive pulmonary disease*. Asthma series no. 4. Cat. no ACM 22. Australian Institute of Health and Welfare, Canberra, 2011. Available from: http://www.aihw.gov.au/publication-detail/?id=10737420159
8. Tovey ER, Rawlinson WD. A modern miasma hypothesis and back-to-school asthma exacerbations. *Med Hypotheses* 2011; 76: 113-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20869177
9. Davies J, Queensland University of Technology. Literature review on thunderstorm asthma and its implications for public health advice. Final report. Melbourne: *Victorian State Government Department of Health and Human Services*; 2017. Available from: https://www2.health.vic.gov.au/about/publications/researchandreports/thunderstorm-asthma-literature-review-may-2107/
10. Girgis ST, Marks GB, Downs SH et al. Thunderstorm-associated asthma in an inland town in south-eastern Australia. Who is at risk? *Eur Respir J* 2000; 16: 3-8.
11. Marks GB, Colquhoun JR, Girgis ST, *et al*. Thunderstorm outflows preceding epidemics of asthma during spring and summer. *Thorax*. 2001; 56: 468-71.
12. D'Amato G, Vitale C, D'Amato M et al. Thunderstorm-related asthma: what happens and why. *Clin Exp Allergy* 2016; 46: 390-6.
13. Victoria State Government Department of Health and Human Services. *The November 2016 Victorian epidemic thunderstorm asthma event: an assessment of the health impacts. The Chief Health Officer's Report, 27 April 2017*. Melbourne: Victorian Government; 2017.
14. Thien F, Beggs PJ, Csutoros D et al. The Melbourne epidemic thunderstorm asthma event 2016: an investigation of environmental triggers, effect on health services, and patient risk factors. *Lancet Planet Health* 2018; 2: e255-e63. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29880157/
15. Andrew E, Nehme Z, Bernard S et al. Stormy weather: a retrospective analysis of demand for emergency medical services during epidemic thunderstorm asthma. *BMJ* 2017; 359: j5636. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29237604/
16. Lohia S, Schlosser RJ, Soler ZM. Impact of intranasal corticosteroids on asthma outcomes in allergic rhinitis: a meta-analysis. *Allergy*. 2013; 68: 569-79. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23590215/
17. O'Hehir RE, Varese NP, Deckert K et al. Epidemic thunderstorm asthma protection with five-grass pollen tablet sublingual immunotherapy: a clinical trial. *Am J Respir Crit Care Med* 2018; 198: 126-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29461859/
18. Vasileiou, E., Sheikh, A., Butler, C., *et al*. Effectiveness of influenza vaccines in asthma: a systematic review and meta-analysis. *Clin Infect Dis*. 2017; 65: 1388-1395. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28591866 Full text at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5850022

19. Brand PL, Baraldi E, Bisgaard H, *et al*. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. *Eur Respir J*. 2008; 32: 1096-1110. Available from: http://erj.ersjournals.com/content/32/4/1096.full
20. Burke H, Leonardi-Bee J, Hashim A, *et al*. Prenatal and passive smoke exposure and incidence of asthma and wheeze: systematic review and meta-analysis. *Pediatrics*. 2012; 129: 735-744. Available from: http://pediatrics.aappublications.org/content/129/4/735.long

Providing asthma management education for parents and children

Recommendations

Provide parents (and children, if old enough) with asthma education that includes information about asthma symptoms and signs, asthma medicines, and how to take inhaled medicines correctly.

Table. Childhood asthma education checklist

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/30

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

Provide a written asthma action plan for all children with asthma, and train parents (and older children) how to follow it.

▶ Go to: National Asthma Council Australia's Asthma Action Plan Library

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

Review the child's written asthma action plan at least yearly and whenever asthma control status changes significantly or medicines are changed or stopped.

Table. Checklist for reviewing a written asthma action plan

- **Ask if the person (or parent) knows where their written asthma action plan is.**
- **Ask if they have used their written asthma action plan because of worsening asthma.**
- **Ask if the person (or parent) has had any problems using their written asthma action plan, or has any comments about whether they find it suitable and effective.**
- **Check that the medication recommendations are appropriate to the person's current treatment.**
- **Check that all action points are appropriate to the person's level of recent asthma symptom control.**
- **Check that the person (or parent) understands and is satisfied with the action points.**
- **If the written asthma action plan has been used because of worsening asthma more than once in the past 12 months: review the person's usual asthma treatment, adherence, inhaler technique, and exposure to avoidable trigger factors.**
- **Check that the contact details for medical care and acute care are up to date.**

Asset ID: 43

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

Provide parents of wheezing preschool children with education that includes information on:

- **causes of wheeze**
- **when wheezing is clinically significant (i.e. when accompanied by increased work of breathing or severe enough to interrupt eating, play, physical activity or sleep)**
- **effective treatment options**
- **how to recognise worsening asthma symptoms (a flare-up).**

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

Provide training for children and parents on how to use inhaler devices correctly, including inhaler technique and the care and cleaning of devices and spacers. Review technique each time asthma medicines are dispensed or prescribed.

▶ **See: Inhaler devices and technique**

How this recommendation was developed

Consensus

Based on clinical experience and expert opinion (informed by evidence, where available).

Last reviewed version 2.0

Advise parents that inhaled medications might affect dental health. Advise rinsing and spitting after taking inhaled medicines to minimise local absorption and the risk of oropharyngeal candidiasis ('thrush') with inhaled corticosteroids, and possibly reduce the risk of dental caries with inhaled beta$_2$ agonists.

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- van Asperen et al. 2010[1]
- National Asthma Council Australia 2018[2]

Last reviewed version 2.0

Advise parents to ensure children have adequate exposure to sunlight to maintain healthy vitamin D levels, while avoiding excess exposure to UV radiation.

Note: Parents can use the Sunsmart app to determine safe exposure times in their region for different times of year.

▶ **Go to: Cancer Council Victoria's and the Victorian Health Promotion Foundation (VicHealth)'s *Sunsmart* initiative**
Go to: *Australian and New Zealand Bone and Mineral Society, the Australasian College of Dermatologists, Cancer Council Australia, Endocrine Society of Australia and Osteoporosis Australia* position statement on sun exposure and vitamin D

How this recommendation was developed

Adapted from existing guidance

Based on reliable clinical practice guideline(s) or position statement(s):

- Cancer Council Australia[3]
- Paxton et al. 2013[4]

Last reviewed version 2.0

More information

Written asthma action plans for children

Every child with asthma should have their own written asthma action plan.

A systematic review found that the use of written asthma action plans significantly reduces the rate of visits to acute care facilities, the number of school days missed and night-time waking, and improves symptoms.[5]

For children and adolescents, written asthma action plans that are based on symptoms appear to be more effective than action plans based on peak expiratory flow monitoring.[5]

A written asthma action plan should include all the following:

- a list of the child's usual medicines (names of medicines, doses, when to take each dose) – including treatment for related conditions such as allergic rhinitis
- clear instructions on what to do in all the following situations:
  - when asthma is getting worse (e.g. when needing more reliever than usual, waking up with asthma, more symptoms than usual, asthma is interfering with usual activities)
  - when asthma symptoms get substantially worse (e.g. when needing reliever again within 3 hours, experiencing increasing difficulty breathing, waking often at night with asthma symptoms)
  - during an asthma emergency.
- instructions on when and how to get medical care (including contact telephone numbers)
- the name and contact details of the child's emergency contact person (e.g. parent)
- the name of the person writing the action plan, and the date it was issued.

Table. Checklist for reviewing a written asthma action plan

- Ask if the person (or parent) knows where their written asthma action plan is.
- Ask if they have used their written asthma action plan because of worsening asthma.
- Ask if the person (or parent) has had any problems using their written asthma action plan, or has any comments about whether they find it suitable and effective.
- Check that the medication recommendations are appropriate to the person's current treatment.
- Check that all action points are appropriate to the person's level of recent asthma symptom control.
- Check that the person (or parent) understands and is satisfied with the action points.
- If the written asthma action plan has been used because of worsening asthma more than once in the past 12 months: review the person's usual asthma treatment, adherence, inhaler technique, and exposure to avoidable trigger factors.
- Check that the contact details for medical care and acute care are up to date.

Asset ID: 43

Templates for written asthma action plans

Templates are available from National Asthma Council Australia:

- National Asthma Council Australia colour-coded plan, available as a printed handout that folds to wallet size and as the *Asthma Buddy* mobile site
- Asthma Cycle of Care asthma action plan
- A plan designed for patients using budesonide/formoterol combination as maintenance and reliever therapy
- Remote Indigenous Australian Asthma Action Plan
- Every Day Asthma Action Plan (designed for remote Indigenous Australians who do not use written English – may also be useful for others for whom written English is inappropriate)
- Children's written asthma action plans.

Some written asthma action plans are available in community languages.

Software for developing electronic pictorial asthma action plans[6, 7] is available online.

▶ Go to: National Asthma Council Australia's *Asthma Action Plan Library*

Download: Imperial College London's *Electronic Asthma Action Plan*

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Asthma education programs for parents/carers and children

Asthma education for children and/or caregivers reduces the risk of emergency department visit for asthma, compared with usual care.[8]

However, the most effective components of education have not been clearly identified.[8, 9] There have been relatively few Australian controlled trials assessing education programs.[9]

There is not enough evidence to tell whether asthma education programs in the child's home are more effective in helping control asthma than asthma education provided somewhere else or standard care,[9] or to identify which types of education is more effective.

All age groups

A systematic review[10] found that asthma education programs were associated with moderate improvement in lung function and with a small reduction in school absence, restriction of physical activity, and emergency department visits. The greatest effects were in children with more severe asthma.[10]

Another systematic review found that educational programmes for the self-management of asthma in children and adolescents improved lung function, reduced the number of school days missed and the number of days with restricted activity, reduced the rate of visits to an emergency department, and possibly reduced the number of disturbed nights.[11]

0-5 years

There is little evidence about the effects of education for parents of preschool-aged children with asthma or wheezing. Most studies have investigated the effects of asthma management education for older children and their parents.[12] Limited evidence suggests that:

- education for parents of preschool children (e.g. written information and review by a health professional, small-group teaching by nurses or education in the family's home) may help improve asthma control[12]
- education programs are more likely to be effective if they involve multiple sessions, each longer than 20 minutes' duration.[12]

Opportunistic asthma education

In addition to the types of structured or formal asthma education evaluated in research trials, all health professionals who work with children with asthma and their parents/carers can provide asthma education whenever the opportunity occurs.

Table. Childhood asthma education checklist

Please view and print this figure separately: http://www.asthmahandbook.org.au/table/show/30

Resources

Education resources are available from the National Asthma Council Australia, Asthma Australia, and the Asthma Foundation in your state or territory.

▶ Go to: *National Asthma Council Australia*
Go to: *Asthma Australia*

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Back-to-school asthma care

Each year during February, a few days after the school year starts, there is an annual increase in asthma flare-ups among children with asthma.

Asthma flare-ups in children, including those resulting in emergency department presentations and hospitalisations, surge during the first month of the school year. [13, 14, 15, 17] There are smaller increases at the beginning of the other school terms.[18] These flare-ups may be due to changes in exposure to virus, allergens, pollution and/or stress during the early days after school return.[19]

Primary care health professionals can help parents/carers prepare for back-to-school flare-ups by:

- recommending a full asthma review at the end of the school holidays to check asthma control, adherence to preventer and inhaler technique
- ensuring that each child has an up-to-date written asthma action plan and the child and/or parents/carers understand how to follow it
- reminding parents/carers to get their child back into their asthma routine before the school year starts, including taking preventer medications every day, if prescribed

▶ Go to: National Asthma Council Australia's Back to school checklist for kids with asthma

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Increasing the inhaled corticosteroid dose to control flare-ups in children

In children taking regular inhaled corticosteroid-containing preventers, there is conflicting evidence for whether, and by how much, the dose should be increased when symptoms worsen or at the onset of an acute flare-up.

Overall, current evidence from highly controlled randomised controlled trials does not support increasing the dose of inhaled corticosteroid as part of a self-initiated action plan to manage flare-ups in children younger than 12 years.[20]

There is some evidence that high doses of inhaled steroids used pre-emptively might be effective in preventing severe acute asthma in children aged under 5 years, based on studies in children not taking regular inhaled corticosteroids.[21] However, very high pre-emptive doses affect children's growth[22] and are not recommended.

Recent randomised controlled trials reported a lack of effect with a range of dose increases:

- A five-fold increase in the inhaled corticosteroid dose at early signs of worsening asthma did not reduce the rate of severe acute asthma in children aged 5–11 years with well-controlled asthma while taking maintenance inhaled corticosteroid treatment (with high adherence).[23] This strategy was associated with a small reduction in linear growth.[23]
- Dose increases of four or eight times usual inhaled corticosteroid maintenance dose at the onset of an acute flare-up in children aged 2–17 years did not reduce requirement for oral corticosteroids, compared with doubling the dose.[24]

A Cochrane systematic review[20] in children and adults reported that increasing the inhaled corticosteroid dose did not prevent severe flare-ups, regardless of how soon the increase was initiated after the onset of symptoms or the magnitude of the dose increase (doubling versus quadrupling). The results did not differ between children under 15 and adults or older adolescents.[20] However, there were too few studies in children to make firm conclusions.

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Parent/carer-initiated oral corticosteroids for wheezing and asthma flare-ups

▶ See also: Managing acute asthma in clinical settings

- Oral corticosteroids are associated with adverse effects on behaviour and bone health. Frequent courses may affect the hypothalamus–pituitary–adrenal axis.

Children aged 1–5 years

Short courses of oral corticosteroids initiated by parents/carers in response to children's wheezing, or at the first sign of a cold, are not effective in managing symptoms in preschool children.[25, 26, 27]

There is inconsistent evidence for the benefits of systemic corticosteroids in preschool children with acute viral-induced wheezing presenting to acute care services.[27, 28, 29] Current evidence does not strongly support their use in this age group.[30]

The Thoracic Society of Australia and New Zealand position statement on the use of corticosteroids in children[1] recommends that oral corticosteroid treatment in preschool children, particularly those with intermittent viral-induced wheezing, should be limited to children with wheeze severe enough to need admission to hospital.

Children aged 6 years and over

A Cochrane systematic review found that there was insufficient evidence supporting the use of parent-initiated courses of oral corticosteroids in school-aged children,[31] although some clinical trials have reported benefits.

In a clinical trial in children aged 6–14 years with a history of recurrent episodes of acute asthma, short courses of oral prednisolone (1 mg/kg a day), initiated by parents in response to an asthma flare-ups, reduced asthma symptoms and the number of missed school days.[32] Another quasi-experimental study found that home initiation of corticosteroids reduced the rate of emergency department visits among school-aged children with moderate-to-severe persistent asthma, compared with rates pre-intervention.[33]

The Thoracic Society of Australia and New Zealand position statement on the use of corticosteroids in children[1] recommends a short course of systemic corticosteroid therapy for children with moderate-to-severe acute asthma or when there is an incomplete response to beta-agonists, and does not recommend against parent/carer-initiated courses.

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Correct use of inhaler devices

Checking and correcting inhaler technique is essential to effective asthma management.

Most patients with asthma or COPD do not use their inhalers properly,[34, 35,36, 36, 37] and most have not had their technique checked or

corrected by a health professional.

Incorrect inhaler technique when using maintenance treatments increases the risk of severe flare-ups and hospitalisation for people with asthma or COPD.[34, 35, 38, 39, 40, 41]

Poor asthma symptom control is often due to incorrect inhaler technique.[42, 43]

Incorrect inhaler technique when using inhaled corticosteroids increases the risk of local side effects like dysphonia and oral thrush.

The steps for using an inhaler device correctly differ between brands. Checklists of correct steps for each inhaler type and how-to videos are available from the National Asthma Council website.

▶ Go to: National Asthma Council Australia's *Using your inhaler* webpage for information, patient resources and videos on inhaler technique
Go to: National Asthma Council Australia's information paper for health professionals on *Inhaler technique for people with asthma or COPD*
Go to: NPS MedicineWise information on *Inhaler devices for respiratory medicines*

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References

1. van Asperen PP, Mellis CM, Sly PD, Robertson C. *The role of corticosteroids in the management of childhood asthma*. The Thoracic Society of Australia and New Zealand, 2010. Available from: https://www.thoracic.org.au/journal-publishing/command/download_file/id/25/filename/The_role_of_corticosteroids_in_the_management_of_childhood_asthma_-_2010.pdf
2. National Asthma Council Australia,. *Inhaler technique in adults with asthma or COPD. An information paper for health professionals*. NACA, Melbourne, 2018. Available from: https://www.nationalasthma.org.au/living-with-asthma/resources/health-professionals/information-paper/hp-inhaler-technique-for-people-with-asthma-or-copd
3. Cancer Council Australia,, Position statement - Sun exposure and vitamin D - risks and benefits. **, . Available from: https://wiki.cancer.org.au/policy/Positionstatement-RisksandbenefitsofsunexposureSun exposure and vitamin D - risks and benefits
4. Paxton, G. A., Teale, G. R., Nowson, C. A., *et al*. Vitamin D and health in pregnancy, infants, children and adolescents in Australia and New Zealand: a position statement. *Med J Aust*. 2013; 198: 142-3. Available from: https://www.mja.com.au/journal/2013/198/3/vitamin-d-and-health-pregnancy-infants-children-and-adolescents-australia-and
5. Zemek RL, Bhogal S, Ducharme FM. Systematic Review of Randomized Controlled Trials Examining Written Action Plans in Children - What Is the Plan?. *Arch Pediatr Adolesc Med*. 2008; 162: 157-63. Available from: http://archpedi.jamanetwork.com/article.aspx?articleid=379087#tab1
6. Roberts NJ, Mohamed Z, Wong PS, *et al*. The development and comprehensibility of a pictorial asthma action plan. *Patient Educ Couns*. 2009; 74: 12-18. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18789626
7. Roberts NJ, Evans G, Blenkhorn P, Partridge M. Development of an electronic pictorial asthma action plan and its use in primary care. *Patient Educ Couns*. 2010; 80: 141-146. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19879092
8. Coffman JM, Cabana MD, Halpin HA, Yelin EH. Effects of asthma education on children's use of acute care services: a meta-analysis. *Pediatrics*. 2008; 121: 575-86. Available from: http://pediatrics.aappublications.org/content/121/3/575.long
9. Welsh EJ, Hasan M, Li P. Home-based educational interventions for children with asthma. *Cochrane Database Syst Rev*. 2011; Issue 10: CD008469. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008469.pub2/full
10. Wolf F, Guevara JP, Grum CM, *et al*. Educational interventions for asthma in children. *Cochrane Database Syst Rev*. 2002; Issue 4: CD000326. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000326/full
11. Guevara JP, Wolf FM, Grum CM, Clark NM. Effects of educational interventions for self management of asthma in children and adolescents: systematic review and meta-analysis. *BMJ*. 2003; 326: 1308-1309. Available from: http://www.bmj.com/content/326/7402/1308
12. Brand PL, Baraldi E, Bisgaard H, *et al*. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. *Eur Respir J*. 2008; 32: 1096-1110. Available from: http://erj.ersjournals.com/content/32/4/1096.full
13. Johnston NW, Johnston SL, Duncan JM et al. The September epidemic of asthma exacerbations in children: a search for etiology. *J Allergy Clin Immunol* 2005; 115: 132-8. Available from: https://www.ncbi.nlm.nih.gov/pubmed/15637559
14. Sears MR, Johnston NW. Understanding the September asthma epidemic. *J Allergy Clin Immunol* 2007; 120: 526-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/17658590
15. Eggo RM, Scott JG, Galvani AP, Meyers LA. Respiratory virus transmission dynamics determine timing of asthma exacerbation peaks: Evidence from a population-level model. *Proc Natl Acad Sci U S A* 2016; 113: 2194-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/26858436
16. Ahmet, A, Kim, H, Spier, S. Adrenal suppression: A practical guide to the screening and management of this under-recognized complication of inhaled corticosteroid therapy. *Allergy Asthma Clin Immunol*. 2011; 7: 13.
17. Australian Institute of Health and Welfare. *Asthma hospitalisations in Australia 2010-11*. Australian Institute of Health and Welfare, Canberra, 2013. Available from: http://www.aihw.gov.au/publication-detail/?id=60129544541
18. Australian Centre for Asthma Monitoring. *Asthma in Australia 2011: with a focus chapter on chronic obstructive pulmonary disease*. Asthma series no. 4. Cat. no ACM 22. Australian Institute of Health and Welfare, Canberra, 2011. Available from: http://www.aihw.gov.au/publication-detail/?id=10737420159

19. Tovey ER, Rawlinson WD. A modern miasma hypothesis and back-to-school asthma exacerbations. *Med Hypotheses* 2011; 76: 113-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20869177
20. Kew KM, Quinn M, Quon BS, Ducharme FM. Increased versus stable doses of inhaled corticosteroids for exacerbations of chronic asthma in adults and children. *Cochrane Database Syst Rev* 2016; Issue 6: CD007524. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27272563
21. Kaiser SV, Huynh T, Bacharier LB et al. Preventing exacerbations in preschoolers with recurrent wheeze: a meta-analysis. *Pediatrics* 2016; 137: Available from: https://www.ncbi.nlm.nih.gov/pubmed/27230765
22. Ducharme FM, Lemire C, Noya FJ, *et al*. Preemptive use of high-dose fluticasone for virus-induced wheezing in young children. *N Engl J Med*. 2009; 360: 339-353. Available from: http://www.nejm.org/doi/full/10.1056/NEJMoa0808907#t=article
23. Jackson DJ, Bacharier LB, Mauger DT et al. Quintupling Inhaled Glucocorticoids to Prevent Childhood Asthma Exacerbations. *N Engl J Med* 2018; 378: 891-901. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29504498
24. Yousef, E., Hossain, J., Mannan, S., *et al*. Early intervention with high-dose inhaled corticosteroids for control of acute asthma exacerbations at home and improved outcomes: a randomized controlled trial. *Allergy Asthma Proc*. 2012; 33: 508-13. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23394509
25. Beigelman A, King TS, Mauger D, *et al*. Do oral corticosteroids reduce the severity of acute lower respiratory tract illnesses in preschool children with recurrent wheezing?. *J Allergy Clin Immunol*. 2013; 131: 1518-1525. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23498594
26. Oommen A, Lambert PC, Grigg J. Efficacy of a short course of parent-initiated oral prednisolone for viral wheeze in children aged 1-5 years: randomised controlled trial. *Lancet*. 2003; 362: 1433-1438. Available from: http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(03)14685-5/fulltext
27. Panickar J, Lakhanpaul M, Lambert PC, *et al*. Oral prednisolone for preschool children with acute virus-induced wheezing. *N Engl J Med*. 2009; 360: 329-328. Available from: https://www.ncbi.nlm.nih.gov/pubmed/19164186
28. Foster SJ, Cooper MN, Oosterhof S, Borland ML. Oral prednisolone in preschool children with virus-associated wheeze: a prospective, randomised, double-blind, placebo-controlled trial. *Lancet Respir Med*. 2018; 6: 97-106. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29373235
29. Therapeutic guidelines [Electronic book]: Therapeutic Guidelines Limited; 2018 [cited 2018 April].
30. Castro-Rodriguez JA, Beckhaus AA, Forno E. Efficacy of oral corticosteroids in the treatment of acute wheezing episodes in asthmatic preschoolers: Systematic review with meta-analysis. *Pediatric pulmonology* 2016; 51: 868-76. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27074244
31. Ganaie MB, Munavvar M, Gordon M et al. Patient- and parent-initiated oral steroids for asthma exacerbations. *Cochrane Database Syst Rev* 2016; 12: Cd012195. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27943237
32. Vuillermin P, Robertson CF, Carlin JB, *et al*. Parent initiated prednisolone for acute asthma in children of school age: randomised controlled crossover trial. *BMJ*. 2010; 340: c843. Available from: http://www.bmj.com/content/340/bmj.c843.long
33. Sarzynski LM, Turner T, Stukus DR, Allen E. Home supply of emergency oral steroids and reduction in asthma healthcare utilization. *Pediatr Pulmonol* 2017; 52: 1546-9. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29034999
34. The Inhaler Error Steering Committee,, Price, D., Bosnic-Anticevich, S., *et al*. Inhaler competence in asthma: common errors, barriers to use and recommended solutions. *Respir Med*. 2013; 107: 37-46. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23098685
35. Bjermer, L.. The importance of continuity in inhaler device choice for asthma and chronic obstructive pulmonary disease. *Respiration; international review of thoracic diseases*. 2014; 88: 346-52. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25195762
36. Basheti, I A, Armour, C L, Bosnic-Anticevich, S Z, Reddel, H K. Evaluation of a novel educational strategy, including inhaler-based reminder labels, to improve asthma inhaler technique. *Patient Educ Couns*. 2008; 72: 26-33. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18314294
37. Bosnic-Anticevich, S. Z., Sinha, H., So, S., Reddel, H. K.. Metered-dose inhaler technique: the effect of two educational interventions delivered in community pharmacy over time. *The Journal of asthma : official journal of the Association for the Care of Asthma*. 2010; 47: 251-6. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20394511
38. Melani AS, Bonavia M, Cilenti V, *et al*. Inhaler mishandling remains common in real life and is associated with reduced disease control. *Respir Med*. 2011; 105: 930-8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21367593
39. Levy ML, Dekhuijzen PN, Barnes PJ, *et al*. Inhaler technique: facts and fantasies. A view from the Aerosol Drug Management Improvement Team (ADMIT). *NPJ Prim Care Respir Med*. 2016; 26: 16017. Available from: https://www.ncbi.nlm.nih.gov/pubmed/27098045
40. Haughney, J., Price, D., Barnes, N. C., *et al*. Choosing inhaler devices for people with asthma: current knowledge and outstanding research needs. *Respiratory medicine*. 2010; 104: 1237-45. Available from: https://www.ncbi.nlm.nih.gov/pubmed/20472415
41. Giraud, V., Roche, N.. Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability. *The European respiratory journal*. 2002; 19: 246-51. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11866004
42. Harnett, C. M., Hunt, E. B., Bowen, B. R., *et al*. A study to assess inhaler technique and its potential impact on asthma control in patients attending an asthma clinic. *J Asthma*. 2014; 51: 440-5.
43. Hardwell, A., Barber, V., Hargadon, T., *et al*. Technique training does not improve the ability of most patients to use pressurised metered-dose inhalers (pMDIs). *Prim Care Respir J*. 2011; 20: 92-6. Available from: http://www.nature.com/articles/pcrj201088