Managing difficult-to-treat asthma in adults and adolescents

Read first

- Assess current asthma symptom control and risk factors
- Assessing and optimising adherence to ICS in adults & adolescents
- Assessing and correcting inhaler technique
- Treatment levels for adults and adolescents

Recommendation

If a patient's asthma is not well controlled on medium-dose ICS-LABA (medium-dose MART or maintenance medium-dose ICS-LABA plus SABA as needed), investigate thoroughly:

1. Assess for and correct common causes of poor control (poor adherence, incorrect inhaler technique, exposure to avoidable triggers (e.g. cigarette smoke, allergens, irritants, respiratory infections, moulds/dampness, indoor/outdoor air pollution), psychosocial factors affecting asthma self-management (e.g. life events, financial problems, or mental health conditions).
2. If patient is using SABA, assess for overuse. Refer patients with marked overuse to a severe asthma clinic (if available) or respiratory physician for supervised reduction.
3. Confirm the diagnosis: check that variable expiratory airflow limitation has been recorded using an objective test.
4. Assess comorbid conditions that could be contributing to asthma symptoms (e.g. rhinosinusitis, aspirin-exacerbated respiratory disease, obesity, gastroesophageal reflux disease, obstructive sleep apnoea) and whether respiratory symptoms may be caused by an alternative diagnosis (e.g. heart failure, inducible laryngeal obstruction, anxiety disorders).

Sources & rationale

Evidence-based recommendation adopted from GINA [GINA 2024]

Among patients with asthma that is uncontrolled despite having been prescribed medium-dose maintenance ICS-LABA or higher-intensity treatment, many can achieve good control after correcting common causes. A minority have severe asthma, which is non-responsive to high doses of ICS and requires specialist treatment with monoclonal antibody therapy.[GINA 2024]

References

Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention, 2024. Updated May 2024. Available from: www.ginasthma.org

Recommendation

If good asthma control cannot be achieved despite treatment with medium-dose ICS-LABA with good adherence and correct inhaler technique, and after assessing and managing other risk factors, refer to an accredited respiratory laboratory for spirometry, assess blood eosinophil level, and arrange specialist referral for investigation for biologic treatment.

This recommendation applies to patients with good adherence and correct inhaler technique, and after assessing and managing other risk factors.

Medium-dose ICS-LABA includes either MART or maintenance ICS-LABA plus as-needed SABA.

If asthma is not well controlled on medium-dose maintenance ICS-LABA plus SABA as needed, consider first switching to medium-dose MART first and monitoring control.

Sources & rationale

The risk of severe exacerbations requiring systemic corticosteroid is very high among adults with asthma that is uncontrolled despite treatment with medium- or high-dose ICS plus LABA, a history of exacerbations in the previous year, elevated blood eosinophil count and elevated FeNO.[Busse 2021]

For patients with severe eosinophilic or allergic asthma, monoclonal antibody therapies added to ICS-LABA significantly lower the rate of severe exacerbations requiring systemic corticosteroids, emergency department visits or hospitalisation, and may allow patients to reduce or stop oral corticosteroid treatment.[Agache 2020] Some patients with previously uncontrolled severe asthma experience complete or near-complete asthma control during monoclonal antibody therapy. [Rupani 2021]

Although eligibility for PBS reimbursement for monoclonal antibody therapy requires treatment with high-dose ICS-LABA (unless contraindicated or not tolerated), prompt referral of patients with inadequate response to medium-dose ICS is recommended to facilitate assessment and minimise time to effective treatment.

References

Agache I, Beltran J, Akdis C, et al. Efficacy and safety of treatment with biologicals (benralizumab, dupilumab, mepolizumab, omalizumab and reslizumab) for severe eosinophilic asthma. A systematic review for the EAACI Guidelines – recommendations on the use of biologicals in severe asthma. Allergy 2020; 75: 1023-1042.

Busse WW, Wenzel SE, Casale TB, et al. Baseline FeNO as a prognostic biomarker for subsequent severe asthma exacerbations in patients with uncontrolled, moderate-to-severe asthma receiving placebo in the LIBERTY ASTHMA QUEST study: a post-hoc analysis. Lancet Respir Med 2021; 9: 1165-1173.

Rupani H, Hew M. Super-responders to severe asthma treatments: defining a new paradigm. J Allergy Clin Immunol Pract 2021; 9: 4005-4006.

Resources

Thoracic Society of Australia and New Zealand's list of accredited respiratory laboratories.

Notes

Raised eosinophil count (≥150 cells/microlitre) in a patient taking medium-dose ICS or daily oral corticosteroids suggests refractory type 2 inflammation. Blood eosinophils may be elevated for reasons other than asthma. A very high blood eosinophil count ≥1500 cells/microlitre suggests other serious complications of asthma (e.g. Allergic Bronchopulmonary Aspergillosis) or other serious conditions (e.g. eosinophilic granulomatosis with polyangiitis that require urgent specialist assessment).

Recommendation

If referral is not immediately available, consider a short (3–6 months) treatment trial with either of:

- high-dose ICS-LABA
- ICS-LABA-LAMA with a medium or high ICS dose.

Alert Do not start high-dose ICS-LABA before assessment including blood eosinophil count.

Alert Avoid long-term treatment with high-dose ICS unless unavoidable to prevent severe exacerbations. Systemic adverse effects of high-dose ICS include reduced bone mineral density, cataracts, and diabetes.

Table

LAMAs and ICS-LABA-LAMA combinations approved for asthma treatment in adults and adolescents

Brand name	Active ingredients	Inhaler brand name (type)	Strength (microg)	Maintenance dose
*Spiriva**	Tiotropium	*Respimat* (SMI)	2.5	2 inhalations daily
Enerzair†	Mometasone-indacaterol-glycopyrronium	*Breezhaler* (DPI)	68/114/46 136/114/46	2 inhalations per capsule daily
Trelegy†	Fluticasone furoate-vilanterol-umeclidinium	*Ellipta* (DPI)	200/25/62.5	1 inhalation daily
Trimbow†	Beclometasone-formoterol-glycopyrronium	(pMDI)	100/6/10 200/6/10	2 inhalations twice daily

Additional information

DPI: dry powder inhaler; ICS: inhaled corticosteroid; LABA: long-acting beta$_2$ agonist; ; LAMA: long-acting muscarinic antagonist; pMDI: pressurised metered-dose inhaler; SMI: soft mist inhaler

* Treatment must be used in combination with a maintenance combination of an ICS (at least 800 microg budesonide per day or equivalent) and a LABA, unless a LABA is contraindicated.

† Patient must be at least 18 years of age for all ICS-LABA-LAMA combinations

Table

Single-inhaler ICS-LABA-LAMA combinations approved for asthma treatment (details)

Active ingredients	Brand names (Type)	Strength (microg)*	Dose	Age	PBS code	PBS streamlined authority code	Maximum quantity (5 repeats for all)	Actuations per device
Beclometasone Formoterol Glycopyrronium	*Trimbow* (pMDI)	100/6/10	2 inhalations twice daily	≥ 18 years	14606R	12603	1	120
		200/6/10	2 inhalations twice daily	≥ 18 years	13200R	12603	1	120
Fluticasone furoate Vilanterol Umeclidinium	*Trelegy Ellipta* (DPI)	200/25/62.5	1 inhalation once daily	≥ 18 years	12917W	12603	1	30
					14382Y†	15601	2	
Mometasone Indacaterol Glycopyrronium	*Enerzair Breezhaler* (DPI)	68/114/46	2 inhalations per capsule once daily	≥ 18 years	12298G	12603	1	30
					14471P†	15601	2	
		136/114/46	2 inhalations per capsule once daily	≥ 18 years	12295D	12603	1	
					14399W†	15601	2	

Additional information

DPI: dry powder inhaler; ICS: inhaled corticosteroid; LABA: long-acting beta$_2$ agonist; LAMA: long-acting muscarinic antagonist; pMDI: pressurised metered-dose inhaler

*ICS dose/LABA dose/LAMA dose

† The condition must be stable for the prescriber to consider the listed maximum quantity of this medicine suitable for this patient (60-day prescribing)

If there is no clinical response after 3–6 months, switch back to medium-dose ICS-LABA.

Sources & rationale

Recommendation type: Consensus recommendation

High-dose ICS-LABA

For most patients with inadequate asthma control (symptoms or exacerbations) on medium-dose ICS-LABA, increasing to high-dose ICS-LABA has little benefit but increases the risk of side-effects.[GINA 2025]

Increasing the ICS dose achieves the greatest reduction in exacerbations in patients with elevated blood eosinophil count or elevated FeNO.[Lee 2021]

Consider this option for patients with an elevated eosinophil count.

Long-term high-dose ICS should be avoided due to increased risk of side effects.[Bloom 2024, von Bülow]

ICS-LABA-LAMA

The addition of a LAMA to medium- or high-dose ICS-LABA is associated with a small improvement in lung function.[GINA 2025] The addition of LAMA to ICS-LABA is more likely to benefit adults with reduced lung function than those with normal lung function, independent of baseline blood eosinophil count.[Lee 2021]

In some studies, ICS-LABA-LAMA reduced exacerbations, compared with medium- or high-dose ICS-LABA.[GINA 2025]

Consider this option for patients with low FEV_1 and an eosinophil count within normal range.

References

Bloom CI, Yang F, Hubbard R, et al. Association of dose of inhaled corticosteroids and frequency of adverse events. Am J Respir Crit Care Med 2024; 211: 54–63.

Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention, 2025. Available from: www.ginasthma.org

Lee LA, Bailes Z, Barnes N, et al. Efficacy and safety of once-daily single-inhaler triple therapy (FF/UMEC/VI) versus FF/VI in patients with inadequately controlled asthma (CAPTAIN): a double-blind, randomised, phase 3A trial. [Erratum in: Lancet Respir Med 2021; 9: e18.] Lancet Respir Med 2021; 9: 69-84.

von Bülow A, Hansen S, Sandin P, et al. Use of high-dose inhaled corticosteroids and risk of corticosteroid related adverse events in asthma -findings from the NORDSTAR cohort. J Allergy Clin Immunol Pract 2025; Feb 1: S2213-2198(25)00100-X.

Recommendation

Avoid prescribing maintenance oral corticosteroids.

Alert Maintenance treatment with oral corticosteroids carries a high risk of serious adverse effects.

Sources & rationale

Recommendation type: Consensus recommendation

Maintenance treatment with corticosteroid increases patients' risk of infections, cardiovascular events, type 2 diabetes mellitus, osteoporosis, cataracts, weight gain, insomnia, depression, and behavioural disturbances. [Price 2018]

Even short courses of oral corticosteroids to manage asthma exacerbations are associated with increased lifetime risk of osteoporosis, pneumonia, cardiovascular or cerebrovascular diseases, cataract, sleep apnoea, renal impairment, depression/anxiety, type 2 diabetes, and weight gain. [Price 2018]

A cumulative dose of more than 1000 mg prednisolone significantly increases the risk of type 2 diabetes, cerebrovascular accidents, heart failure, and cardiovascular or cerebrovascular disease, compared with cumulative doses below 500 mg. [Price 2018] A cumulative dose of only 500 mg to <1000 mg increases the risk of type 2 diabetes, compared with lower use.

References

Price DB, Trudo F, Voorham J, et al. Adverse outcomes from initiation of systemic corticosteroids for asthma: long-term observational study. J Asthma Allergy 2018; 11: 193-204.

Notes

Maintenance treatment with systemic corticosteroids is very occasionally a last resort for a patient at high risk of severe and life-threatening exacerbations, when all other treatment options have failed to control asthma.

Any patient who requires maintenance oral corticosteroid treatment to manage asthma should be under the care of a severe asthma clinic or specialist.

Consideration

Consider ICS-LABA-LAMA for adults with longstanding asthma who have developed persistent expiratory airflow limitation.

This recommendation applies to patients in whom pre-bronchodilator spirometry consistently shows $FEV_1/FVC < 0.07$ and FEV_1 below 80% of predicted value, despite ICS-LABA treatment with good adherence and correct inhaler technique. These patients may or may not have a positive bronchodilator responsiveness test or some degree of bronchodilator response.

Alert

Common LAMA side effects include dry mouth (usually mild). Serious adverse effects consistent with anticholinergic effects include glaucoma, constipation, intestinal obstruction (including paralytic ileus) and urinary retention. Consult TGA-approved product information for warnings and precautions.

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Additional information

DPI: dry powder inhaler; ICS: inhaled corticosteroid; LABA: long-acting $beta_2$ agonist; ; LAMA: long-acting muscarinic antagonist; pMDI: pressurised metered-dose inhaler; SMI: soft mist inhaler

* Treatment must be used in combination with a maintenance combination of an ICS (at least 800 microg budesonide per day or equivalent) and a LABA, unless a LABA is contraindicated.

† Patient must be at least 18 years of age for all ICS-LABA-LAMA combinations

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Single-inhaler ICS-LABA-LAMA combinations approved for asthma treatment (details)

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*ICS dose/LABA dose/LAMA dose

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See coexisting asthma and COPD

Sources & rationale

Recommendation type: Consensus recommendation

Patients with longstanding asthma may develop persistent expiratory airflow limitation, defined as FEV_1/FVC <0.7 or < lower limit of normal.[Rutting 2022] Among this group, approximately two-thirds have a negative bronchodilator response on spirometry [Rutting 2022] (sometimes called fixed airway limitation). These findings, which are mainly due to airway remodelling,[Rutting 2022] are also features of COPD.

ICS treatment is mandatory for patients with features or diagnosis of both asthma and COPD.[GINA 2025] Such patients usually also require treatment with LABA, or both LABA and LAMA, for adequate symptom control.[GINA 2025]

In patients with coexisting asthma and COPD, characterised by both persistent airflow obstruction and airway hyperresponsiveness, ICS-LABA-LAMA treatment improves lung function compared with ICS-LABA treatment.[Park 2021]

References

Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention, 2025. Available from: **www.ginasthma.org**

Park SY, Kim S, Kim JH, et al. A randomized, noninferiority trial comparing ICS + LABA with ICS + LABA + LAMA in asthma-COPD overlap (ACO) treatment: The ACO Treatment with Optimal Medications (ATOMIC) Study. J Allergy Clin Immunol Pract 2021; 9: 1304-1311.

Rutting S, Thamrin C, Cross TJ, et al. Fixed airflow obstruction in asthma: a problem of the whole lung not of just the airways. Front Physiol 2022; 13: 898208.

Consideration

Consider the environmental impact of inhalers when prescribing and when discussing treatment options with patients.

Sources & rationale

Recommendation type: Consensus recommendation

Resources

National Asthma Council Australia information paper: Reducing the environmental impact of asthma treatment. Information for health professionals (2024)

Practice point

To check SABA overuse, ask how many actuations taken per day, and how long SABA reliever inhaler lasts, check prescribing records, and ask whether patient also uses non-prescription reliever:

- **Dispensing of 3 or more salbutamol canisters in a year (average 1.6 actuations per day) is associated with increased risk of exacerbations.**
- **Dispensing 12 or more canisters in a year (average 6.6 actuations per day) is associated with increased risk of asthma death.**
- **Patients with habitual SABA over-use may need supervised weaning off – consider specialist referral.**

Practice point

Consider arranging a Home Medicines Review or Residential Medication Management Review for patients with difficult-to-treat asthma, to check inhaler technique and adherence.

Resources

Medicare Benefits Schedule - Item 900
https://www9.health.gov.au/mbs/fullDisplay.cfm?type=item&q=900

Medicare Benefits Schedule - Item 903
https://www9.health.gov.au/mbs/fullDisplay.cfm?type=item&q=903

Practice point

If prescribing add-on LAMA for a patient on medium-dose ICS-LABA:

- check PBS restrictions. Budesonide-formoterol-glycopyrronium is not reimbursed by PBS for asthma, but patients with persistent airflow limitation are eligible if they have a concurrent diagnosis of COPD.
- consider prescribing a single-inhaler combination to reduce the number of different inhalers required. If using a separate LAMA inhaler, train patients to use the different inhalers correctly. If switching to a single-inhaler combination in a different inhaler device from the patient's ICS-LABA, train patients to use the new inhaler correctly.

Resources

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† Patient must be at least 18 years of age for all ICS-LABA-LAMA combinations

Practice point

Arrange referral for patients with asthma that is unresponsive to medium-dose ICS-LABA, regardless of result of blood eosinophil count.

Practice point

Primary care clinicians can facilitate access to monoclonal antibody therapy through early identification of patients with type 2 airway inflammation that persists despite medium-doses ICS, and prompt referral to an appropriate specialist. Specialist assessment should be arranged as soon as possible in a patient with asthma that is not well controlled on medium-dose ICS-LABA (Level 3), despite good adherence and correct inhaler technique, and after assessing and managing other risk factors such as comorbid conditions and exposure to avoidable triggers.

Alert Do not delay specialist referral until a patient requires long-term high-dose ICS or maintenance or systemic corticosteroids. Failure of asthma to respond to medium-dose ICS-containing treatment suggests a high risk of exacerbations and the need for monoclonal antibody therapy.

Practice point

Bone mineral density and blood glucose should be monitored in patients using high-dose ICS long term and those with frequent oral corticosteroid courses for severe exacerbations.

Practice point

If frequent short courses of oral corticosteroids or maintenance oral corticosteroid treatment (prescribed only as a last resort) seem necessary to control asthma, the patient needs urgent specialist referral to assess for safer options.

Practice point

Patients with difficult-to-control or severe asthma have usually received multiple treatments. Ask them to bring all their inhalers to visits for asthma review, so you can check and clarify which are to be used and which are to be discontinued.

Practice point

After monoclonal antibody therapy is initiated by the specialist, doses are usually administered in primary care or self-administered by the patient or carer.

Alert Patients on monoclonal antibody therapy should not reduce or stop their other asthma medicines, except in consultation with the specialist.

Resources

National Asthma Council Australia's information paper Monoclonal antibody therapy for severe asthma

https://www.nationalasthma.org.au/living-with-asthma/resources/health-professionals/information-paper/monoclonal-antibody-therapy-for-severe-asthma

Practice point

Patients using monoclonal antibody therapy should continue to take ICS-containing treatment, even if they achieve good asthma control.

Resources

National Asthma Council Australia's information paper Monoclonal antibody therapy for severe asthma

https://www.nationalasthma.org.au/living-with-asthma/resources/health-professionals/information-paper/monoclonal-antibody-therapy-for-severe-asthma

National Asthma Council Australia's Monoclonal antibody therapy for severe asthma chart

https://www.nationalasthma.org.au/living-with-asthma/resources/health-professionals/charts/monoclonal-antibody-therapy-for-severe-asthma-chart

Practice point

For patients receiving monoclonal antibody therapy, continue to monitor adherence to maintenance ICS-containing treatment, inhaler technique, symptom control, exacerbations, oral corticosteroid use, adverse effects, comorbidities (including those that may respond to the monoclonal antibody therapy, such as eczema and nasal polyps), mental health and patient satisfaction.

Resources

National Asthma Council Australia's information paper Monoclonal antibody therapy for severe asthma
https://www.nationalasthma.org.au/living-with-asthma/resources/health-professionals/information-paper/monoclonal-antibody-therapy-for-severe-asthma

National Asthma Council Australia's Monoclonal antibody therapy for severe asthma chart
https://www.nationalasthma.org.au/living-with-asthma/resources/health-professionals/charts/monoclonal-antibody-therapy-for-severe-asthma-chart

Practice point

For patients with a marked response to monoclonal antibody therapy, the specialist may reduce or stop maintenance oral corticosteroid treatment, and may reduce the ICS-LABA dose.

Practice point

For patients prescribed azithromycin for severe asthma, monitor adverse effects: manage diarrhoea if it occurs, monitor for macrolide-resistant pathogens, and consider potential drug-drug interactions (e.g. cytochrome P450 interactions, and rhabdomyolysis in patients also using statins).

Alert Contraindications to azithromycin use include prolonged QTc interval > 0.48 sec assessed by ECG (potentially fatal) and cardiac arrhythmia. Caution applies to people with hearing loss.

Resources

Centre of Excellence in Severe Asthma's Clinical recommendations for the use of azithromycin in severe asthma in adults. Version 1. 24.10.2019.
https://www.severeasthma.org.au/wp-content/uploads/2019/11/CRE-Azithromycin-Recommendation-v1-24102019.pdf

Centre of Excellence in Severe Asthma's severe asthma toolkit.
https://www.severeasthma.org.au/tools-resources/toolkits/