Specialist assessment and treatment for severe asthma in adults and adolescents

Read first

- Treatment levels for adults and adolescents
- Adjusting treatment for adults and adolescents
- Managing difficult-to-treat asthma in adults and adolescents

Severe asthma has been defined as asthma that remains uncontrolled despite high-dose ICS-LABA (with correct inhaler technique and good adherence) or maintenance oral corticosteroids, or that requires such treatment to prevent it becoming uncontrolled.[Chung 2014] However, these are not recommended long-term treatments.

Asthma is uncontrolled if the patient experiences frequent symptoms, activity limitation, night waking, or has exacerbations that require systemic corticosteroid treatment.

Among people with persisting asthma symptoms, low lung function, or exacerbations despite ICS-containing treatment, only a small proportion have severe asthma. The most common reasons for failure to achieve good asthma control (few symptoms and few exacerbations) are suboptimal adherence, poor inhaler technique, continued exposure to environmental triggers (e.g. smoking), and untreated comorbid medical conditions such as chronic rhinosinusitis. When these problems are identified and corrected, asthma control improves for many people.

References

Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. Eur Respir J 2014; 43: 343-373.

Type 2 inflammation in asthma

Type 2 inflammation of the airways represents multiple inflammatory pathways involving recruitment of eosinophils and resulting in mucus hypersecretion and airway hyperresponsiveness.[Brusselle 2022] Clinical tests for type 2 airway inflammation include blood eosinophil count, sputum eosinophil count (less common), and FeNO, a non-invasive test available in lung function laboratories.

Most people with asthma have type 2 inflammation,[Fahy 2015] which typically responds well to low-dose ICS. However, a small proportion of patients have type 2 inflammation that does not respond to high-dose ICS and is relatively non-responsive to oral corticosteroids.[Fahy 2015] Despite ICS treatment, these patients show persistently raised blood eosinophil count, raised FeNO or both, with or without atopy and elevated serum total IgE.[Fahy 2015]

Persistent type 2 airway inflammation is a strong predictor of exacerbations.[Fahy 2015] The risk of severe exacerbations 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]

References

Brusselle GG, Koppelman GH. Biologic therapies for severe asthma. N Engl J Med 2022; 386: 157-171.

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.

Fahy JV. Type 2 inflammation in asthma–present in most, absent in many. Nat Rev Immunol 2015; 15: 57-65.

Specialist investigations to guide severe asthma treatment

Specialist investigations for a patient referred for suspected severe asthma might include some or all of the following:

- fractional exhaled nitric oxide (FeNO) – FeNO ≥20 ppb in a patient taking high-dose* ICS or daily oral corticosteroids suggests refractory type 2 inflammation.[GINA 2025]
- blood eosinophil count – eosinophil count ≥150 cells/microlitre in a patient taking high-dose* ICS or daily oral corticosteroids suggests ICS-refractory type 2 inflammation.[GINA 2025] Blood eosinophils may be elevated for reasons other than asthma. A very high blood eosinophil count ≥1500 cells/microlitre suggests the presence of other serious complications of asthma (e.g. Allergic Bronchopulmonary Aspergillosis) or other serious conditions (e.g. eosinophilic granulomatosis with polyangiitis).
- sputum eosinophil count (rarely performed) – eosinophils ≥2% in a patient taking high-dose* ICS or daily oral corticosteroids suggests refractory type 2 inflammation
- other blood tests (e.g. complete blood count, CRP, total serum IgG, IgA, IgM, total IgE, fungal precipitins including Aspergillus, if ABPA considered)
- allergy testing for clinically relevant allergens: skin prick test or allergen-specific IgE
- chest X-ray or high-resolution chest computed tomography
- CT sinuses (if symptoms suggest chronic rhinosinusitis).

* See notes.

Alert Long-term high-dose ICS treatment and maintenance systemic corticosteroid treatment should be avoided

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

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.

Notes

Most research investigating cut-points for anti-inflammatory markers has been conducted in patients with severe asthma using high doses of ICS. However, long-term use of high-dose ICS is not recommended due increased risk of systemic side-effects such as cardiovascular events, osteoporosis, cataract and glaucoma.[Bloom 2024, von Bülow 2025]

Elevated inflammatory markers in patients using medium-dose ICS also suggests type 2 inflammation that is nonresponsive to ICS and requires prompt investigation.

Monoclonal antibody therapy

Monoclonal antibody therapy is the first-choice treatment for patients with severe allergic or eosinophilic asthma that does not respond adequately to treatment with ICS and LABAs. Some monoclonal antibody therapies can only be prescribed by a specialist or in consultation with a specialist, and all are reimbursed by PBS only for patients under specialist care.

Monoclonal antibody therapy is very effective in improving symptoms, reducing the rate of exacerbations and reducing use of oral corticosteroids in people with severe asthma and persistent type 2 inflammation.[Chandrasekara 2024]

To facilitate patients' access to these treatments, assessment by a specialist 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.

Four monoclonal antibody therapies are available in Australia:

- Benralizumab (anti-IL5Rα) is approved by TGA for as an add-on treatment for patients ≥12 years with severe eosinophilic asthma (blood eosinophil count 300 cells/microlitre or 150 cells/microlitre while on oral corticosteroid treatment). [Australian PI benralizumab]
- Mepolizumab (anti-IL-5) is approved by TGA as an add-on treatment for patients ≥12 years with severe eosinophilic asthma.[Australian PI mepolizumab]
- Dupilumab (anti-IL-4Rα) is approved by TGA as add-on treatment for patients ≥6 years with moderate to severe asthma with type 2 inflammation (elevated eosinophils or elevated FeNO) that is inadequately controlled despite other maintenance treatment.[Australian PI dupilumab]
- Omalizumab (anti-IgE) is approved by TGA for adults and adolescents ≥12 years with moderate-to-severe allergic asthma who are using ICS and have serum IgE levels within a range specified in TGA-approved product information (different indications apply to children 6 to <12 years).[Australian PI omalizumab]

For PBS reimbursement patients must meet strict criteria for uncontrolled asthma despite optimised treatment, criteria for allergic status (omalizumab and dupilumab) and/or for eosinophilia (benralizumab, mepolizumab, dupilumab), and must be treated by a specialist (respiratory physician, clinical immunologist, allergist, or general physician experienced in the management of patients with severe asthma).

References

Australian product information – Dupixent (dupilumab) solution for injection. [Revised 5 July 2024] Therapeutic Goods Administration (www.ebs.tga.gov.au)

Australian product information. Fasenra (benralizumab) solution for injection prefilled syringe and prefilled pen (Fasenra Pen). [Revised 7 July 2023] Therapeutic Goods Administration (www.ebs.tga.gov.au)

Australian product information. Nucala (mepolizumab) powder for injection and solution for injection. [Revised 14 January 2022] Therapeutic Goods Administration (www.ebs.tga.gov.au)

Australian product information – Xolair (omalizumab) solution for injection and powder for solution for injection. [Revised 4 September 2024] Therapeutic Goods Administration (www.ebs.tga.gov.au)

Chandrasekara S, Wark P. Biologic therapies for severe asthma with persistent type 2 inflammation. Aust Prescr 2024; 47: 36-42.

Resources

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

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

Other severe asthma treatments

Other treatment strategies sometimes used in specialist care for patient with severe asthma under specialist care include:

- azithromycin – limited evidence suggests that treatment macrolides reduce asthma exacerbations in patients with severe asthma. The recommended azithromycin dose is 500 mg 3 times per week, or 250 mg daily for 12 months.[Centre of Excellence in Severe Asthma] Macrolides should only be prescribed for asthma by specialists with expertise in managing severe asthma.[Centre of Excellence in Severe Asthma]
- breathing exercises
- bronchial thermoplasty.

References

Centre of Excellence in Severe Asthma. Clinical recommendations for the use of azithromycin in severe asthma in adults. Version 1. 24.10.2019.