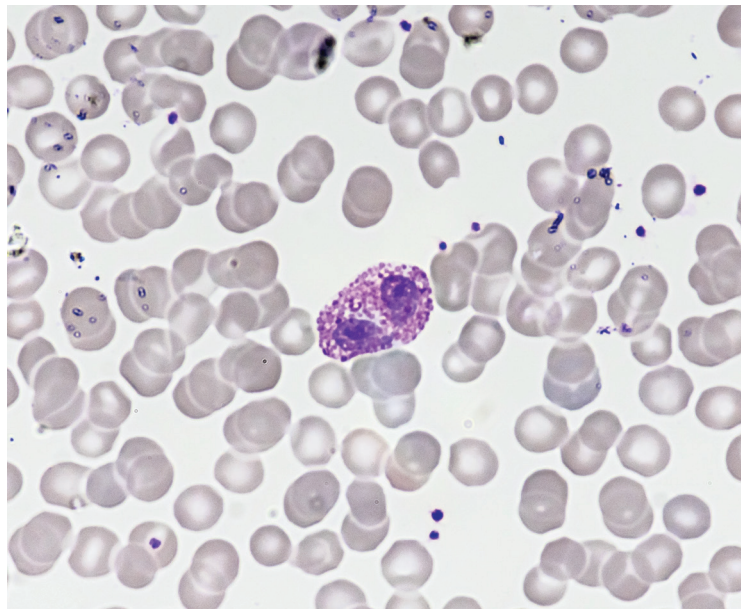


# Monoclonal antibody therapy for severe asthma

## KEY POINTS

- Benralizumab, mepolizumab and omalizumab are monoclonal antibody therapies used in the treatment of people with severe asthma whose asthma is uncontrolled despite optimised standard treatment, including high-dose inhaled corticosteroids and long-acting beta<sub>2</sub> agonists.
- Monoclonal antibody therapies target inflammatory pathways that activate immune responses leading to airway inflammation.
- Monoclonal antibody therapies can be prescribed with Pharmaceutical Benefits Scheme (PBS) subsidy by certain specialists for patients attending an approved public or private hospital.
- After treatment has been initiated by a specialist, ongoing maintenance doses can be administered in primary care.
- Monoclonal antibody therapies have been shown to reduce the frequency of severe asthma flare-ups (worsening asthma requiring oral corticosteroids, emergency department visit or hospitalisation),<sup>1-7</sup> reduce the requirement for oral corticosteroids,<sup>1,3,6</sup> and in some cases improve quality of life<sup>8,9</sup> and asthma symptoms.<sup>2,3,10</sup> Some may also improve lung function.<sup>8</sup>
- Patients taking monoclonal antibody therapies still need an up-to-date written asthma action plan and to follow it when symptoms worsen.
- All the monoclonal antibody therapies currently available in Australia are generally well tolerated. Injection site reactions are among the most common adverse events.<sup>11,12</sup> Systemic reactions, including anaphylaxis, are rare but can occur.<sup>11,12</sup>
- Before becoming eligible for PBS subsidy for monoclonal antibody therapy treatment, patients must either have been treated by the same specialist for at least 6 months, or have been diagnosed by a multidisciplinary severe asthma clinic team.<sup>13</sup>



## Currently available monoclonal antibody therapies for asthma

Three monoclonal antibody therapies (benralizumab, mepolizumab and omalizumab) are available in Australia for the treatment of patients with severe asthma whose asthma is uncontrolled despite optimised standard treatment including high-dose inhaled corticosteroids and long-acting beta<sub>2</sub> agonists (Table 1).

These medicines are funded by PBS only when prescribed by respiratory specialists, allergy specialists, or general physicians (or, in the case of omalizumab, paediatricians) with expertise in severe asthma management, for patients attending a public or private hospital, and when patients meet certain general and product-specific criteria. After treatment is initiated by a specialist, ongoing maintenance doses can be administered in primary care, but reviews required for continuing PBS-funded treatment must be carried out by the specialist.

Guidelines for asthma management:  
[astmahandbook.org.au](http://astmahandbook.org.au)

## RECOMMENDATIONS

Identify patients with uncontrolled asthma who might benefit from monoclonal antibody therapy and offer referral for specialist assessment without delay, after checking and correcting common causes of uncontrolled asthma such as incorrect inhaler technique and suboptimal adherence.

Arrange specialist referral for any patient for whom long-term maintenance oral corticosteroids for asthma have been prescribed or are being considered, or who requires frequent short courses of oral corticosteroids for acute asthma (if no recent specialist review).

Advise patients who have been prescribed a monoclonal antibody therapy to keep taking their inhaled corticosteroid preventer. Continue to check adherence and inhaler technique regularly.

Ensure that each patient has an up-to-date written asthma action plan: review it at least yearly or whenever the medication regimen is changed. Remind patients taking monoclonal antibody therapy to follow their written asthma action plan when symptoms worsen.

Ensure that patients understand that they must attend all scheduled specialist visits in order to remain eligible for access to monoclonal antibody therapy through the PBS.

When administering monoclonal antibody therapies, instructions for storing, preparing and administering doses should be followed carefully. The patient must be monitored under direct observation by a health professional (e.g. registered nurse or GP) for at least 30 minutes after the injection for maintenance doses.

## What is the clinical definition of severe asthma?

Severe asthma (also called severe refractory asthma) is asthma that remains uncontrolled despite maximal standard treatment (*Australian Asthma Handbook*<sup>14</sup> step 4 or higher), or which can only be controlled with such treatment.

Asthma severity is classified according to the level of treatment needed to achieve or maintain good asthma control – not by the intensity or frequency of symptoms, or by clinical findings before treatment.<sup>14, 15</sup>

Asthma in most people can be effectively treated with standard preventer treatment, such as long-term regular use of preventer containing a low dose of inhaled corticosteroids. Among people who have persisting symptoms, low lung function or asthma flare-ups despite regular preventer treatment, only a small proportion have severe asthma.

In practice, the most common reasons for failure to achieve good asthma control are suboptimal adherence, poor inhaler technique, continued exposure to environmental triggers including smoking, and untreated comorbid medical conditions such as chronic rhinosinusitis. When these problems are identified and corrected, many people's asthma control improves.

For more information, refer to the *Australian Asthma Handbook* information on:

- **management challenges**
- **managing asthma in adults**
- **managing asthma in children**

## Definitions

**Severe asthma:** asthma that remains uncontrolled despite the highest recommended level of inhaled medication (e.g. high-dose inhaled corticosteroids plus long-acting beta<sub>2</sub> agonist) or maintenance oral corticosteroids, or that requires such treatment to prevent it becoming uncontrolled.<sup>14, 16</sup>

**Uncontrolled asthma:** asthma with one or more of the following features:<sup>16</sup>

- poor symptom control, e.g. during previous 4 weeks, the person has experienced symptoms during night or on waking or limitation of activities due to asthma, has experienced daytime symptoms on more than 2 days per week, or has needed to take short-acting beta<sub>2</sub> agonist reliever on more than 2 days per week (not including doses taken prophylactically before exercise)<sup>14</sup>
- frequent severe flare-ups (e.g. more than one flare-up requiring treatment with oral corticosteroids in the previous year)
- serious flare-ups (e.g. hospital admission, intensive care unit admission, or mechanical ventilation in the previous year)
- persistent airflow limitation.

Table 1. Monoclonal antibody therapies currently available in Australia for severe asthma<sup>11, 12, 17</sup>

Name	Description	Indication*	Dosage & route of administration
Benralizumab (Fasenra)	<b>Anti-IL-5 receptor</b> Humanised monoclonal antibody directed against IL-5 receptor R $\alpha$ on surface of eosinophils and basophils	Add-on treatment for uncontrolled severe eosinophilic asthma in adults and adolescents aged $\geq 12$ years	Prefilled syringe for injection 30 mg SC every 4 weeks for three injections then every 8 weeks
Mepolizumab (Nucala)	<b>Anti-IL-5</b> Humanised monoclonal antibody directed against IL-5	Add-on treatment for uncontrolled severe eosinophilic asthma in adults and adolescents $\geq 12$ years	Powder for injection in a single-use vial 100 mg SC every 4 weeks
Omalizumab (Xolair)	<b>Anti-IgE</b> Humanised monoclonal antibody directed against IgE	Add-on treatment for uncontrolled severe allergic asthma in adults, adolescents and children aged $\geq 6$ years	Prefilled syringe for SC injection Dose calculated according to baseline IgE and body weight Usual dose every 2–4 weeks (larger doses divided in 2 and administered every 2 weeks)

ICS: inhaled corticosteroids; IgE: immunoglobulin E; IL-5: interleukin 5; SC: subcutaneous

\*Broad indication only (PBS criteria summarised on page 6)

### Mechanisms of action

Monoclonal antibody therapies for asthma are humanised monoclonal antibodies directed against immunoglobulin E (IgE) in the case of omalizumab, interleukin-5 (IL-5) in the case of mepolizumab, or the IL-5 receptor in the case of benralizumab. IgE and IL-5 are important components of inflammatory pathways that activate immune responses leading to airway inflammation.

#### Anti-IL-5 (mepolizumab) and anti-IL-5 receptor (benralizumab)

IL-5 is the main cytokine involved in the growth and differentiation, recruitment, activation and survival of eosinophils,<sup>11, 18</sup> which contribute to airway inflammation in many, but not all, patients with asthma. In early-onset asthma, but not in late-onset asthma, eosinophilic airway inflammation is usually associated with allergy.<sup>19</sup>

Mepolizumab targets human IL-5, blocking its ability to bind to receptors on the surface of eosinophils.<sup>11</sup> Inhibition of IL-5 signalling reduces the production and survival of eosinophils.<sup>11</sup>

Benralizumab targets the IL-5 receptor R $\alpha$ , leading directly to cell-mediated destruction of eosinophils and basophils.<sup>17</sup>

Blood levels of eosinophils are markedly reduced by mepolizumab and almost totally depleted by benralizumab.<sup>18</sup>

#### Anti-IgE therapy (omalizumab)

The allergic cascade is initiated when IgE bound to the surface of mast cells and basophils is crosslinked by allergen, resulting in cell degranulation and release of inflammatory mediators including histamine, leukotrienes and cytokines. These mediators contribute to airway oedema, smooth muscle contraction and altered cellular activity, which produce asthma symptoms of bronchoconstriction, mucus production, wheezing, dyspnoea and chest tightness.

Omalizumab selectively binds to human IgE and prevents it being available to bind to the IgE receptor on the surface of mast cells and basophils.<sup>12</sup> Omalizumab treatment also reduces the number of these receptors on basophils in allergic people, so less histamine is released when exposed to allergens.<sup>12</sup>

## Which patients may benefit from monoclonal antibody therapy?

Monoclonal antibody therapies target specific inflammatory pathways (see Mechanisms of action), so they will not benefit all patients or modify all aspects of asthma.

Systematic reviews of randomised clinical trials (RCTs) have demonstrated benefits of anti-IgE therapy<sup>6,9</sup> anti-IL-5 therapy<sup>18</sup> and anti-IL-5 receptor therapy<sup>18</sup> in patients with severe asthma who were experiencing clinically significant asthma flare-ups (requiring treatment with systemic corticosteroids) despite regular treatment with inhaled corticosteroids at medium-to-high doses.

An IgE level of at least 30 IU/mL must be documented before a patient is eligible for PBS subsidy for omalizumab treatment.<sup>13</sup> However, pre-treatment IgE level does not predict efficacy among patients taking omalizumab.<sup>20,21</sup> In one study, pre-treatment blood eosinophils  $\geq 260 \times 10^9/L$  or exhaled nitric oxide  $\geq 19.5$  ppb was associated with significantly greater reduction in flare-ups with omalizumab treatment,<sup>21</sup> but in a real-world study, similar reductions were seen across patients with a wide range of blood eosinophil levels.<sup>22</sup>

The benefits of anti-IL-5 therapy increase with the blood eosinophil levels before treatment, and the number of severe flare-ups in the previous year.<sup>23,24</sup> Mepolizumab is less effective in patients with baseline eosinophil counts below 150 cells per microlitre and shows greatest benefits in those with baseline eosinophil counts of at least 500 cells per microlitre.<sup>23</sup> PBS subsidy for mepolizumab or benralizumab treatment requires documentation of an eosinophil count of at least 300 cells per microlitre within the previous 12 months.<sup>13</sup>

## What are the clinical benefits of monoclonal antibody therapies?

Monoclonal antibody therapy reduces flare-ups, improves asthma symptoms and quality of life, and reduces corticosteroid requirements in patients with severe asthma. It might have additional benefits in other airway diseases (e.g. allergic rhinitis or chronic sinusitis).

### Benefits demonstrated in RCTs versus placebo

**Benralizumab:** Patients with severe eosinophilic asthma taking benralizumab as add-on treatment had fewer clinically significant asthma flare-ups,<sup>1,2</sup> including among patients with recurrent asthma flare-ups despite treatment with high-dose inhaled corticosteroids plus long-acting beta<sub>2</sub> agonists,<sup>2</sup> and experienced improvement in asthma symptoms.<sup>2,10</sup> Among patients with severe eosinophilic asthma relying on

maintenance oral corticosteroids to control asthma, there was an overall reduction in dose requirements and some patients were able to stop taking oral corticosteroids.<sup>1</sup> There was also a small improvement in lung function in some, but not all, RCTs.<sup>8</sup>

**Mepolizumab:** Patients with severe eosinophilic asthma taking mepolizumab as add-on treatment had fewer clinically significant asthma flare-ups requiring care in the emergency department or admission to hospital,<sup>3-5</sup> including among those taking high doses of inhaled corticosteroids<sup>4</sup> or long-term maintenance systemic corticosteroids,<sup>3</sup> and experienced improvement in asthma symptom control<sup>3</sup> and asthma-related quality of life.<sup>8</sup> There was a reduction in corticosteroid dose requirements among those relying on oral corticosteroids to control asthma.<sup>3</sup> A small improvement in lung function was seen in some, but not all, RCTs.<sup>8</sup>

**Omalizumab:** Patients with severe allergic asthma taking omalizumab as add-on treatment had fewer clinically significant asthma flare-ups<sup>6,7</sup> including flare-ups requiring hospitalisation,<sup>7</sup> and experienced improved quality of life<sup>9</sup> and a reduction in reliever use.<sup>7</sup> Reductions in flare-up rates have been shown in adults, adolescents and children with severe persistent allergic asthma.<sup>6</sup> There is some evidence that omalizumab reduced oral corticosteroid requirements,<sup>6</sup> and also reduced the dose requirement for inhaled corticosteroids in some, but not all, RCTs.<sup>25</sup> In children with asthma, who are prone to acute flare-ups associated with viral infections, treatment with omalizumab reduced rates of seasonal acute asthma flare-ups and may improve the antiviral immune response to the common cold virus.<sup>26</sup>

There have been no head-to-head studies comparing any of the currently available monoclonal antibody therapies for severe asthma. Indirect comparisons suggest that, overall, efficacy and tolerability are similar for benralizumab and mepolizumab at comparable doses.<sup>24</sup> Among patients with severe asthma eligible for both mepolizumab and omalizumab, efficacy and tolerability are largely similar for both options.<sup>27</sup>

### Real-world effectiveness studies

A substantial body of evidence for omalizumab is also available from real-world effectiveness studies.<sup>22</sup> Systematic reviews of real-world studies have confirmed benefits seen in RCTs, including reductions in rates of asthma flare-ups,<sup>25,28</sup> emergency department visits and hospitalisations,<sup>25,28</sup> and improvements in lung function,<sup>25,28</sup> asthma symptom control,<sup>25,28</sup> and quality of life.<sup>28</sup> Reduced requirements for inhaled corticosteroids were also reported in some, but not all, real-world studies.<sup>25</sup> Follow-up of up to 4 years has confirmed long-term benefits.<sup>28</sup>

Data from registries of patients taking omalizumab also confirm effectiveness. Analysis of data from patients with severe allergic asthma enrolled in the Australian Xolair



Registry<sup>29</sup> showed that 83% of patients could be classified as responders based on PBS criteria (i.e. experienced a clinically important improvement in asthma symptom control), and that oral corticosteroid use was reduced. In an observational study conducted through an international omalizumab registry<sup>30</sup> approximately 70% of patients were classified as responders after approximately 16 weeks of treatment, based on a physician's global assessment. The rate of flare-ups was reduced over time. Symptom levels, use of short-acting beta<sub>2</sub> agonist and requirement for long-term oral corticosteroids were reduced over 2 years. To date, there are no published real-world studies of effectiveness of benralizumab or mepolizumab.

## What are the main safety issues?

All the monoclonal antibody therapies currently available in Australia are generally well tolerated. Injection site reactions are among the most common adverse events. Systemic reactions, including anaphylaxis, are rare but can occur.<sup>31</sup>

There is very limited information about effects in pregnancy. The only study of monoclonal antibody therapy specifically in pregnancy was conducted among women taking omalizumab. Initial data showed that the rates of prematurity, low birth weight, and small size for gestational age were similar to those found in other studies of patients with severe asthma, with no increase in congenital abnormalities.<sup>32</sup>

## Anti-IL-5 (mepolizumab) and anti-IL-5 receptor (benralizumab)

A Cochrane systematic review<sup>18</sup> of RCTs evaluating anti-IL-5 monoclonal antibody therapies concluded there was no excess of serious adverse events in patients taking active treatment compared with placebo.

### Benralizumab

The Cochrane meta-analysis found there was a significantly higher rate of discontinuations due to adverse events among patients taking benralizumab compared with those taking placebo, but both rates were small (2.3% versus 0.9%).<sup>18</sup> In clinical trials of benralizumab the most common adverse events were worsening asthma and other respiratory events.<sup>1, 2, 10</sup> Hypersensitivity reactions, including urticaria and papular rash, have been observed. When these occur, it is usually within hours, but sometimes within days.<sup>17</sup>

Patients with pre-existing helminth infections should be treated before starting benralizumab.<sup>18</sup> During benralizumab treatment, if a new helminth infection occurs that does not respond to anti-helminth treatment, temporary discontinuation of benralizumab should be considered.<sup>18</sup>

### Mepolizumab

The Cochrane meta-analysis found no difference in rates of adverse events leading to discontinuation among patients taking mepolizumab, compared with those taking placebo.<sup>18</sup> In clinical trials of mepolizumab the most common adverse events included injection site reactions.<sup>11</sup> Systemic reactions, including anaphylaxis, urticaria, angioedema, rash, bronchospasm and hypotension, have been observed. When these occur, it is usually within hours, but sometimes within days.<sup>11</sup> Systemic reactions can also occur after long-term use.<sup>11</sup>

Opportunistic infections such as herpes zoster are possible in patients treated with mepolizumab.<sup>11</sup> Patients with pre-existing helminth infections should be treated before starting mepolizumab.<sup>11</sup> During mepolizumab treatment, if a new helminth infection occurs that does not respond to anti-helminth treatment, temporary discontinuation of mepolizumab should be considered.

The safety of mepolizumab has not been established in adolescents weighing less than 45 kg.<sup>11</sup>

### Anti-IgE (omalizumab)

A Cochrane systematic review of omalizumab RCTs<sup>7</sup> found there were fewer serious adverse events among patients taking omalizumab than those taking placebo. In clinical trials, the most common adverse events reported with omalizumab treatment were injection site reactions and headaches.<sup>12</sup> In children, the most commonly reported adverse events were headache, pyrexia and upper abdominal pain.<sup>12</sup>

Local or systemic allergic reactions, including anaphylaxis (estimated at 0.2% in post-marketing reports), have been observed after treatment with omalizumab.<sup>12</sup> In clinical use, anaphylaxis has been reported after the first dose or after a later dose.<sup>12</sup> Most have occurred within 2 hours of administration, but some have occurred more than 24 hours later.<sup>12</sup> Rare adverse effects of omalizumab include serum sickness and serum sickness-like reactions (e.g. arthritis, arthralgia, urticaria or other rash, fever, lymphadenopathy), allergic eosinophilic granulomatous vasculitis (previously called Churg-Strauss syndrome).<sup>12, 31</sup>

A meta-analysis of phase I–IV placebo-controlled RCTs<sup>33</sup> found no association between omalizumab treatment and risk of malignancy. Omalizumab treatment was not associated with an increased risk of malignancy in an observational study with median 5 years follow-up.<sup>34</sup>



## Who can prescribe monoclonal antibody therapy?

Monoclonal antibody therapies are subsidised by PBS only when prescribed by respiratory physicians, allergists, clinical immunologists, general physicians (or, in the case of omalizumab, paediatricians) with experience in severe asthma management, for patients attending an approved public or private hospital (on discharge or as an outpatient) at the time of prescription.‡

Before making the PBS application, the prescribing specialist documents clinical information demonstrating the asthma diagnosis and severity, and arranges required tests (e.g. total

IgE assay to determine omalizumab dose or blood eosinophil count to fulfil PBS eligibility criteria for treatment with mepolizumab or benralizumab). The specialist also arranges further follow-up assessments as required to fulfil PBS criteria for continuing treatment.

Ensure that patients understand that, in order to remain eligible for access to monoclonal antibody therapy through the PBS, it is important that they attend all scheduled specialist visits.

## Overview of PBS criteria for monoclonal antibody therapy<sup>13</sup>

### General criteria:

- diagnosis of asthma demonstrated by lung function tests (spirometry showing reversible expiratory airflow limitation, bronchial provocation test showing airway hyperresponsiveness, or peak expiratory flow monitoring showing variable airflow limitation), confirmed and documented by a specialist (respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma)
- asthma present for at least 1 year
- treated by the same specialist for at least 6 months or diagnosis by a multidisciplinary severe asthma clinic team
- inadequate asthma control despite documented adherence to optimised standard treatment that includes high-dose inhaled corticosteroids plus long-acting beta<sub>2</sub> agonist for at least 12 months, with at least one severe flare-up requiring hospitalisation or systemic corticosteroids in the past year. (Some exemptions from medication criteria are permitted according to intolerance or contraindications.)

### Specific criteria for benralizumab and mepolizumab:

- adults and adolescents ≥ 12 years
- (to start) blood eosinophil count ≥ 300 cells per microlitre in the last 12 months
- (to continue) demonstrated adequate response to treatment

### Specific criteria for omalizumab:

- adults and children ≥ 6 years
- (to start) documented evidence of atopy (skin prick testing or specific IgE test), and total serum IgE ≥ 30 IU/mL
- (to continue) documented demonstration of adequate response to treatment

### Switching between monoclonal antibody therapies

Some patients may meet PBS criteria for more than one monoclonal antibody therapy. In cases where one product has failed to achieve a clinical response, the prescribing specialist might consider switching to a different agent.

PBS criteria specify a minimum waiting time of 6 months between courses of different agents or of the same agent (in the case of failure to achieve or maintain therapeutic response).

Note: This overview is for purposes of comparison and highlighting key requirements only. Please refer to full PBS listing.

‡TGA-approved product information specifies that:

- benralizumab should be prescribed by a health care professional in consultation with a specialist physician experienced in the diagnosis and treatment of severe asthma<sup>17</sup>
- mepolizumab should be prescribed by a specialist experienced in the diagnosis and treatment of severe asthma<sup>11</sup>
- omalizumab for children should be prescribed only in conjunction with a paediatrician, respiratory physician or immunologist.<sup>12</sup>

## Who administers the treatment?

Monoclonal antibody therapies must be prepared and administered by a doctor or registered nurse, using standard aseptic techniques and with appropriate facilities and monitoring for reactions such as anaphylaxis.

Generally, the first 2–3 doses are administered in the specialist's rooms, a day hospital or day procedure unit. The patient should be directly observed by a health professional for 1 hour after the first dose of benralizumab or mepolizumab, and for 2 hours after the first three doses of omalizumab.<sup>35-37</sup>

Subsequent maintenance doses can be given in the specialist's office or in a primary care clinic. Current practice differs between states and territories. Instructions for storing, preparing and administering the dose should be followed carefully. For mepolizumab, the dose should be given as soon as practical after reconstituting.<sup>11, 12</sup>

At each maintenance dose, the patient should be monitored under direct observation by a health professional (e.g. registered nurse or GP) for at least 30 minutes after the injection.<sup>35, 36, 37</sup>

### Practice points

- Patients on monoclonal antibody therapy still require usual asthma care from their GP. They should keep taking their inhaled corticosteroid regularly, and their usual doctor should continue to check adherence and inhaler technique from time to time.
- Some patients relying on oral corticosteroids to control their asthma may be able to reduce the dose or stop taking it after gradually reducing the dose. Patients should not stop taking corticosteroids abruptly after starting monoclonal antibody therapy. Any reduction in the dose of oral corticosteroid should be carefully considered and the patients should be monitored carefully because of the risk of adrenal suppression.
- Flare-ups can still occur while taking a monoclonal antibody therapy, so patients should be advised to follow their written asthma action plan. Written asthma action plans should be updated every 12 months, or whenever there is any change in the treatment regimen.
- Most patients who require monoclonal antibody therapy would be eligible for a GP Management Plan and Team Care Arrangements. Refer to Medical Benefits Schedule (MBS) <http://www.health.gov.au/internet/main/publishing.nsf/content/mbsprimarycare-chronicdiseasemanagement>
- Patients with severe asthma may also benefit from referral to an asthma educator, MedsCheck by a community pharmacist, or Home Medicines Review (MBS item 900) by an accredited pharmacist (if eligible).
- Refer to National Asthma Council Australia <https://www.nationalasthma.org.au/living-with-asthma/resources/health-professionals/reports-and-statistics/asthma-cycle-of-care> and MBS for information on the Asthma Cycle of Care (MBS items 2546–2559 and 2664–2677) and the Practice Incentives Program (PIP) Asthma Incentive.

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# INFORMATION PAPER FOR PRIMARY HEALTHCARE PROFESSIONALS

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## More information

Australian Asthma Handbook [www.astmahandbook.org.au](http://www.astmahandbook.org.au)

Severe asthma toolkit [toolkit.severeasthma.org.au](http://toolkit.severeasthma.org.au)

Clinical recommendations for the use of benralizumab in severe asthma. Available at: [www.severeasthma.org.au/benralizumab](http://www.severeasthma.org.au/benralizumab)

Clinical recommendations for the use of mepolizumab in severe asthma. Available at: [www.severeasthma.org.au/mepolizumab](http://www.severeasthma.org.au/mepolizumab)

Clinical recommendations for the use of omalizumab in severe asthma in adults. Available at: [www.severeasthma.org.au/omalizumab](http://www.severeasthma.org.au/omalizumab)

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