

6.16 BENRALIZUMAB

30 mg in 1 mL solution for injection prefilled syringe Fasenra[®], AstraZeneca

1 Purpose of Application

- 1.1 The minor submission requested changes to the current PBS restrictions for medications for uncontrolled severe eosinophilic asthma.
- 1.2 Mepolizumab is the only medication that is currently PBS-listed for uncontrolled severe eosinophilic asthma. Omalizumab is PBS-listed for uncontrolled severe allergic asthma, which overlaps with eosinophilic asthma in some patients.
- 1.3 A major submission seeking PBS-listing of benralizumab was also considered at the March 2018 PBAC meeting. In that submission, listing was requested for the treatment of uncontrolled severe eosinophilic asthma on a cost-minimisation basis with mepolizumab. This minor submission intended that any changes to the restrictions would flow-on to benralizumab, should it be recommended for PBS-listing.
- 1.4 The PBAC noted that a minor submission requesting changes to the mepolizumab restriction was also on the March 2018 PBAC meeting agenda (Item 6.11).

2 Requested listing

- 2.1 The submission sought the following changes to the restrictions for biologics used to treat uncontrolled severe eosinophilic asthma:
 - removal of the requirement for a patient to be under the care of the same physician for at least 12 months, which the submission termed “continuity of care”;
 - removal of the requirement for patients to have had a blood eosinophil count ≥ 300 cells per microlitre in the last 6 weeks; and
 - removal of six month interval when switching between biologic therapies for uncontrolled severe asthma.
- 2.2 The submission requested changes to the PBS restrictions for medications for uncontrolled severe eosinophilic asthma. Omalizumab is PBS-listed for uncontrolled severe allergic asthma, rather than eosinophilic asthma. The PBAC noted that corresponding changes may also be required to the omalizumab restriction for consistency.
- 2.3 The minor submission based its requested changes on the restriction for mepolizumab (hence the mepolizumab restriction is outlined below).
- 2.4 Changes proposed by the submission are shown in **bold**; additions proposed by the submission are added in italics and deletions are crossed out with strikethrough.

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Parts of the restriction that would require amendment associated with the proposed changes, as identified by the Secretariat, are shaded grey. Note that an abridged restriction is provided for continuing therapy with only the relevant sections included.

Mepolizumab and requested restriction for benralizumab	
Category / Program	Section 100 – Highly Specialised Drugs Program – public and private
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
PBS Indication:	Uncontrolled severe eosinophilic asthma
Treatment phase:	Initial treatment
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing
Treatment criteria:	Must be treated by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma.
Clinical criteria:	<p>Patient must be under the care of the same physician for at least 12 months, AND Patient must have a diagnosis of asthma confirmed and documented by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma, defined by the following standard clinical features: (i) forced expiratory volume (FEV1) reversibility greater than or equal to 12% and greater than or equal to 200 mL at baseline within 30 minutes after administration of salbutamol (200 to 400 micrograms), or (ii) airway hyperresponsiveness defined as a greater than 20% decline in FEV1 during a direct bronchial provocation test or greater than 15% decline during an indirect bronchial provocation test, or (iii) peak expiratory flow (PEF) variability of greater than 15% between the two highest and two lowest peak expiratory flow rates during 14 days, AND Patient must have a duration of asthma of at least 1 year, AND Patient must have forced expiratory volume (FEV1) less than or equal to 80% predicted, documented on 1 or more occasions in the previous 12 months, AND Patient must have, or have had, blood eosinophil count greater than or equal to 300 cells per microlitre in the last 6 weeks, AND Patient must have signed a patient or parent/guardian acknowledgement indicating they understand and acknowledge that PBS subsidised treatment will cease if they do not meet the predetermined response criteria for ongoing PBS subsidised treatment, as outlined in the restriction for continuing treatment, AND Patient must have failed to achieve adequate control with optimised asthma therapy, despite formal assessment of and adherence to correct inhaler technique, which has been documented, AND The treatment must not be used in combination with or within 6 months of treatment with, PBS subsidised omalizumab.</p>
Population criteria:	Patient must be aged 12 years or older.

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Prescriber Instructions	<p>Optimised asthma therapy includes:</p> <p>(i) Adherence to maximal inhaled therapy, including high dose inhaled corticosteroid (ICS) plus long acting beta 2 agonist (LABA) therapy for at least 12 months, unless contraindicated or not tolerated;</p> <p>AND</p> <p>(ii) treatment with oral corticosteroids, either daily oral corticosteroids for at least 6 weeks, OR a cumulative dose of oral corticosteroids of at least 500 mg prednisolone equivalent in the previous 12 months, unless contraindicated or not tolerated.</p> <p>If the requirement for treatment with optimised asthma therapy cannot be met because of contraindications according to the relevant TGA approved Product Information and/or intolerances of a severity necessitating permanent treatment withdrawal, details of the contraindication and/or intolerance must be provided in the Authority application.</p> <p>The following initiation criteria indicate failure to achieve adequate control and must be demonstrated in all patients at the time of the application:</p> <p>(a) an Asthma Control Questionnaire (ACQ 5) score of at least 2.0, as assessed in the previous month, AND</p> <p>(b) while receiving optimised asthma therapy in the past 12 months, experienced at least 1 admission to hospital for a severe asthma exacerbation, OR 1 severe asthma exacerbation, requiring documented use of systemic corticosteroids (oral corticosteroids initiated or increased for at least 3 days, or parenteral corticosteroids) prescribed/supervised by a physician.</p> <p>The Asthma Control Questionnaire (5 item version) assessment of the patient must be made at time of application (in the previous month) for treatment (to establish baseline score) and again around 26 to 30 weeks after the first dose so that there is adequate time for a response to be demonstrated and for the application for continuing therapy to be processed.</p> <p>This assessment at around 26 to 30 weeks, which will be used to determine eligibility for continuing treatment, must be submitted within 4 weeks of the date of assessment, and no later than 2 weeks prior to the patient completing their current treatment course, to avoid an interruption to supply. Where a response assessment is not undertaken and submitted within this timeframe, the patient will be deemed to have failed to respond to treatment with mepolizumab.</p> <p>A patient who fails to respond to a course of PBS subsidised mepolizumab for the treatment of uncontrolled severe eosinophilic asthma will not be eligible to receive further PBS subsidised treatment with mepolizumab or omalizumab within 6 months of the date on which treatment was ceased.</p> <p>At the time of the authority application, medical practitioners should request 7 repeats to provide for an initial course of mepolizumab sufficient for 32 weeks of therapy.</p> <p>Mepolizumab and omalizumab may not be used concurrently or within 6 months of each other. A patient is required to have ceased treatment with omalizumab for 6 months prior to initiating treatment with mepolizumab.</p> <p><i>The prescriber must state in the Authority application that the patient has received at least 12 months of optimised asthma therapy before commencing PBS subsidised biologic therapy for this condition</i></p>
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<p>Administrative Advice</p>	<p>The authority application must be made in writing and must include:</p> <ul style="list-style-type: none"> (a) a completed authority prescription form; and (b) a completed Severe Eosinophilic Asthma Initial PBS Authority Application Supporting Information Form, which includes the following: <ul style="list-style-type: none"> (i) details of prior optimised asthma drug therapy (date of commencement and duration of therapy); and (ii) details of severe exacerbation/s experienced in the past 12 months while receiving optimised asthma therapy (date and treatment); and (iii) the signed patient or parent/guardian acknowledgement; and (c) a copy of the eosinophil pathology report; and (d) a completed Asthma Control Questionnaire (ACQ 5) calculation sheet including the date of assessment of the patient's symptoms.
<p>Note (abridged)</p>	<p>TREATMENT OF ADULT AND ADOLESCENT PATIENTS WITH UNCONTROLLED SEVERE EOSINOPHILIC ASTHMA</p> <p>Patients are eligible to commence a 'mepolizumab treatment cycle' (initial treatment course with or without continuing treatment course/s) if they satisfy the eligibility criteria as detailed under the initial treatment restriction.</p> <p>Once a patient has either failed to achieve or maintain a response to mepolizumab, they are deemed to have completed a treatment cycle and they must have, at a minimum, a 6 month break in PBS-subsidised mepolizumab therapy before they are eligible to commence the next mepolizumab treatment cycle, or if eligible, an 'omalizumab treatment cycle'. The length of a treatment break is measured from the date the most recent treatment with PBS-subsidised mepolizumab is stopped to the date of the first application for initial treatment with mepolizumab under the new treatment cycle.</p> <p>There is no limit to the number of treatment cycles a patient may undertake in their lifetime.</p> <p>(1) How to prescribe PBS-subsidised mepolizumab therapy:</p> <p>(a) Initial treatment:</p> <p>Applications for initial treatment should be made where:</p> <ul style="list-style-type: none"> i) A patient has received no prior PBS-subsidised mepolizumab treatment and wishes to commence such therapy; or ii) A patient wishes to recommence treatment with mepolizumab following a break in PBS-subsidised therapy of more than 6 months; or iii) A patient has received prior PBS-subsidised omalizumab and wishes to commence treatment with mepolizumab after a treatment break of 6 months. <p>All applications for initial treatment for non-grandfather patients will be limited to provide for a maximum of 32 weeks of therapy for mepolizumab.</p> <p><<(2) unchanged>></p> <p>(3) Re-commencement of treatment after a 6 month break in PBS-subsidised therapy:</p> <p>A patient who wishes to trial a second or subsequent mepolizumab treatment cycle, or an initial omalizumab treatment cycle, following a break in PBS-subsidised therapy of at least 6 months, must re-qualify for initial treatment with respect to the indices of disease severity (oral corticosteroid dose, Asthma Control Questionnaire (ACQ-5) score, and relevant exacerbation history). Patients must have received optimised standard therapy, at adequate doses and for the minimum period specified, immediately prior to the time the new baseline assessments are performed.</p>

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Mepolizumab restriction (abridged, only pertinent sections are included)	
Treatment phase:	Continuing treatment
Treatment criteria:	As per existing restriction (no changes proposed)
Clinical criteria:	Patient must have demonstrated or sustained an adequate response to PBS subsidised treatment with this drug, AND The treatment must not be used in combination with, or within 6 months of treatment with, PBS subsidised omalizumab.
Population criteria	As per existing restriction (no changes proposed)
Prescriber Instructions (abridged)	A patient who fails to respond to a course of PBS subsidised mepolizumab for the treatment of uncontrolled severe eosinophilic asthma will not be eligible to receive further PBS subsidised treatment with mepolizumab for this condition within 6 months of the date on which treatment was ceased.

For more detail on PBAC's view, see section 5 PBAC outcome.

3 Background

- 3.1 A major submission for PBS-listing of benralizumab, which was also considered at the March 2018 PBAC meeting, was made under the TGA-PBAC parallel process. At the time of PBAC consideration, the Delegates Overview and Advisory Committee on Medicines Minutes were available. The pre-PBAC response stated that, following the Advisory Committee on Medicines meeting, the TGA Delegate had recommended the indication: “[benralizumab] is indicated as an add-on maintenance treatment in patients aged ≥ 12 years of age, with severe eosinophilic asthma (with blood eosinophil count of ≥ 300 cells/ μ L or ≥ 150 if on chronic OCS treatment).”
- 3.2 There are currently two biologic agents that are PBS-listed for uncontrolled severe asthma: mepolizumab and omalizumab.
- 3.3 Mepolizumab was PBS listed on 1 January 2017 for the treatment of uncontrolled severe eosinophilic asthma in patients aged 12 years and over, as a Section 100 (Highly Specialised Drugs Program) written authority. It was recommended by the PBAC at its July 2016 meeting on a cost-minimisation basis with omalizumab.
- 3.4 Omalizumab was first recommended for listing in November 2010 and is currently PBS-listed for the treatment of patients aged six years and over with uncontrolled severe allergic asthma who have a total serum immunoglobulin E ≥ 30 IU/mL. It was recommended on a cost-effectiveness basis compared with standard of care.
- 3.5 The submission did not propose a change to the clinical place in therapy.

4 Basis for requested restriction changes

Sponsor hearing

4.1 There was no hearing for this item as it was a minor submission.

Consumer comments

4.2 The PBAC noted that no consumer comments were received for this item. However, the PBAC noted that general input relating to the restrictions for biologics in asthma was provided by two organisations prior to the PBAC meeting: the Thoracic Society of Australia and New Zealand; and the Centre of Research Excellence in Severe Asthma (which included comment from the principal investigators of the Australian Mepolizumab Registry).

4.3 The PBAC noted that both organisations also suggested changes to the restriction relating to: the requirements for a patient to be under the care of the same physician for at least 12 months; and the six month interval between biologic therapies. The PBAC further noted that the Centre of Research Excellence in Severe Asthma also proposed numerous other changes to the restriction including: removal of the requirement for six weeks of prior oral corticosteroid therapy; and changes to the timing for re-assessments.

Basis for submission's proposed changes

4.4 The submission proposed changing the current restrictions for severe refractory eosinophilic asthma, which it intended would flow on to benralizumab should it be PBS-listed. The submission stated that proposed changes would remove what it claimed were “potential barriers for eligible patients to receive timely treatment with PBS-subsidised biologic agents”.

Duration of treatment by the same physician (referred to as ‘Continuity of care criteria’):

4.5 The submission proposed the following changes to the initial treatment restriction:

- removal of the criteria: “Patient must be under the care of the same physician for at least 12 months”; and
- addition of the following note in the prescriber instructions: “The prescriber must state in the Authority application that the patient has received at least 12 months of optimised asthma therapy before commencing PBS subsidised biologic therapy for this condition”.

4.6 The submission stated that patients who move into the care of a new specialist might have to re-start the 12 month period before they could receive PBS-subsidised biologic treatment (e.g. when a patient is referred to a specialist by a General Practitioner, or when a change in the treating physician occurs). The submission stated that this may increase the risk of asthma exacerbations or adverse events from oral corticosteroid treatment.

- 4.7 The submission interpreted that the implicit intention of the criteria was so that the treating physician would have optimised the patient’s inhaled and oral therapies and ensured their inhaler technique was correct before prescribing a biologic agent. The submission considered that the requested amendment would preserve this intent.
- 4.8 The submission noted that the restriction also includes other criteria which would also preserve this intent, including that: the “patient must have a duration of asthma of at least 1 year”; “Optimised asthma therapy includes: adherence to maximal inhaled therapy, including high dose inhaled corticosteroid (ICS) plus long-acting beta-2 agonist (LABA) therapy for at least 12 months, unless contraindicated or not tolerated”; and treatment must be initiated by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma. The submission did not propose changes to these components of the restriction.
- 4.9 The PBAC noted that the Thoracic Society of Australia and New Zealand and the Centre of Research Excellence in Severe Asthma stated that the current requirements delay treatment and put patients at risk of severe asthma exacerbations. Both organisations proposed changing this criterion to allow use in patients: under specialist care for at least 6 months; or confirmed to have uncontrolled severe asthma, following assessment by a severe asthma clinic. The Centre of Research Excellence in Severe Asthma proposed that the latter method of assessment should be available through hospital-based severe asthma multidisciplinary clinics, comprising at least a respiratory physician and a nurse or pharmacist or trained asthma educator.

Eosinophil levels

- 4.10 The submission requested the following change to the clinical criteria for benralizumab:
- “Patient must have, or have had, a blood eosinophil count greater than or equal to 300 cells per microlitre ~~in the last six weeks~~.”
- 4.11 The submission’s rationale for the proposed change was that a patient’s eosinophil levels may have previously been ≥ 300 cells/ μL but may currently be suppressed by oral corticosteroid therapy.
- 4.12 The submission acknowledged that the sponsor of mepolizumab had made a submission to the November 2017 PBAC meeting to extend the testing period to 12 months, though the outcome was not published at the time the minor submission was made.
- 4.13 The PBAC noted that on 1 February 2018, the restriction for mepolizumab was changed to: “Patient must have blood eosinophil count greater than or equal to 300 cells per microlitre in the last 12 months” following its recommendation at its November 2017 meeting. Per the November 2017 PBAC outcomes, the PBAC noted

that this would allow improved access to mepolizumab treatment by reducing the time and administrative burden for patients and clinicians.

Six-month wait between biologics for asthma

- 4.14 The submission proposed removal of the requirement for patients with inadequate response to a particular biologic to have a six month interval between biologics for asthma. The submission stated this requirement was based on the restriction for omalizumab when it was the only biologic listed for asthma, but may no longer be reasonable given multiple biologic agents are available with differing mechanisms of action. The submission further stated that delaying a switch to a potentially effective agent could be considered clinically inappropriate.
- 4.15 The PBAC noted that the the Thoracic Society of Australia and New Zealand and the Centre of Research Excellence in Severe Asthma both proposed changing the six month interval when switching between different biologics. The organisations proposed that the requirement be either removed or replaced with an interval of one or two months.
- 4.16 The PBAC considered that the period of time between re-trial of biologics and the time for switching biologics may differ, and so would need to be reflected separately in the restrictions.

Basis for six month treatment break: re-trial of the same biologic

- 4.17 The PBAC noted that the six month treatment break was originally based on the omalizumab restriction, and related to re-trial of omalizumab in patients with inadequate response. Omalizumab was the first biologic listed for uncontrolled severe asthma, and included the requirement that “A patient who fails to respond to a course of PBS-subsidised omalizumab for the treatment of uncontrolled severe allergic asthma will not be eligible to receive further PBS-subsidised treatment with omalizumab for this condition within 6 months of the date on which treatment was ceased.”
- 4.18 The PBAC further noted that the existing mepolizumab restriction was largely based on the omalizumab restriction, and included a parallel six month treatment break between re-trial of mepolizumab for those patients who did not achieve an adequate response and a consistent six month treatment break between switching between the two biologics.

Switching between different biologics

- 4.19 The key trials of benralizumab, CALIMA and SIROCCO (which are discussed in the parallel major submission, item 5.01), excluded patients who received another biologic within four months or five half-lives, whichever was longer (source: Clinical Study Reports for CALIMA and SIROCCO).
- 4.20 The PBAC noted that the half-lives of the biologics used to treat asthma are:

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- benralizumab has an elimination half-life of 15 days (source: page 4, Draft Benralizumab Product Information),
 - mepolizumab has an elimination half-life of 16 to 22 days (source: page 3, Mepolizumab Product Information); and
 - omalizumab has an elimination half-life of 22 days (\pm 8 days). The Omalizumab Product Information states: “Omalizumab has a long serum half-life (mean 22 + 8.2 days). The long half-life is characteristic of IgG class immunoglobulins and a result of IgG recycling via its salvage receptor (FcRn). At the doses recommended for therapeutic use, average clearance is expected to represent dominantly IgG clearance and to be relatively slow (2.27-4.12 mL/kg/day)” (source: page 3, Omalizumab Product Information).
- 4.21 Thus, these medications would not be expected to be eliminated from the body until 75 to 110 days (2.5 to 4 months) after the last injection, based on clearance requiring five elimination half-lives.
- 4.22 The three biologic agents have different modes of action. Mepolizumab and benralizumab both target the interleukin-5 (IL-5) pathway (i.e. eosinophil-mediated inflammation). Benralizumab is an IL-5 receptor α antagonist, while mepolizumab targets the IL-5 ligand. On the other hand, omalizumab targets the immunoglobulin E pathway (allergic asthma). The submission stated that these differences in mechanism of action could result in differences in patient responsiveness to particular agents.

Re-trial of the same agent

- 4.23 It was unclear whether the submission also sought removal of the six-month break between re-trial of benralizumab in patients who had either failed to achieve or maintain a response to benralizumab. Removal of the six-month break between re-trial of the same agent following inadequate response would negate the intent of the response criteria.
- 4.24 The PBAC noted that there is currently no limit to the number of times that a patient can re-trial the same biologic agent following previous inadequate response. In other conditions, patients cannot keep re-trialling a biologic agent they have previously failed to respond to. For example biologics for chronic plaque psoriasis include the clinical criteria: “patient must not have failed, or ceased to respond to, PBS-subsidised therapy with this drug for the treatment of this condition in the current Treatment Cycle”.

Separate initial restriction for patients switching between biologics

- 4.25 The current initial restriction requires patients to have:
- an Asthma Control Questionnaire (ACQ-5) score of at least 2.0, as assessed in the previous month;
 - experienced a severe asthma exacerbation requiring either a hospital admission or use of systemic corticosteroids in the past 12 months;

- forced expiratory volume (FEV1) \leq 80% predicted in the previous 12 months; and
 - failed to achieve adequate control with optimised asthma therapy, which includes treatment with oral corticosteroids (doses specified).
- 4.26 The PBAC considered that these requirements may not be appropriate for patients who are switching to a new biologic, rather than first initiating biologic therapy. That is, the PBAC noted that patients may experience an inadequate response to a biologic (i.e. not achieve either (a) reduction in ACQ-5 score \geq 0.5 from baseline, or (b) maintenance oral corticosteroid dose reduced by \geq 25% from baseline, and no deterioration in ACQ-5 score from baseline), but may still not meet the initial restriction criteria outlined above. The PBAC noted that without a separate “initial” restriction for patients who are switching from a different biologic, there may be additional barriers to patients switching from one biologic to another.

Other information provided in the submission

- 4.27 The submission compared the six month break between biologics for asthma with the treatment break that had previously been required for biologic disease modifying anti-rheumatic drugs (bDMARDs) for severe active rheumatoid arthritis. This had comprised a minimum five year break after a patient had failed to respond to three bDMARDs. The submission referred to the ‘PBAC Review of bDMARDs for the treatment of severe active rheumatoid arthritis’ (2009 Public Summary Document), which stated that:
- “The PBAC considered that the five year break in therapy required under the PBS restrictions after failure to respond to three bDMARDs was no longer clinically appropriate given the existence of multiple drugs with different mechanisms of actions and recommended that this requirement be removed from the restrictions. PBAC recalled it had settled on this exclusion period during its early considerations of the bDMARDs when only a limited number of these medicines were available. At that time, the five year period was seen as a reasonable timeframe to allow sponsors to obtain new data about the efficacy of one bDMARD following failure of another bDMARD.”... “(t)he Committee considered that revising the restriction to allow patients to trial up to five bDMARDs would be appropriate to enable patients to try more treatments with different modes of action.”
- 4.28 Following the review, the restrictions for bDMARDs in rheumatoid arthritis were changed to allow patients to try a maximum of five bDMARDs within a life-time. Note that there were six bDMARDs listed on the PBS for rheumatoid arthritis at the time of the review.
- 4.29 The minor submission did not provide any specific evidence of the efficacy of one biologic commenced immediately following inadequate response to another agent, nor of potential harms associated with switching between biologics without a wash-out period. The latter may be relevant given the long half-lives of these medications.

Economic analysis

- 4.30 As a minor submission, no economic comparison was presented.
- 4.31 The parallel major submission for PBS-listing of benralizumab was made on a cost-minimisation basis to mepolizumab.

Estimated PBS usage & financial implications

- 4.32 The minor submission estimated that there would be no additional financial implications for the Commonwealth associated with the proposed amendments to the restrictions. However, the requested changes may be associated with increased costs to the PBS/RPBS, for example due to increased drug costs during the six-month treatment break or earlier commencement of therapy. This is particularly pertinent given the changes were requested to “improve access” to biologic therapies.

5 PBAC Outcome

- 5.1 The PBAC recommended changing the restriction for biologics for severe asthma to reduce the duration of time that a patient must be under the care of the same physician to six months. The PBAC noted that the submission’s request to extend the eosinophil blood test validity period had already been made, pursuant to a positive recommendation made at the Committee’s November 2017 meeting for mepolizumab. The PBAC deferred making a decision on the request to remove the six month treatment break when switching between different biologics. The PBAC considered that removal of the treatment break would have flow-on implications and would require consideration of issues around re-trialling of the same biologic, switching between and cycling of biologics in asthma. The deferral was to enable further consideration and broader discussion given the complexity of these matters.
- 5.2 The PBAC noted that there was support from a number of clinician groups for changes to the PBS restrictions for biologics, particularly relating to the duration of treatment by the same physician and to the six-month treatment break when switching between different biologics.

Duration of treatment by the same physician

- 5.3 The PBAC recommended changing the clinical criterion stipulating that a “patient must be under the care of the same physician for at least 12 months”. The PBAC recommended that this criterion be replaced with a requirement for patients to be either under the care of the same physician for at least six months, or be diagnosed as having uncontrolled severe asthma by a multidisciplinary severe asthma clinic team, consistent with the intention of the changes proposed by the Centre of Research Excellence in Severe Asthma and the Thoracic Society of Australia and New Zealand. The PBAC considered that these changes should be made to all biologics for uncontrolled, severe asthma.
- 5.4 As suggested by the Centre of Research Excellence in Severe Asthma, the PBAC

recommended that a multidisciplinary severe asthma clinic team would comprise of at least a respiratory physician and a nurse, pharmacist or trained asthma educator.

- 5.5 The PBAC noted that this would make the period of time under the care of the same physician consistent with the PBS listing of omalizumab for uncontrolled severe allergic asthma in children aged 6 to 12 years.
- 5.6 The PBAC considered that this change may improve continuity of care and access to effective treatment when patients with uncontrolled severe asthma change physicians prior to initiating a biologic.

Eosinophil count in the past six weeks

- 5.7 The PBAC noted that on 1 February 2018, the eosinophil blood test validity period was changed from six weeks to 12 months in the mepolizumab restriction; the criterion now states: “Patient must have blood eosinophil count greater than or equal to 300 cells per microlitre in the last 12 months”. The PBAC considered that this adequately addressed the submission’s request to change the time period for validity of this test. The PBAC noted that this change would flow-on to the listing for benralizumab for uncontrolled severe eosinophilic asthma for consistency with the listing for mepolizumab.

Six month waiting period between biologics for asthma

- 5.8 The PBAC noted the six month treatment break was originally based on the omalizumab restriction when it was the only biologic listed for asthma and the requirement initially only related to re-trialling omalizumab in patients with inadequate response.
- 5.9 The PBAC noted that the treatment breaks when switching between different biologics were somewhat consistent with the exclusion criteria of the key trials of biologics in asthma. The key trials had generally required wash-out periods between different biologics. For example, the key trials of benralizumab excluded patients who received another biologic within four months or five half-lives, whichever was longer. The PBAC further noted the long elimination half-lives of the biologics for asthma (15 to 22 days).
- 5.10 The PBAC noted input from the Centre of Research Excellence in Severe Asthma and the Thoracic Society of Australia and New Zealand, which stated that patients may be at risk of severe exacerbations during treatment breaks. As such, the PBAC considered that the requirements warranted further review. The PBAC considered that any changes to the time periods between use of biologics should take into account the inter-related issues associated with re-trialling, switching and cycling of biologics in asthma, which are each discussed in turn below. Given the complexity, the PBAC considered that such matters would best be informed by broader discussion at a stakeholder meeting.

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- 5.11 With respect to re-trialling of the same biologic, the PBAC considered that broader discussion was required as to:
- the circumstances under which it would be appropriate to re-trial the same biologic agent rather than trial other treatment options; and
 - whether the same agent could be re-trialled following previous inadequate response. If so, consideration would be required as to how many times an agent could be re-trialled and the time period between re-trialling of the same agent.
- 5.12 With respect to switching between different biologics, the PBAC considered that broader discussion was required as to:
- the criteria for switching to an alternative biologic therapy;
 - whether the six month break should be replaced with a break of a different duration. The PBAC noted that clinical organisations had proposed that the requirement be either removed or replaced with a treatment break of one or two months;
 - whether there should be limits on the number of times that a patient can use each agent (refer to cycling between biologics, discussed below); and
 - whether a separate initial restriction would be required to enable patients to switch from one biologic to another without having to meet the current initial restriction requirements (i.e. separate initial restrictions may be required for: patients who are newly eligible for biologic therapy; and those who were previously eligible and now initiating different biologic).
- 5.13 With respect to cycling between the biologics, the PBAC considered that broader discussion was required regarding the number of agents that could be used over a defined time period, including evidence supporting the clinical plausibility of cycling between agents. This could potentially include consideration of: a maximum number of biologics for the treatment of asthma over a certain timeframe (e.g. similar to the PBS arrangements for chronic plaque psoriasis, wherein patients with an inadequate response to three biologic agents must have a minimum five year break before re-trialling biologics); or a maximum number of biologics for the treatment of asthma in a lifetime (e.g. similar to the PBS arrangements for rheumatoid arthritis, wherein patients can trial a maximum of five biologics within a life-time).
- 5.14 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommend a change to the duration of treatment by the same physician.

Deferred amendments to the six-month waiting period between switching biologic therapies for uncontrolled severe asthma.

6 Recommended listing

Amend the existing listing for mepolizumab and omalizumab for the treatment of uncontrolled severe eosinophilic asthma and uncontrolled severe allergic asthma in adults respectively and include in the recommended listing for benralizumab for the treatment of uncontrolled severe eosinophilic asthma as follows:

- reduce the time frame in the clinical criterion: “patient must be under the care of the same physician for at least 12 months” to “at least 6 months” and;
- Include an alternative criterion (that is an ‘or’ criterion) of “Patient must have been diagnosed by a multidisciplinary severe asthma clinic team.” A multidisciplinary severe asthma clinic team will be comprised of at least a respiratory physician and a nurse, pharmacist or trained asthma educator.

The full restrictions are provided below.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
BENRALIZUMAB 30 mg in 1 mL injection, (prefilled syringe)	1	4	Fasenra® AstraZenica Pty Ltd
Category / Program	Section 100 Highly Specialised Drugs Program – public and private		
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives		
PBS Indication:	Uncontrolled severe eosinophilic asthma		
Treatment phase:	Initial treatment		
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined		
Treatment criteria	Must be treated by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma.		

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<p>Clinical criteria:</p>	<p>Patient must be under the care of the same physician for at least 6 months, OR Patient must have been diagnosed by a multidisciplinary severe asthma clinic team AND Patient must have a diagnosis of asthma confirmed and documented by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma, defined by the following standard clinical features: (i) forced expiratory volume (FEV1) reversibility greater than or equal to 12% and greater than or equal to 200 mL at baseline within 30 minutes after administration of salbutamol (200 to 400 micrograms), or (ii) airway hyperresponsiveness defined as a greater than 20% decline in FEV1 during a direct bronchial provocation test or greater than 15% decline during an indirect bronchial provocation test, or (iii) peak expiratory flow (PEF) variability of greater than 15% between the two highest and two lowest peak expiratory flow rates during 14 days, AND Patient must have a duration of asthma of at least 1 year, AND Patient must have forced expiratory volume (FEV1) less than or equal to 80% predicted, documented on 1 or more occasions in the previous 12 months, AND Patient must have blood eosinophil count greater than or equal to 300 cells per microlitre in the last 12 months, AND Patient must have failed to achieve adequate control with optimised asthma therapy, despite formal assessment of and adherence to correct inhaler technique, which has been documented, AND The treatment must not be used in combination with, or within 6 months of treatment with, PBS-subsidised omalizumab or mepolizumab.</p>
<p>Population criteria</p>	<p>Patient must be aged 12 years or older.</p>
<p>Prescriber Instructions</p>	<p>Optimised asthma therapy includes: (i) Adherence to maximal inhaled therapy, including high dose inhaled corticosteroid (ICS) plus long-acting beta-2 agonist (LABA) therapy for at least 12 months, unless contraindicated or not tolerated; AND (ii) treatment with oral corticosteroids, either daily oral corticosteroids for at least 6 weeks, OR a cumulative dose of oral corticosteroids of at least 500 mg prednisolone equivalent in the previous 12 months, unless contraindicated or not tolerated. If the requirement for treatment with optimised asthma therapy cannot be met because of contraindications according to the relevant TGA-approved Product Information and/or intolerances of a severity necessitating permanent treatment withdrawal, details of the contraindication and/or intolerance must be provided in the Authority application. The following initiation criteria indicate failure to achieve adequate control and must be demonstrated in all patients at the time of the application: (a) an Asthma Control Questionnaire (ACQ-5) score of at least 2.0, as assessed in the previous month, AND (b) while receiving optimised asthma therapy in the past 12 months, experienced at least 1 admission to hospital for a severe asthma exacerbation, OR 1 severe asthma exacerbation, requiring documented use of systemic corticosteroids (oral corticosteroids initiated or increased for at least 3 days, or parenteral corticosteroids) prescribed/supervised by a</p>

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	<p>physician.</p> <p>The Asthma Control Questionnaire (5 item version) assessment of the patient must be made at time of application for treatment (to establish baseline score) and again around 24 weeks after the first dose so that there is adequate time for a response to be demonstrated and for the application for continuing therapy to be processed.</p> <p>This assessment at around 24 weeks, which will be used to determine eligibility for continuing treatment, must be submitted within 4 weeks of the date of assessment, and no later than 2 weeks prior to the patient completing their current treatment course, to avoid an interruption to supply. Where a response assessment is not undertaken and submitted within this timeframe, the patient will be deemed to have failed to respond to treatment with benralizumab.</p> <p>A patient who fails to respond to a course of PBS-subsidised benralizumab for the treatment of uncontrolled severe eosinophilic asthma will not be eligible to receive further PBS-subsidised treatment with benralizumab, mepolizumab or omalizumab within 6 months of the date on which treatment was ceased.</p> <p>A multidisciplinary severe asthma clinic team comprises of:</p> <ul style="list-style-type: none"> • A respiratory physician; and • A pharmacist, nurse or asthma educator. <p>At the time of the authority application, medical practitioners should request 4 repeats to provide for an initial course of benralizumab sufficient for 32 weeks of therapy.</p> <p>Benralizumab may not be used concurrently with mepolizumab or omalizumab or within 6 months of each other. A patient is required to have ceased treatment with mepolizumab or omalizumab for 6 months prior to initiating treatment with benralizumab.</p> <p>The authority application must be made in writing and must include:</p> <p>(a) a completed authority prescription form; and</p> <p>(b) a completed Severe Eosinophilic Asthma Initial PBS Authority Application - Supporting Information Form,</p> <p>which includes the following:</p> <p>(i) details of prior optimised asthma drug therapy (date of commencement and duration of therapy); and</p> <p>(ii) details of severe exacerbation/s experienced in the past 12 months while receiving optimised asthma therapy (date and treatment); and</p> <p>(iii) the signed patient or parent/guardian acknowledgement; and</p> <p>(c) a copy of the eosinophil pathology report; and</p> <p>(d) a completed Asthma Control Questionnaire (ACQ-5) calculation sheet including the date of assessment of the patient's symptoms.</p>
<p>Administrative Advice</p>	<p>The Department of Human Services website (www.humanservices.gov.au) has details of the accepted toxicities, including severity, which will be accepted for the purposes of exempting a patient from the requirement of treatment with optimised asthma therapy.</p> <p>For copies of the ACQ, please contact AstraZenica on [phone number to be advised].</p> <p>It is recommended that an application for continuing treatment is submitted at the time of the 24 week assessment, to ensure continuity of treatment for those patients who meet the continuation criteria for PBS-subsidised benralizumab treatment.</p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to:</p> <p>Department of Human Services</p>

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	<p>Complex Drugs Reply Paid 9826 HOBART TAS 7001 TREATMENT OF ADULT AND ADOLESCENT PATIENTS WITH UNCONTROLLED SEVERE EOSINOPHILIC ASTHMA</p> <p>Patients are eligible to commence a 'benralizumab treatment cycle' (initial treatment course with or without continuing treatment course/s) if they satisfy the eligibility criteria as detailed under the initial treatment restriction.</p> <p>Once a patient has either failed to achieve or maintain a response to benralizumab, they are deemed to have completed a treatment cycle and they must have, at a minimum, a 6 month break in PBS-subsidised benralizumab therapy before they are eligible to commence the next 'benralizumab treatment cycle', or if eligible, a 'mepolizumab treatment cycle' or an 'omalizumab treatment cycle'. The length of a treatment break is measured from the date the most recent treatment with PBS-subsidised benralizumab is stopped to the date of the first application for initial treatment with benralizumab, mepolizumab or omalizumab under the new treatment cycle.</p> <p>There is no limit to the number of treatment cycles a patient may undertake in their lifetime.</p> <p>(1) How to prescribe PBS-subsidised benralizumab therapy:</p> <p>(a) Initial treatment:</p> <p>Applications for initial treatment should be made where:</p> <ul style="list-style-type: none">i) A patient has received no prior PBS-subsidised benralizumab treatment and wishes to commence such therapy; orii) A patient wishes to recommence treatment with benralizumab following a break in PBS-subsidised therapy of more than 6 months; oriii) A patient has received prior PBS-subsidised mepolizumab or omalizumab and wishes to commence treatment with benralizumab after a treatment break of 6 months. <p>All applications for initial treatment for non-grandfather patients will be limited to provide for a maximum of 32 weeks of therapy for benralizumab.</p> <p>(b) Grandfather patients:</p> <p>For patients who commenced treatment with benralizumab for uncontrolled severe eosinophilic asthma prior to <i>[insert date of listing]</i> and who continues to receive treatment at the time of application, may qualify for treatment under the initial 'grandfather' treatment restriction. A patient may only qualify for PBS-subsidised treatment under this restriction once. A maximum of 24 weeks of treatment with benralizumab will be authorised under this criterion. Approval will be based on the criteria included in the relevant restriction. Following completion of the Initial PBS-subsidised course, further applications for treatment with benralizumab will be assessed under the continuing treatment restriction.</p> <p>'Grandfather' arrangements will only apply for the first treatment cycle (initial treatment course with or without continuing treatment course/s). If a 'Grandfathered' patient recommences on second and subsequent cycles after a treatment break, the 'Grandfathered' patient must re-qualify for Initial treatment under the criteria that apply to a new patient. See 'Re-commencement of treatment after a 6 month break in PBS-subsidised therapy' below for further details.</p> <p>(c) Continuing treatment:</p> <p>Following the completion of the initial treatment course with benralizumab, a patient may qualify to receive up to a further 24 weeks of continuing treatment with benralizumab providing they have demonstrated an adequate response to treatment. The patient remains eligible to receive continuing benralizumab treatment in courses of up to 24 weeks providing they continue to sustain the response.</p> <p>(2) Baseline measurements to determine response:</p> <p>The Department of Human Services will determine whether a response to treatment has been demonstrated based on the baseline measurements of the Asthma Control</p>
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	<p>Questionnaire (ACQ; 5 item version) and oral corticosteroid dose, submitted with the Initial authority application for benralizumab. However, prescribers may provide new baseline measurements when a new Initial treatment authority application is submitted and the Department of Human Services will assess response according to these revised baseline measurements.</p> <p>(3) Re-commencement of treatment after a 6 month break in PBS-subsidised therapy: A patient who wishes to trial a second or subsequent benralizumab treatment cycle, or an initial mepolizumab or omalizumab treatment cycle, following a break in PBS-subsidised therapy of at least 6 months, must re-qualify for initial treatment with respect to the indices of disease severity (oral corticosteroid dose, Asthma Control Questionnaire (ACQ-5) score, and relevant exacerbation history). Patients must have received optimised standard therapy, at adequate doses and for the minimum period specified, immediately prior to the time the new baseline assessments are performed.</p> <p>Formal assessment and correction of inhaler technique should be performed in accordance with the National Asthma Council (NAC) Information Paper for Health Professionals on Inhaler Technique (available at www.humanservices.gov.au or www.nationalasthma.org.au); the assessment and adherence to correct technique should be documented in the patient's medical records. Patients can obtain support with inhaler technique through their local Asthma Foundation (1800 645 130).</p> <p>No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.</p>
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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
BENRALIZUMAB 30 mg in 1 mL injection, (prefilled syringe)	1	4	Fasenra® AstraZenica Pty Ltd
Category / Program	Section 100 Highly Specialised Drugs Program – public and private		
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives		
PBS Indication:	Uncontrolled severe eosinophilic asthma		
Treatment phase:	Initial treatment – balance of supply		
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Streamlined		
Treatment criteria	Must be treated by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma.		
Clinical criteria:	Patient must have received insufficient therapy with this drug under the Initial treatment restriction to complete 32 weeks treatment, AND The treatment must provide no more than the balance of up to 32 weeks treatment available under the above restriction.		
Population criteria	Patient must be aged 12 years or older.		
Administrative Advice	Authority approval for sufficient therapy to complete a maximum of 32 weeks of treatment may be requested by telephone by contacting the Department of Human Services on 1800		

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	<p>700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Written application for authority approval for sufficient therapy to complete a maximum of 32 weeks of treatment should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001 TREATMENT OF ADULT AND ADOLESCENT PATIENTS WITH UNCONTROLLED SEVERE EOSINOPHILIC ASTHMA (Per note for initial treatment) No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.</p>
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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
BENRALIZUMAB 30 mg in 1 mL injection, (prefilled syringe)	1	2	Fasenra® AstraZenica Pty Ltd
Category / Program	Section 100 Highly Specialised Drugs Program – public and private		
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives		
PBS Indication:	Uncontrolled severe eosinophilic asthma		
Treatment phase:	Continuing treatment		
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined		
Treatment criteria	Must be treated by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma.		
Clinical criteria:	Patient must have demonstrated or sustained an adequate response to PBS subsidised treatment with this drug, AND The treatment must not be used in combination with, or within 6 months of treatment with, PBS subsidised omalizumab or mepolizumab.		
Population criteria	Patient must be aged 12 years or older.		
Prescriber Instructions	An adequate response to benralizumab treatment is defined as: (a) a reduction in the Asthma Control Questionnaire (ACQ 5) score of at least 0.5 from baseline, OR (b) maintenance oral corticosteroid dose reduced by at least 25% from baseline, and no deterioration in ACQ 5 score from baseline. All applications for continuing treatment with benralizumab must include a measurement of		

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	<p>response to the prior course of therapy. The Asthma Control Questionnaire (5 item version) assessment of the patient's response to the prior course of treatment, and the assessment of oral corticosteroid dose, must be made at around 24 weeks after the first dose of PBS subsidised benralizumab so that there is adequate time for a response to be demonstrated and for the application for continuing therapy to be processed.</p> <p>The first assessment should, where possible, be completed by the same physician who initiated treatment with benralizumab. This assessment, which will be used to determine eligibility for continuing treatment, must be submitted within 4 weeks of the date of assessment, and no later than 2 weeks prior to the patient completing their current treatment course, to avoid an interruption to supply. Where a response assessment is not undertaken and submitted within this timeframe, the patient will be deemed to have failed to respond to treatment with benralizumab.</p> <p>A patient who fails to respond to a course of PBS subsidised benralizumab for the treatment of uncontrolled severe eosinophilic asthma will not be eligible to receive further PBS subsidised treatment with benralizumab for this condition within 6 months of the date on which treatment was ceased.</p> <p>At the time of the authority application, medical practitioners should request the appropriate number of repeats to provide for a continuing course of benralizumab sufficient for 24 weeks of therapy.</p> <p>The authority application must be made in writing and must include:</p> <ul style="list-style-type: none"> (a) a completed authority prescription form; and (b) a completed Severe Eosinophilic Asthma Continuing PBS Authority Application Supporting Information Form which includes details of maintenance oral corticosteroid dose; and (c) a completed Asthma Control Questionnaire (ACQ 5) calculation sheet including the date of assessment of the patient's symptoms
<p>Administrative Advice</p>	<p>If the same physician cannot assess the patient please call the Department of Human Services on 1800 700 270.</p> <p>It is recommended that second and subsequent applications for continuing treatment are submitted at the time of a 16 week assessment, to ensure continuity of treatment for those patients who meet the continuation criteria for PBS subsidised benralizumab treatment.</p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to:</p> <p>Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>
<p>Administrative advice (additional note)</p>	<p>For copies of the ACQ, please contact AstraZenica on [phone number to be advised].</p> <p>TREATMENT OF ADULT AND ADOLESCENT PATIENTS WITH UNCONTROLLED SEVERE EOSINOPHILIC ASTHMA <i>(Per note for initial treatment)</i></p> <p>No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.</p>

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
BENRALIZUMAB 30 mg in 1 mL injection, (prefilled syringe)	1	2	Fasenra® AstraZenica Pty Ltd
Category / Program	Section 100 Highly Specialised Drugs Program – public and private		
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives		
PBS Indication:	Uncontrolled severe eosinophilic asthma		
Treatment phase:	Continuing treatment – balance of supply		
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input checked="" type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Streamlined		
Treatment criteria	Must be treated by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma.		
Clinical criteria:	Patient must have received insufficient therapy with this drug under the continuing treatment restriction to complete 24 weeks treatment, AND The treatment must provide no more than the balance of up to 24 weeks treatment available under the above restriction.		
Population criteria	Patient must be aged 12 years or older.		
Administrative Advice	Authority approval for sufficient therapy to complete a maximum of 24 weeks of treatment may be requested by telephone by contacting the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Written application for authority approval for sufficient therapy to complete a maximum of 24 weeks of treatment should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001 TREATMENT OF ADULT AND ADOLESCENT PATIENTS WITH UNCONTROLLED SEVERE EOSINOPHILIC ASTHMA (Per note for initial treatment) No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.		

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
BENRALIZUMAB 30 mg in 1 mL injection, (prefilled syringe)	1	2	Fasenra® AstraZenica Pty Ltd
Category / Program	Section 100 Highly Specialised Drugs Program – public and private		
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives		
PBS Indication:	Uncontrolled severe eosinophilic asthma		
Treatment phase:	Initial treatment – grandfather patients		
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined		
Treatment criteria	Must be treated by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma.		

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<p>Clinical criteria:</p>	<p>Patient must have received non-PBS treatment with this drug for this condition prior to [Date to be finalised], AND Patient must be receiving treatment with this drug for this condition at the time of application, AND Patient must have had, prior to commencement of benralizumab, a diagnosis of asthma confirmed and documented by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma, defined by the following standard clinical features: (i) Forced expiratory volume (FEV1) reversibility greater than or equal to 12% and greater than or equal to 200 mL at baseline within 30 minutes after administration of salbutamol (200 to 400 micrograms), or(ii) airway hyperresponsiveness defined as a greater than 20% decline in FEV1 during a direct bronchial provocation test or greater than 15% decline during an indirect bronchial provocation test, or(iii) peak expiratory flow (PEF) variability of greater than 15% between the two highest and two lowest peak expiratory flow rates during 14 days, AND Patient must have had blood eosinophil count greater than or equal to 300 cells per microlitre prior to commencement of benralizumab, AND Patient must have had a duration of asthma of at least 1 year prior to commencement of benralizumab, AND Patient must have failed to achieve adequate control with optimised asthma therapy prior to benralizumab therapy despite formal assessment of and adherence to correct inhaler technique, which has been documented, AND Patient must have demonstrated an adequate response to treatment with benralizumab, AND The treatment must not be used in combination with mepolizumab or omalizumab.</p>
<p>Population criteria</p>	<p>Patient must be aged 12 years or older.</p>
<p>Prescriber Instructions</p>	<p>Optimised asthma therapy includes: (i) Adherence to maximal inhaled therapy, including high dose inhaled corticosteroid (ICS) plus long-acting beta-2 agonist (LABA) therapy for at least 12 months, unless contraindicated or not tolerated; AND (ii) treatment with oral corticosteroids, either daily oral corticosteroids for at least 6 weeks, OR a cumulative dose of oral corticosteroids of at least 500 mg prednisolone equivalent in the previous 12 months, unless contraindicated or not tolerated. If the requirement for treatment with optimised asthma therapy cannot be met because of contraindications according to the relevant TGA-approved Product Information and/or intolerances of a severity necessitating permanent treatment withdrawal, details of the contraindication and/or intolerance must be provided in the Authority application. A review of the patient's records should be conducted to extract pre- and post-benralizumab data on symptoms, quality of life, medication doses, exacerbations and hospitalisations. Parameters to establish response are: (i) a reduction in Asthma Control Questionnaire (ACQ-5) score of at least 0.5; and/or (ii) maintenance oral corticosteroid dose reduced by at least 25% from baseline. The assessment of the patient's response to the initial PBS subsidised course of treatment must be made at around 16 weeks after the first dose so that there is adequate time for a response to be demonstrated and for the application for continuing therapy to be</p>

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	<p>processed. The same parameters used to establish response to non-PBS-subsidised therapy with benralizumab should be used for the assessment.</p> <p>This assessment, which will be used to determine eligibility for continuing treatment, must be submitted within 4 weeks of the date of assessment, and no later than 2 weeks prior to the patient completing their current treatment course, to avoid an interruption to supply. Where a response assessment is not undertaken and submitted within this timeframe, the patient will be deemed to have failed to respond to treatment with benralizumab.</p> <p>Patients will be eligible to receive continuing courses of benralizumab treatment of up to 24 weeks providing they continue to demonstrate an adequate response to treatment.</p> <p>A patient may qualify for PBS-subsidised treatment under this restriction once only.</p> <p>A patient who fails to respond to a course of PBS-subsidised benralizumab for the treatment of uncontrolled severe eosinophilic asthma will not be eligible to receive further PBS-subsidised treatment with benralizumab, mepolizumab or omalizumab within 6 months of the date on which treatment was ceased.</p> <p>At the time of the authority application, medical practitioners should request the appropriate maximum quantity and number of repeats to provide for a continuing course of benralizumab sufficient for 24 weeks of therapy.</p> <p>The authority application must be made in writing and must include:</p> <ul style="list-style-type: none"> (a) a completed authority prescription form; and (b) a completed Severe Eosinophilic Asthma Grandfather PBS Authority Application - Supporting Information Form, <p>which includes the following:</p> <ul style="list-style-type: none"> (i) details of prior optimised asthma drug therapy (date of commencement and duration of therapy); and (ii) details of pre- and post-benralizumab data on symptoms, quality of life, medication doses, severe exacerbation/s and hospitalisations, and (iii) the signed patient or parent/guardian acknowledgement; and (c) a copy of the pre-benralizumab eosinophil pathology report.
<p>Administrative Advice</p>	<p>The Department of Human Services website (www.humanservices.gov.au) has details of the accepted toxicities, including severity, which will be accepted for the purposes of exempting a patient from the requirement of treatment with optimised asthma therapy.</p> <p>It is recommended that an application for continuing treatment is submitted at the time of the 16 week assessment, to ensure continuity of treatment for those patients who meet the continuation criterion for PBS subsidised benralizumab treatment.</p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to:</p> <p>Department of Human Services Complex Drugs Programs Reply Paid 9826 HOBART TAS 7001</p> <p>Formal assessment and correction of inhaler technique should be performed in accordance with the National Asthma Council (NAC) Information Paper for Health Professionals on Inhaler Technique (available at www.humanservices.gov.au or www.nationalasthma.org.au); the assessment and adherence to correct technique should be documented in the patient's medical records. Patients can obtain support with inhaler technique through their local Asthma Foundation (1800 645 130).</p>

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Administrative advice (additional note)	<p>For copies of the ACQ, please contact AstraZenica on [phone number to be advised].</p> <p>TREATMENT OF ADULT AND ADOLESCENT PATIENTS WITH UNCONTROLLED SEVERE EOSINOPHILIC ASTHMA</p> <p>(Per note for initial treatment)</p> <p>No increase in the maximum quantity or number of units may be authorised.</p> <p>No increase in the maximum number of repeats may be authorised.</p> <p>Special Pricing Arrangements apply.</p>
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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
MEPOLIZUMAB 100 mg injection, 1 vial	1	7	Nucala® GlaxoSmithKline Australia Pty Ltd
Category / Program	Section 100 Highly Specialised Drugs Program – public and private		
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives		
PBS Indication:	Uncontrolled severe eosinophilic asthma		
Treatment phase:	Initial treatment		
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined		
Treatment criteria	Must be treated by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma.		

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<p>Clinical criteria:</p>	<p><i>Patient must be under the care of the same physician for at least 12 6 months,</i> OR <i>Patient must have been diagnosed by a multidisciplinary severe asthma clinic team</i> AND Patient must have a diagnosis of asthma confirmed and documented by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma, defined by the following standard clinical features: (i) forced expiratory volume (FEV1) reversibility greater than or equal to 12% and greater than or equal to 200 mL at baseline within 30 minutes after administration of salbutamol (200 to 400 micrograms), or (ii) airway hyperresponsiveness defined as a greater than 20% decline in FEV1 during a direct bronchial provocation test or greater than 15% decline during an indirect bronchial provocation test, or (iii) peak expiratory flow (PEF) variability of greater than 15% between the two highest and two lowest peak expiratory flow rates during 14 days, AND Patient must have a duration of asthma of at least 1 year, AND Patient must have forced expiratory volume (FEV1) less than or equal to 80% predicted, documented on 1 or more occasions in the previous 12 months, AND Patient must have blood eosinophil count greater than or equal to 300 cells per microlitre in the last 12 months, AND Patient must have signed a patient or parent/guardian acknowledgement indicating they understand and acknowledge that PBS subsidised treatment will cease if they do not meet the predetermined response criteria for ongoing PBS subsidised treatment, as outlined in the restriction for continuing treatment, AND Patient must have failed to achieve adequate control with optimised asthma therapy, despite formal assessment of and adherence to correct inhaler technique, which has been documented, AND The treatment must not be used in combination with, or within 6 months of treatment with, PBS-subsidised omalizumab or benralizumab.</p>
<p>Population criteria</p>	<p>Patient must be aged 12 years or older.</p>
<p>Prescriber Instructions</p>	<p>Optimised asthma therapy includes: (i) Adherence to maximal inhaled therapy, including high dose inhaled corticosteroid (ICS) plus long-acting beta-2 agonist (LABA) therapy for at least 12 months, unless contraindicated or not tolerated; AND (ii) treatment with oral corticosteroids, either daily oral corticosteroids for at least 6 weeks, OR a cumulative dose of oral corticosteroids of at least 500 mg prednisolone equivalent in the previous 12 months, unless contraindicated or not tolerated. If the requirement for treatment with optimised asthma therapy cannot be met because of contraindications according to the relevant TGA-approved Product Information and/or intolerances of a severity necessitating permanent treatment withdrawal, details of the contraindication and/or intolerance must be provided in the Authority application. The following initiation criteria indicate failure to achieve adequate control and must be demonstrated in all patients at the time of the application: (a) an Asthma Control Questionnaire (ACQ-5) score of at least 2.0, as assessed in the</p>

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	<p>previous month, AND</p> <p>(b) while receiving optimised asthma therapy in the past 12 months, experienced at least 1 admission to hospital for a severe asthma exacerbation, OR 1 severe asthma exacerbation, requiring documented use of systemic corticosteroids (oral corticosteroids initiated or increased for at least 3 days, or parenteral corticosteroids) prescribed/supervised by a physician.</p> <p>The Asthma Control Questionnaire (5 item version) assessment of the patient must be made at time of application for treatment (to establish baseline score) and again around 26 to 30 weeks after the first dose so that there is adequate time for a response to be demonstrated and for the application for continuing therapy to be processed.</p> <p>This assessment at around 26 to 30 weeks, which will be used to determine eligibility for continuing treatment, must be submitted within 4 weeks of the date of assessment, and no later than 2 weeks prior to the patient completing their current treatment course, to avoid an interruption to supply. Where a response assessment is not undertaken and submitted within this timeframe, the patient will be deemed to have failed to respond to treatment with benralizumab.</p> <p>A patient who fails to respond to a course of PBS-subsidised mepolizumab for the treatment of uncontrolled severe eosinophilic asthma will not be eligible to receive further PBS-subsidised treatment with mepolizumab, <i>benralizumab</i> or omalizumab within 6 months of the date on which treatment was ceased.</p> <p>At the time of the authority application, medical practitioners should request 7 repeats to provide for an initial course of mepolizumab sufficient for 32 weeks of therapy.</p> <p><i>A multidisciplinary severe asthma clinic team comprises of:</i></p> <ul style="list-style-type: none"> • <i>A respiratory physician; and</i> • <i>A pharmacist, nurse or asthma educator.</i> <p>Mepolizumab and omalizumab may not be used concurrently with <i>benralizumab</i> or <i>omalizumab</i>, or within 6 months of each other. A patient is required to have ceased treatment with <i>benralizumab</i> or <i>omalizumab</i> for 6 months prior to initiating treatment with mepolizumab.</p> <p>The authority application must be made in writing and must include:</p> <p>(a) a completed authority prescription form; and</p> <p>(b) a completed Severe Eosinophilic Asthma Initial PBS Authority Application - Supporting Information Form,</p> <p>which includes the following:</p> <p>(i) details of prior optimised asthma drug therapy (date of commencement and duration of therapy); and</p> <p>(ii) details of severe exacerbation/s experienced in the past 12 months while receiving optimised asthma therapy (date and treatment); and</p> <p>(iii) the signed patient or parent/guardian acknowledgement; and</p> <p>(c) a copy of the eosinophil pathology report; and</p> <p>(d) a completed Asthma Control Questionnaire (ACQ-5) calculation sheet including the date of assessment of the patient's symptoms.</p>
<p>Administrative Advice</p>	<p>The Department of Human Services website (www.humanservices.gov.au) has details of the accepted toxicities, including severity, which will be accepted for the purposes of exempting a patient from the requirement of treatment with optimised asthma therapy.</p> <p>For copies of the ACQ, please contact GlaxoSmithKline Medical Information on 1800 033 109.</p> <p>It is recommended that an application for continuing treatment is submitted at the time of the 26 to 30 week assessment, to ensure continuity of treatment for those patients who meet the continuation criteria for PBS-subsidised mepolizumab treatment.</p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department</p>

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	<p>of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to:</p> <p>Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p> <p>TREATMENT OF ADULT AND ADOLESCENT PATIENTS WITH UNCONTROLLED SEVERE EOSINOPHILIC ASTHMA</p> <p>Patients are eligible to commence a 'mepolizumab treatment cycle' (initial treatment course with or without continuing treatment course/s) if they satisfy the eligibility criteria as detailed under the initial treatment restriction.</p> <p>Once a patient has either failed to achieve or maintain a response to mepolizumab, they are deemed to have completed a treatment cycle and they must have, at a minimum, a 6 month break in PBS-subsidised mepolizumab therapy before they are eligible to commence the next mepolizumab treatment cycle, or if eligible, a '<i>benralizumab treatment cycle</i>' or an '<i>omalizumab treatment cycle</i>'. The length of a treatment break is measured from the date the most recent treatment with PBS-subsidised mepolizumab is stopped to the date of the first application for initial treatment with mepolizumab, <i>benralizumab</i> or <i>omalizumab</i> under the new treatment cycle.</p> <p>There is no limit to the number of treatment cycles a patient may undertake in their lifetime.</p> <p>(1) How to prescribe PBS-subsidised mepolizumab therapy:</p> <p>(a) Initial treatment:</p> <p>Applications for initial treatment should be made where:</p> <p>i) A patient has received no prior PBS-subsidised mepolizumab treatment and wishes to commence such therapy; or</p> <p>ii) A patient wishes to recommence treatment with mepolizumab following a break in PBS-subsidised therapy of more than 6 months; or</p> <p>iii) A patient has received prior PBS-subsidised <i>benralizumab</i> or <i>omalizumab</i> and wishes to commence treatment with mepolizumab after a treatment break of 6 months.</p> <p>All Applications for initial treatment for non-grandfather patients will be limited to provide for a maximum of 32 weeks of therapy for mepolizumab.</p> <p>(b) Grandfather patients:</p> <p>For patients who commenced treatment with mepolizumab for uncontrolled severe eosinophilic asthma prior to 1 January 2017 and who continues to receive treatment at the time of application, may qualify for treatment under the initial 'grandfather' treatment restriction. A patient may only qualify for PBS subsidised treatment under this restriction once. A maximum of 24 weeks of treatment with mepolizumab will be authorised under this criterion. Approval will be based on the criteria included in the relevant restriction. Following completion of the Initial PBS-subsidised course, further applications for treatment with mepolizumab will be assessed under the continuing treatment restriction.</p> <p>'Grandfather' arrangements will only apply for the first treatment cycle (initial treatment course with or without continuing treatment course/s). If a 'Grandfathered' patient recommences on second and subsequent cycles after a treatment break, the 'Grandfathered' patient must re-qualify for Initial treatment under the criteria that apply to a new patient. See 'Re-commencement of treatment after a 6 month break in PBS-subsidised therapy' below for further details.</p> <p>(cb) Continuing treatment:</p>
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	<p>Following the completion of the initial treatment course with mepolizumab, a patient may qualify to receive up to a further 24 weeks of continuing treatment with mepolizumab providing they have demonstrated an adequate response to treatment. The patient remains eligible to receive continuing mepolizumab treatment in courses of up to 24 weeks providing they continue to sustain the response.</p> <p>(2) Baseline measurements to determine response: The Department of Human Services will determine whether a response to treatment has been demonstrated based on the baseline measurements of the Asthma Control Questionnaire (ACQ; 5 item version) and oral corticosteroid dose, submitted with the Initial authority application for mepolizumab. However, prescribers may provide new baseline measurements when a new Initial treatment authority application is submitted and the Department of Human Services will assess response according to these revised baseline measurements.</p> <p>(3) Re-commencement of treatment after a 6 month break in PBS-subsidised therapy: A patient who wishes to trial a second or subsequent mepolizumab treatment cycle, or an initial <i>benralizumab</i> or omalizumab treatment cycle, following a break in PBS-subsidised therapy of at least 6 months, must re-qualify for initial treatment with respect to the indices of disease severity (oral corticosteroid dose, Asthma Control Questionnaire (ACQ-5) score, and relevant exacerbation history). Patients must have received optimised standard therapy, at adequate doses and for the minimum period specified, immediately prior to the time the new baseline assessments are performed.</p> <p>Formal assessment and correction of inhaler technique should be performed in accordance with the National Asthma Council (NAC) Information Paper for Health Professionals on Inhaler Technique (available at www.humanservices.gov.au or www.nationalasthma.org.au); the assessment and adherence to correct technique should be documented in the patient's medical records. Patients can obtain support with inhaler technique through their local Asthma Foundation (1800 645 130).</p> <p>No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.</p>
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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
MEPOLIZUMAB 100 mg injection, 1 vial	1	5	Nucala® GlaxoSmithKline Australia Pty Ltd
Category / Program	Section 100 Highly Specialised Drugs Program – public and private		
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives		
PBS Indication:	Uncontrolled severe eosinophilic asthma		
Treatment phase:	Continuing treatment		

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Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria	Must be treated by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma.
Clinical criteria:	<p>Patient must have demonstrated or sustained an adequate response to PBS subsidised treatment with this drug, AND</p> <p>The treatment must not be used in combination with, or within 6 months of treatment with, PBS subsidised <i>benralizumab</i> or <i>omalizumab</i>.</p>
Population criteria	Patient must be aged 12 years or older.
Prescriber Instructions	<p>An adequate response to mepolizumab treatment is defined as:</p> <p>(a) a reduction in the Asthma Control Questionnaire (ACQ 5) score of at least 0.5 from baseline, OR</p> <p>(b) maintenance OCS dose reduced by at least 25% from baseline, and no deterioration in ACQ 5 score from baseline.</p> <p>All applications for continuing treatment with mepolizumab must include a measurement of response to the prior course of therapy. The Asthma Control Questionnaire (5 item version) assessment of the patient's response to the prior course of treatment, and the assessment of oral corticosteroid dose, must be made at around 26 to 30 weeks after the first dose of PBS subsidised mepolizumab so that there is adequate time for a response to be demonstrated and for the application for continuing therapy to be processed.</p> <p>The first assessment should, where possible, be completed by the same physician who initiated treatment with mepolizumab. This assessment, which will be used to determine eligibility for continuing treatment, must be submitted within 4 weeks of the date of assessment, and no later than 2 weeks prior to the patient completing their current treatment course, to avoid an interruption to supply. Where a response assessment is not undertaken and submitted within this timeframe, the patient will be deemed to have failed to respond to treatment with mepolizumab.</p> <p>A patient who fails to respond to a course of PBS subsidised mepolizumab for the treatment of uncontrolled severe eosinophilic asthma will not be eligible to receive further PBS subsidised treatment with mepolizumab for this condition within 6 months of the date on which treatment was ceased.</p> <p>At the time of the authority application, medical practitioners should request the appropriate number of repeats to provide for a continuing course of mepolizumab sufficient for 24 weeks of therapy.</p> <p>The authority application must be made in writing and must include:</p> <p>(a) a completed authority prescription form; and</p> <p>(b) a completed Severe Eosinophilic Asthma Continuing PBS Authority Application Supporting Information Form which includes details of maintenance oral corticosteroid dose; and</p> <p>(c) a completed Asthma Control Questionnaire (ACQ 5) calculation sheet including the date of assessment of the patient's symptoms</p>
Administrative Advice	<p>If the same physician cannot assess the patient please call the Department of Human Services on 1800 700 270.</p> <p>It is recommended that second and subsequent applications for continuing treatment are</p>

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	<p>submitted at the time of an 18 to 22 week assessment, to ensure continuity of treatment for those patients who meet the continuation criteria for PBS subsidised mepolizumab treatment.</p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001 Authority Required Uncontrolled severe eosinophilic asthma</p>
<p>Administrative (additional note)</p>	<p>advice</p> <p>For copies of the ACQ, please contact GlaxoSmithKline Medical Information on 1800 033 109.</p> <p>TREATMENT OF ADULT AND ADOLESCENT PATIENTS WITH UNCONTROLLED SEVERE EOSINOPHILIC ASTHMA <i>(Per note for initial treatment)</i></p> <p>No increase in the maximum quantity or number of units may be authorised. No increase in the maximum number of repeats may be authorised. Special Pricing Arrangements apply.</p>

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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
OMALIZUMAB 75 mg in 0.5 mL injection, 1 syringe	1	0	Xolair® Novartis Pharmaceuticals Australia Pty Ltd
OMALIZUMAB 150 mg in 1 mL injection, 1 syringe	1	0	
Category / Program	Section 100 Highly Specialised Drugs Program – public and private		
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives		
PBS Indication:	Uncontrolled severe allergic asthma		
Treatment phase:	Initial treatment		
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined		
Treatment criteria	Must be treated by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma.		

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<p>Clinical criteria:</p>	<p>Patient must be under the care of the same physician for at least 426 months, OR Patient must have been diagnosed by a multidisciplinary severe asthma clinic team AND Patient must have a diagnosis of asthma confirmed and documented by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma, defined by the following standard clinical features: (i) forced expiratory volume (FEV1) reversibility greater than or equal to 12% and greater than or equal to 200 mL at baseline within 30 minutes after administration of salbutamol (200 to 400 micrograms), or (ii) airway hyperresponsiveness defined as a greater than 20% decline in FEV1 during a direct bronchial provocation test or greater than 15% decline during an indirect bronchial provocation test, or (iii) peak expiratory flow (PEF) variability of greater than 15% between the two highest and two lowest peak expiratory flow rates during 14 days, AND Patient must have a duration of asthma of at least 1 year, AND Patient must have forced expiratory volume (FEV1) less than or equal to 80% predicted, documented on 1 or more occasions in the previous 12 months, AND Patient must have past or current evidence of atopy, documented by skin prick testing or RAST, AND Patient must have total serum human immunoglobulin E greater than or equal to 30 IU/mL, AND Patient must have signed a patient or parent/guardian acknowledgement indicating they understand and acknowledge that PBS-subsidised treatment will cease if they do not meet the predetermined response criteria for ongoing PBS-subsidised treatment, as outlined in the restriction for continuing treatment, AND Patient must have failed to achieve adequate control with optimised asthma therapy, despite formal assessment of and adherence to correct inhaler technique, which has been documented, AND Patient must not receive more than 28 weeks of treatment under this restriction, AND The treatment must not be used in combination with, or within 6 months of treatment with, PBS-subsidised mepolizumab or benralizumab.</p>
<p>Population criteria</p>	<p>Patient must be aged 12 years or older.</p>
<p>Prescriber Instructions</p>	<p>Optimised asthma therapy includes: (i) Adherence to maximal inhaled therapy, including high dose inhaled corticosteroid (ICS) plus long-acting beta-2 agonist (LABA) therapy for at least 12 months, unless contraindicated or not tolerated; AND (ii) treatment with oral corticosteroids, either daily oral corticosteroids for at least 6 weeks, OR a cumulative dose of oral corticosteroids of at least 500 mg prednisolone equivalent in the previous 12 months, unless contraindicated or not tolerated. If the requirement for treatment with optimised asthma therapy cannot be met because of contraindications according to the relevant TGA-approved Product Information and/or intolerances of a severity necessitating permanent treatment withdrawal, details of the contraindication and/or intolerance must be provided in the Authority application. The initial IgE assessment must be no more than 12 months old at the time of application. The following initiation criteria indicate failure to achieve adequate control and must be</p>

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	<p>demonstrated in all patients at the time of the application:</p> <p>(a) an Asthma Control Questionnaire (ACQ-5) score of at least 2.0, as assessed in the previous month, AND</p> <p>(b) while receiving optimised asthma therapy in the past 12 months, experienced at least 1 admission to hospital for a severe asthma exacerbation, OR 1 severe asthma exacerbation, requiring documented use of systemic corticosteroids (oral corticosteroids initiated or increased for at least 3 days, or parenteral corticosteroids) prescribed/supervised by a physician.</p> <p>The Asthma Control Questionnaire (5 item version) assessment of the patient's response to this initial course of treatment, and the assessment of oral corticosteroid dose, must be made at around 22 to 26 weeks after the first dose so that there is adequate time for a response to be demonstrated and for the application for continuing therapy to be processed.</p> <p>This assessment, which will be used to determine eligibility for continuing treatment, must be submitted within 4 weeks of the date of assessment, and no later than 2 weeks prior to the patient completing their current treatment course, to avoid an interruption to supply. Where a response assessment is not undertaken and submitted within this timeframe, the patient will be deemed to have failed to respond to treatment with omalizumab.</p> <p>A patient who fails to respond to a course of PBS-subsidised omalizumab for the treatment of uncontrolled severe allergic asthma will not be eligible to receive further PBS-subsidised treatment with omalizumab, or mepolizumab or benralizumab for this condition within 6 months of the date on which treatment was ceased.</p> <p>At the time of the authority application, medical practitioners should request the appropriate maximum quantity and number of repeats to provide for an initial course of omalizumab consisting of the recommended number of doses for the baseline IgE level and body weight of the patient (refer to the TGA-approved Product Information) to be administered every 2 or 4 weeks.</p> <p><i>A multidisciplinary severe asthma clinic team comprises of:</i></p> <ul style="list-style-type: none"> • <i>A respiratory physician; and</i> • <i>A pharmacist, nurse or asthma educator.</i> <p><i>Omalizumab may not be used concurrently with benralizumab or mepolizumab, or within 6 months of each other. A patient is required to have ceased treatment with benralizumab or mepolizumab for 6 months prior to initiating treatment with omalizumab.</i></p> <p>The authority application must be made in writing and must include:</p> <p>(a) a completed authority prescription form; and</p> <p>(b) a completed Severe Allergic Asthma PBS Authority Application - Supporting Information Form,</p> <p>which includes the following:</p> <p>(i) details of prior optimised asthma drug therapy (date of commencement and duration of therapy); and</p> <p>(ii) details of severe exacerbation/s experienced in the past 12 months while receiving optimised asthma therapy (date and treatment); and</p> <p>(iii) the signed patient or parent/guardian acknowledgement; and</p> <p>(c) the IgE pathology report; and</p> <p>(d) a completed Asthma Control Questionnaire (ACQ-5) calculation sheet including the date of assessment of the patient's symptoms.</p>
<p>Administrative Advice</p>	<p>The Department of Human Services website (www.humanservices.gov.au) has details of the accepted toxicities, including severity, which will be accepted for the purposes of exempting a patient from the requirement of treatment with optimised asthma therapy.</p> <p>For copies of the ACQ and the calculation sheets please contact Novartis Medical Information on 1800 671 203 or medinfo.phauno@novartis.com</p>

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	<p>It is recommended that an application for continuing treatment is submitted at the time of the 22 to 26 week assessment, to ensure continuity of treatment for those patients who meet the continuation criterion for PBS-subsidised omalizumab treatment.</p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p> <p>Note</p> <p>TREATMENT OF ADULT AND ADOLESCENT PATIENTS WITH UNCONTROLLED SEVERE ALLERGIC ASTHMA</p> <p>Patients are eligible to commence an 'omalizumab treatment cycle' (initial treatment course with or without continuing treatment course/s) if they satisfy the eligibility criteria as detailed under the initial treatment restriction.</p> <p>Once a patient has either failed to achieve or maintain a response to omalizumab, they are deemed to have completed a treatment cycle and they must have, at a minimum, a 6 month break in PBS-subsidised omalizumab therapy before they are eligible to commence the next omalizumab treatment cycle, or if eligible, a 'mepolizumab treatment cycle' or a 'benralizumab treatment cycle'. The length of a treatment break is measured from the date the most recent treatment with PBS-subsidised omalizumab, or mepolizumab or benralizumab is stopped to the date of the first application for initial treatment with omalizumab, or mepolizumab or benralizumab under the new treatment cycle.</p> <p>There is no limit to the number of treatment cycles a patient may undertake in their lifetime.</p> <p>(1) How to prescribe PBS-subsidised omalizumab therapy:</p> <p>(a) Initial treatment:</p> <p>Applications for initial treatment should be made where:</p> <p>i) A patient has received no prior PBS-subsidised omalizumab treatment and wishes to commence such therapy; or</p> <p>ii) A patient wishes to recommence treatment with omalizumab following a break in PBS-subsidised therapy of more than 6 months; or</p> <p>iii) A patient has received prior PBS-subsidised mepolizumab or benralizumab and wishes to commence treatment with omalizumab after a treatment break of 6 months.</p> <p>All applications for initial treatment for non-grandfather patients will be limited to provide for a maximum of 28 weeks of therapy of omalizumab.</p> <p>(b) Continuing treatment:</p> <p>Following the completion of the initial treatment course with omalizumab, a patient may qualify to receive up to a further 24 weeks of continuing treatment with omalizumab providing they have demonstrated an adequate response to treatment. The patient remains eligible to receive continuing omalizumab treatment in courses of up to 24 weeks providing they continue to sustain the response.</p> <p>(2) Baseline measurements to determine response:</p> <p>The Department of Human Services will determine whether a response to treatment has been demonstrated based on the baseline measurements of the Asthma Control Questionnaire (ACQ; 5 item version) or oral corticosteroid dose submitted with the Initial authority application for omalizumab. For patients transitioned from the paediatric to the</p>
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	<p>adolescent/adult restriction, the exacerbation history may also be used to determine response. However, prescribers may provide new baseline measurements when a new Initial treatment authority application is submitted and the Department of Human Services will assess response according to these revised baseline measurements.</p> <p>(3) Re-commencement of treatment after a 6 month break in PBS-subsidised therapy: A patient who wishes to trial a second or subsequent omalizumab treatment cycle, or an initial mepolizumab or <i>benralizumab</i> treatment cycle, following a break in PBS-subsidised therapy of at least 6 months, must re-qualify for initial treatment with respect to the indices of disease severity (oral corticosteroid dose, Asthma Control Questionnaire (ACQ-5) score, and relevant exacerbation history). Patients must have received optimised standard therapy, at adequate doses and for the minimum period specified, immediately prior to the time the new baseline assessments are performed.</p> <p>(4) Monitoring of patients: Anaphylaxis and anaphylactoid reactions have been reported following first or subsequent administration of omalizumab (see Product Information). Patients should be monitored post-injection, and medications for the treatment of anaphylactic reactions should be available for immediate use following administration of omalizumab. Patients should be informed that such reactions are possible and prompt medical attention should be sought if allergic reactions occur.</p> <p>Formal assessment and correction of inhaler technique should be performed in accordance with the National Asthma Council (NAC) Information Paper for Health Professionals on Inhaler Technique (available at www.humanservices.gov.au or www.nationalasthma.org.au); the assessment and adherence to correct technique should be documented in the patient's medical records. Patients can obtain support with inhaler technique through their local Asthma Foundation (1800 645 130).</p> <p>Special Pricing Arrangements apply.</p>
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Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
OMALIZUMAB 75 mg in 0.5 mL injection, 1 syringe	1	0	Xolair® Novartis Pharmaceuticals Australia Pty Ltd
OMALIZUMAB 150 mg in 1 mL injection, 1 syringe	1	0	

Category / Program	Section 100 Highly Specialised Drugs Program – public and private
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
PBS Indication:	Uncontrolled severe allergic asthma
Treatment phase:	Continuing treatment
Restriction Level / Method:	<input type="checkbox"/> Restricted benefit <input checked="" type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined

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Treatment criteria	Must be treated by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma.
Clinical criteria:	<p>Patient must have a documented history of severe allergic asthma,</p> <p>AND</p> <p>Patient must have demonstrated or sustained an adequate response to PBS-subsidised treatment with this drug,</p> <p>AND</p> <p>Patient must not receive more than 24 weeks of treatment under this restriction,</p> <p>AND</p> <p>he treatment must not be used in combination with, or within 6 months of treatment with, PBS-subsidised mepolizumab or benralizumab.</p>
Population criteria	Patient must be aged 12 years or older.
Prescriber Instructions	<p>An adequate response to omalizumab treatment is defined as:</p> <p>(a) a reduction in the Asthma Control Questionnaire (ACQ-5) score of at least 0.5 from baseline, OR</p> <p>(b) maintenance oral corticosteroid dose reduced by at least 25% from baseline, and no deterioration in ACQ-5 score from baseline, OR</p> <p>(c) a reduction in the time-adjusted exacerbation rates compared to the 12 months prior to baseline (this criterion is only applicable for patients transitioned from the paediatric to the adolescent/adult restriction).</p> <p>All applications for continuing treatment with omalizumab must include a measurement of response to the prior course of therapy. The Asthma Control Questionnaire (5 item version) assessment of the patient's response to the prior course of treatment, the assessment of oral corticosteroid dose, and the assessment of time adjusted exacerbation rate must be made at around 18 to 22 weeks after the first dose of PBS-subsidised omalizumab so that there is adequate time for a response to be demonstrated and for the application for continuing therapy to be processed.</p> <p>The first assessment should, where possible, be completed by the same physician who initiated treatment with omalizumab. This assessment, which will be used to determine eligibility for continuing treatment, must be submitted within 4 weeks of the date of assessment, and no later than 2 weeks prior to the patient completing their current treatment course, to avoid an interruption to supply. Where a response assessment is not undertaken and submitted within this timeframe, the patient will be deemed to have failed to respond to treatment with omalizumab.</p> <p>A patient who fails to respond to a course of PBS-subsidised omalizumab for the treatment of uncontrolled severe allergic asthma will not be eligible to receive further PBS-subsidised treatment with omalizumab for this condition within 6 months of the date on which treatment was ceased.</p> <p>At the time of the authority application, medical practitioners should request the appropriate quantity and number of repeats to provide for a continuing course of omalizumab consisting of the recommended number of doses for the baseline IgE level and body weight of the patient (refer to the TGA-approved Product Information), sufficient for 24 weeks of therapy.</p> <p>The authority application must be made in writing and must include:</p> <p>(a) a completed authority prescription form(s); and</p> <p>(b) a completed Severe Allergic Asthma PBS Authority Application and Supporting Information Form which includes details of maintenance oral corticosteroid dose; and</p> <p>(c) a completed Asthma Control Questionnaire (ACQ-5) calculation sheet including the date of assessment of the patient's symptoms and is endorsed with the signature of the prescriber; for patients transitioned from the paediatric to the adolescent/adult restrictions an exacerbation calculation sheet may be submitted.</p>

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Administrative Advice	<p>If the same physician cannot assess the patient please call the Department of Human Services on 1800 700 270.</p> <p>For copies of the ACQ and the calculation sheets please contact Novartis Medical Information on 1800 671 203 or medinfo.phauno@novartis.com</p> <p>It is recommended that an application for continuing treatment is submitted at the time of the 18 to 22 week assessment, to ensure continuity of treatment for those patients who meet the continuation criterion for PBS-subsidised omalizumab treatment.</p> <p>Any queries concerning the arrangements to prescribe may be directed to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Department of Human Services website at www.humanservices.gov.au</p> <p>Applications for authority to prescribe should be forwarded to:</p> <p>Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001 TREATMENT OF ADULT AND ADOLESCENT PATIENTS WITH UNCONTROLLED SEVERE ALLERGIC ASTHMA <i>(Per note for initial treatment)</i></p> <p>Formal assessment and correction of inhaler technique should be performed in accordance with the National Asthma Council (NAC) Information Paper for Health Professionals on Inhaler Technique (available at www.humanservices.gov.au or www.nationalasthma.org.au); the assessment and adherence to correct technique should be documented in the patient's medical records. Patients can obtain support with inhaler technique through their local Asthma Foundation (1800 645 130).</p> <p>Special Pricing Arrangements apply.</p>
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7 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

8 Sponsor's Comment

The sponsor had no comment.