

## 6.12 OMALIZUMAB

**75 mg/0.5 mL injection, 1 x 0.5 mL syringe, 150 mg/mL injection, 1 x 1 mL syringe; 150 mg injection [1 x 150 mg vial] (&) inert substance diluent [1 x 1.2 mL ampoule], 1 pack; Xolair®; Novartis Pharmaceuticals Australia Pty Ltd.**

### 1 Purpose of Application

- 1.1 The minor submission sought to amend the current restriction for omalizumab.

### 2 Background

- 2.1 The PBAC rejected omalizumab for listing for the treatment of patients with uncontrolled severe allergic asthma in November 2009. Following this outcome, a post-PBAC meeting was held in December 2009 and a PBAC-convened stakeholder meeting was held in April 2010. A resubmission was considered and approved by the PBAC for listing in November 2010. The resubmission included the restrictions that were agreed to at the April 2010 stakeholder meeting.
- 2.2 In February 2013, DUSC considered the utilisation of omalizumab over the first 12 months of listing, which was approximately █% of predicted. In April 2013, the PBAC considered that access to appropriately qualified prescribers, establishing eligibility to access PBS-subsidised omalizumab; and the requirement to maintain patients on long-term corticosteroids contributed to the low uptake of omalizumab.
- 2.3 In June 2014, DUSC considered the utilisation of omalizumab over the first 24 months of listing, which was approximately █% of predicted in the second year. In July 2014, the PBAC recalled that a stakeholder meeting in 2010 had been required to finalise the restriction, and requested that such a group be reconvened to discuss potential changes. The PBAC particularly noted the elements of the current restriction referring to oral corticosteroid use were developed in consultation with the stakeholder group and reflected the best practice guidelines at the time. The PBAC recalled that oral corticosteroid use had been an important element in cost effectiveness analysis underpinning the original recommendation. The PBAC considered therefore that a change to the restriction could influence the cost effectiveness of omalizumab.
- 2.4 The sponsor noted that while the restriction for omalizumab would be considered through the review of Authority Required listings, the scope may not allow for a detailed analysis of the eligibility criteria and this would not occur until the third round of reviews.

### 3 Requested listing

3.1 The submission sought a number of changes to the existing restriction, outlined in the following table. The submission claimed these changes are aimed at improving patient care and reducing the administrative burden for health professionals.

Row	Current criteria	Requested revision/comments
1	<b>ELIGIBILITY CRITERIA for INITIAL treatment</b>	
1.1	Initial PBS-subsidised treatment with omalizumab by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma, of a patient aged 12 years or older with uncontrolled severe allergic asthma who has been under the care of this physician for at least 12 months	Initial PBS-subsidised treatment with omalizumab by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma, of a patient aged 12 years or older with uncontrolled severe allergic asthma who has been under the care of this physician for at least 6 months.  On the Medicare application form change the tick box question from “has been in my care for at least 12 months” to “has been in my care for at least 6 months”, and remove the requirement to provide the <i>date of initial visit</i> . Also allow co-signing of applications by treating physicians where appropriate (on a case-by-case basis).
1.2	(a) has 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 standard clinical features, including:  (i) forced expiratory volume (FEV <sub>1</sub> ) 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 - 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.	Has a diagnosis of asthma confirmed by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma, defined by standard clinical features and in accordance with the Australian Asthma Handbook 2014 ( <a href="http://www.asthmahandbook.org.au/diagnosis/adults/making-a-diagnosis">http://www.asthmahandbook.org.au/diagnosis/adults/making-a-diagnosis</a> ).  For patients taking preventer medication where variable airflow limitation cannot be demonstrated, further investigations may be required ( <a href="http://www.asthmahandbook.org.au/table/show/9">http://www.asthmahandbook.org.au/table/show/9</a> ) and diseases other than asthma must be excluded ( <a href="http://www.asthmahandbook.org.au/diagnosis/adults/alternative-diagnoses">http://www.asthmahandbook.org.au/diagnosis/adults/alternative-diagnoses</a> )  On the Medicare application form retain the question: “has a diagnosis of asthma defined by standard clinical features” but remove the sub-questions on FEV <sub>1</sub> reversibility, airway hyperresponsiveness and peak expiratory flow variability.

Row	Current criteria	Requested revision/comments
1.3	(b) duration of asthma of at least 1 year	Propose to retain the question on the Medicare form: <i>“has a diagnosis of asthma for at least one year”</i> , but remove the <i>“provide date of initial diagnosis”</i> field.
1.4	(c) FEV <sub>1</sub> less than or equal to 80% predicted, documented on 3 or more occasions in the previous 12 months	FEV <sub>1</sub> ≤80% predicted, documented on 1 or more occasion in the previous 12 months  On the Medicare application form change the question to <i>“has FEV<sub>1</sub> ≤80% predicted, documented on at least one occasion in the previous 12 months”</i> And remove the requirement to provide the dates and results of the 3 FEV <sub>1</sub> assessments and replace with: <i>“Provide the FEV<sub>1</sub> % predicted result”</i> or delete this requirement as well.
1.5	(d) past or current evidence of atopy, documented by skin prick testing or RAST	Past or current evidence of atopy, documented by skin prick testing or an in vitro measure of specific IgE (see NOTE if unable to identify the specific allergen).  NOTE: Allergy testing should be performed in accordance with the National Asthma Council & Australasian Society of Clinical Immunology and Allergy (ASCIA) Paper for Health Professionals on Asthma & Allergy (available at <a href="http://www.nationalasthma.org.au">www.nationalasthma.org.au</a> ) and resources available on the ASCIA website (available at <a href="http://www.allergy.org.au">www.allergy.org.au</a> ). Assessments should be documented in the patient's medical records and if a specific allergen cannot be identified the application for omalizumab should be discussed with Medicare.  On the Medicare application form: Update the question to include FEIA: <i>“has past or current evidence of atopy, documented by skin prick testing or an in vitro measure of specific IgE”</i> and remove the <i>“provide date of test”</i> field.
1.6	(e) total serum human immunoglobulin E (IgE) greater than or equal to 76 IU/ml and assessed in the previous 12 months	Total serum human immunoglobulin E (IgE) greater than or equal to 30 IU/ml and assessed in the previous 12 months

Row	Current criteria	Requested revision/comments
1.8	<p>(g) has failed to achieve adequate control with optimised asthma therapy, despite formal assessment of and adherence to correct inhaler technique, which has been documented (see NOTE).</p> <p>NOTE: 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 <a href="http://www.medicareaustralia.gov.au">www.medicareaustralia.gov.au</a> or <a href="http://www.nationalasthma.org.au">www.nationalasthma.org.au</a>); 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 (1800645130).</p>	<p>Has failed to achieve adequate control with optimised asthma therapy, despite formal assessment of and adherence to correct inhaler technique, which has been documented (see NOTE).</p> <p>NOTE: Formal assessment and correction of inhaler technique should be performed in accordance with the National Asthma Council (NAC) <i>information papers and checklists for health professionals on inhaler techniques</i> (available at <a href="http://www.medicareaustralia.gov.au">www.medicareaustralia.gov.au</a> or <a href="http://www.nationalasthma.org.au">www.nationalasthma.org.au</a>); 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 (1800645130).</p>
1.8b	<p>(g) has failed to achieve adequate control with optimised asthma therapy, despite formal assessment of and adherence to correct inhaler technique, which has been documented.</p> <p>OAT includes:</p> <p>(i) adherence to maximal inhaled therapy ... AND</p> <p>(ii) oral corticosteroids (at least 10 mg/day prednisolone (or equivalent)) for at least 6 weeks, unless contraindicated or not tolerated.</p>	<p>Has failed to achieve adequate control with optimised asthma therapy, despite formal assessment of and adherence to correct inhaler technique, which has been documented.</p> <p>OAT includes:</p> <p>(i) adherence to maximal inhaled therapy ... AND</p> <p>(ii) treatment with oral corticosteroids, either:</p> <ul style="list-style-type: none"> <li>• daily oral corticosteroids for at least 6 weeks [option to include the statement: <i>recommended dose is ≤7.5mg/day prednisolone equivalent</i> (<a href="http://www.ginasthma.org">http://www.ginasthma.org</a>), unless contraindicated or not tolerated</li> </ul> <p>OR</p> <ul style="list-style-type: none"> <li>• a cumulative dose of oral corticosteroids of at least 500mg prednisolone equivalent in the previous 12 months.</li> </ul> <p>Amendment of the Medicare application form to allow for the OR criteria</p>

2	<b>ELIGIBILITY CRITERIA – failure to achieve adequate control</b>	
2.1	<p>Failure to achieve adequate control as demonstrated by:</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 on oral corticosteroids and in the past 12 months experienced at least: 1 admission to hospital for a severe asthma exacerbation, OR</p> <p>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>Failure to achieve adequate control as demonstrated by:</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) <i>despite continuous or frequent treatment with oral corticosteroids</i>, experienced in the past 12 months at least:</p> <p>1 admission to hospital for a severe asthma exacerbation, OR</p> <p>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>At Medicare level – remove the need for the exacerbation date to match the OCS dates</p>
3	<b>RESPONSE CRITERIA</b>	
	Administrative requirement to assess the patient for response within a 2 week window	A longer window of 4 weeks for assessment of response is requested: weeks 22-26 for initial response and weeks 18-22 for continuation response.
	Continuing patients are required to have an assessment of response every 20 to 22 weeks and based on this are authorised to receive 24 weeks of omalizumab. Thus a written application needs to be completed every 5 months.	<p>It is proposed that the criteria for assessment of response remain unchanged, but that administrative burden of written authorities is removed once a patient has clearly and consistently demonstrated response to omalizumab.</p> <p>Request consideration of allowing transition from a written authority for all approvals to a streamlined (public hospital) and phone authority (private hospital) approval process for patients who have maintained their response to omalizumab for at least 2 years.</p>

For more detail on PBAC’s view, see section 5 “PBAC outcome”

#### 4 Consideration of the evidence

##### Sponsor hearing

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

##### Consumer comments

4.2 The PBAC noted and welcomed the input from individuals (5), health care professionals (2) and organisations (2) via the Consumer Comments facility on the

PBS website. The comments described a range of benefits of treatment with omalizumab (including a reduction in other medications required and reduction in exacerbations), as well as issues regarding patients excluded under the current listing.

**Estimated PBS usage & financial implications**

- 4.3 The submission presented financial estimates based on the expected increase in uptake and response/continuation rates of omalizumab if the requested changes to the restriction were to be implemented. The submission noted that while less than 10,000 patients are expected to be treated with omalizumab in year 1 under the current restriction, in 2011 the number of patients expected to be treated with omalizumab in that year was less than 10,000.
- 4.4 The minor submission estimated a net cost to the PBS of less than \$10 million in Year 5 of listing, with a total net cost to the PBS of \$ [REDACTED] over the first 5 years of listing at the published DPMQ. This is summarised in the table below.

**Estimated use and financial implications**

	Year 1	Year 2	Year 3	Year 4	Year 5
<b>Estimated extent of use</b>					
Number currently treated	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Number treated under proposed restriction changes	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
<b>Estimated net cost to PBS</b>					
Net cost to PBS – published DPMQ	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Net cost to PBS – effective price	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]

Source: Table 14 p 44 of the submission and the Financial Workbook.

- 4.5 The submission noted that omalizumab is subject to a Deed of Agreement [REDACTED].

*For more detail on PBAC’s view, see section 5 “PBAC outcome”*

**5 PBAC Outcome**

- 5.1 The PBAC recommended amending the restriction wording of omalizumab to align the definition of optimal asthma therapy with current clinical guidelines (refers to row 1.8b in the table) and to extend the period for assessment of response from 2 weeks to 4 weeks (refers to row 3).
- 5.2 The PBAC considered that accepting the change to the definition of optimal asthma therapy, with regards to treatment with oral corticosteroids, in line with clinical treatment guidelines was appropriately pragmatic. The recommended change made to the definition is shown by strikethrough and italics as below:  
 ‘Optimised asthma therapy includes:

(i) adherence to maximal inhaled therapy, including high dose inhaled corticosteroid (budesonide 1600 micrograms per day or fluticasone propionate 1000 micrograms per day or equivalent), plus long-acting beta-2 agonist therapy (at least salmeterol 50 micrograms bd or eformoterol 12 micrograms bd) for at least 12 months, unless contraindicated or not tolerated, AND

(ii) *treatment with oral corticosteroids (at least 10 mg per day prednisolone (or equivalent)), either daily oral corticosteroids for at least 6 weeks, unless contraindicated or not tolerated or a cumulative dose of oral corticosteroids of at least 500 mg prednisolone equivalent in the previous 12 months.*'

- 5.3 The PBAC noted that the pre-PBAC response included a stepped economic evaluation for omalizumab, from the current to the proposed PBS criteria under the original and pre-filled syringe prices. The PBAC noted that the ICERs were verified against the sponsor's 2010 model prior to the meeting. However, a more extensive evaluation of the economic analysis could not be conducted in the available time.
- 5.4 The PBAC noted that the remaining requested changes to the restriction for omalizumab would require formal evaluation prior to consideration by PBAC. Accordingly, the PBAC recommended that the sponsor submit a major resubmission to justify reducing the baseline IgE threshold as well as other requested changes to the wording of the restriction.

**Outcome:**

Recommended

**6 Recommended listing**

- 6.1 Amend existing listing.
- 6.2 The amended restriction will need to be remodelled to comply with PharmCIS format. The Secretariat will provide a suggested restriction in the PharmCIS format as soon as it's available.

**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**

Novartis welcomes the positive recommendation made by the PBAC with regard to the baseline oral corticosteroid criteria and the expanded assessment window for patients with severe allergic asthma. We also acknowledge the input from patients, patient organisations and health care professionals, provided through the PBAC

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consumer comments process. Novartis believes that the Stakeholder meeting requested by the PBAC (in consideration of the DUSC utilisation review mid 2014) would provide an appropriate forum for discussing the remaining proposed changes to the restrictions, application forms and background therapy toxicity criteria.