

6.12 OMALIZUMAB

prefilled syringe, 150 mg/mL

Xolair[®], Novartis Pharmaceuticals Australia Pty Ltd

1 Purpose of Application

- 1.1 The minor submission requested a Section 85 Authority Required (Written) and Authority Required (Telephone) listing for the initial and continuing treatment respectively, for patients with severe chronic spontaneous urticaria (CSU), in addition to the existing Section 100 Highly Specialised Drugs (S100 HSD) Authority Required listings for CSU.

2 Requested listing

- 2.1 The submission requested the following new listing. Suggestions and additions proposed by the Secretariat to the requested listing are added in italics and suggested deletions are crossed out with strikethrough.

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
OMALIZUMAB 150 mg/mL injection, 1 mL syringe	2	2 (initial) 5 (continuing)	To be confirmed	Xolair® Novartis Pharmaceuticals Australia Pty Ltd

Treatment phase: Initial treatment

Category / Program	GENERAL – General Schedule (Code GE)
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
Severity:	Severe
Condition:	Chronic spontaneous urticaria
PBS Indication:	<i>Severe chronic spontaneous urticaria</i>
Treatment phase:	Initial
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 clinical immunologist; OR Must be treated by an allergist; OR Must be treated by a dermatologist; OR Must be treated by a general physician with expertise in the management of chronic spontaneous urticaria (CSU).

<p>Clinical criteria:</p>	<p>The condition must be based on both physical examination and patient history (to exclude any factors that may be triggering the urticaria), AND Patient must have experienced itch and hives that persist on a daily basis for at least 6 weeks despite treatment with H1 antihistamines, AND Patient must have failed to achieve an adequate response after a minimum of 2 weeks treatment with a standard therapy, AND Patient must not receive more than 12 weeks of treatment under this restriction.</p> <p>A standard therapy is defined as a combination of therapies that includes H1 antihistamines at maximally tolerated doses in accordance with clinical guidelines, and one of the following: 1) a H2 receptor antagonist (150 mg twice per day); or 2) a leukotriene receptor antagonist (LTRA) (10 mg per day); or 3) doxepin (up to 25 mg three times a day)</p> <p>If the requirement for treatment with H1 antihistamines and a H2 receptor antagonist, or a leukotriene receptor antagonist or doxepin 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>A failure to achieve an adequate response to standard therapy is defined as a current Urticaria Activity Score 7 (UAS7) score of equal to or greater than 28 with an itch score of greater than 8, as assessed while still on standard therapy.</p>
<p>Population criteria:</p>	<p>Severe chronic spontaneous urticaria</p>
<p>Administrative Advice</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 Chronic Spontaneous Urticaria Omalizumab Initial PBS Authority Application - Supporting Information Form which must include:</p> <p>(i) demonstration of failure to achieve an adequate response to standard therapy; and</p> <p>(ii) drug names and doses of standard therapies that the patient has failed; and</p> <p>(iii) a signed patient acknowledgment that cessation of therapy should be considered after the patient has demonstrated clinical benefit with omalizumab to re-evaluate the need for continued therapy. Any patient who ceases therapy and whose CSU relapses will need to re-initiate PBS-subsidised omalizumab as a new patient.</p> <p><i>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). 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</i></p> <p><i>Applications for authority to prescribe should be forwarded to:</i> Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>

Treatment phase: Continuing treatment

Category / Program	GENERAL – General Schedule (Code GE)
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
Severity:	Severe
Condition:	Chronic spontaneous urticaria
PBS Indication:	Severe chronic spontaneous urticaria
Treatment phase:	Continuing
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"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	Must be treated by a clinical immunologist; OR Must be treated by an allergist; OR Must be treated by a dermatologist; OR Must be treated by a general physician with expertise in the management of chronic spontaneous urticaria (CSU).
Clinical criteria:	Patient must have demonstrated a response to the most recent PBS-subsidised treatment with this drug for this condition, AND Patient must not receive more than 24 weeks per authorised course of treatment under this restriction.
Prescriber Instructions	<p>A proportion of patients respond to 150 mg 4-weekly so where a substantial improvement has been obtained with a 300 mg dose it is reasonable to back-titrate dose after initial treatment.</p> <p>Cessation of therapy should be considered after the patient has demonstrated clinical benefit with omalizumab to re-evaluate the need for continued therapy. Any patient who ceases therapy and whose CSU relapses will need to re-initiate PBS-subsidised omalizumab as a new patient.</p> <p>Applications for authorisation under this criterion may be made 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).</p>

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

3 Background

3.1 Omalizumab received a positive recommendation at the November 2015 PBAC meeting to extend listing to include patients with severe CSU (at that time referred to as chronic idiopathic urticaria), on the basis of cost minimisation against cyclosporin. The equi-effective doses recommended by the PBAC were omalizumab 300mg and cyclosporin 3mg/kg (PSD, November 2015, paragraph 7.1). A resubmission in November 2016 requested a reassessment of the equi-effective

dose of omalizumab compared with cyclosporin. The PBAC henceforth recommended a change in the equi-effective doses to omalizumab 300 mg and cyclosporin 4 mg/kg (PSD, November 2016, paragraph 5.1).

- 3.2 Omalizumab was listed on the PBS as a S100 HSD drug with an initial written authority and continuing telephone authority for the treatment of severe CSU on 1 September 2017. Omalizumab is also PBS listed as a S100 HSD drug for uncontrolled severe allergic asthma.
- 3.3 The PBAC noted that to prescribe S100 HSDs under the PBS, a prescriber must be:
- affiliated with the hospital the patient is receiving treatment from and be either a staff hospital specialist, or a visiting or consulting specialist of the hospital,
 - an accredited prescriber of medication for the treatment of hepatitis C who is approved by a state or territory to prescribe medication for the treatment of hepatitis C and act under a special arrangement for maintenance therapy only,
 - an accredited prescriber of medication for the treatment of HIV or AIDS who is approved by a state or territory to prescribe medication for the treatment of HIV or AIDS under a special arrangement,
 - a medical practitioner prescribing maintenance therapy when it is impractical to get a prescription from the treating affiliated specialist medical practitioner and the specialist has agreed to the prescription, or
 - a medical practitioner whom the Commonwealth and the state or territory government has agreed may prescribe medication for maintenance therapy.
- 3.4 The minor submission stated (p5) that approximately █% of relevant specialists, predominately dermatologists (█%), who see patients who would otherwise be eligible for omalizumab for severe CSU on the PBS, cannot prescribe omalizumab due to a lack of a hospital provider number. Therefore, a dual listing in S85 was requested.

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 that no consumer comments were received for this item.

Estimated PBS usage & financial implications

- 4.3 The minor submission made a number of assumptions to estimate the uptake of omalizumab as a S85 listing, as presented below.

Table 1: Assumption on the financial estimates

Number of dermatologists prescribing biologics	█
Number of immunologists/allergists prescribing biologics	█
Total likely prescribers of omalizumab for CSU	█
Estimated % of CSU patients seen by immunologist/allergists	█%
Estimated % of CSU patients seen by dermatologists	█%
Immunologists without a hospital provider number	█%
Dermatologists without a hospital provider number	█%

Source: p17 of the minor submission

4.4 The minor submission estimated that approximately █% of all CSU patient encounters are likely to be with a non-hospital affiliated specialist. It assumed that █% of immunologists and allergists who are eligible for S100 prescribing may also prescribe omalizumab as a S85 item. The minor submission further assumed that █% of prescriptions from dermatologists will be through the S85 listing. Overall, this resulted in a weighted average of █% of omalizumab prescriptions estimated to be S85 items.

4.5 The dispensed price for maximum quantity (DPMQ) is increased for a S85 listing if the ex-manufacturer price (AEMP) remains unchanged. This represented financial implications to government, as presented below. These estimates were not verified.

Table 2: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5
Total prescriptions (from agreed estimates)	█	█	█	█	█
% prescriptions moving to S85	█%	█%	█%	█%	█%
Number prescriptions moving to S85	█	█	█	█	█
Average cost/prescription as S100 item	\$ █	\$ █	\$ █	\$ █	\$ █
Cost of scripts as S100 items (Net DPMQ)	\$ █	\$ █	\$ █	\$ █	\$ █
Average cost/prescription as S85 item	\$ █	\$ █	\$ █	\$ █	\$ █
Cost of scripts as S85 items (Net DPMQ)	\$ █	\$ █	\$ █	\$ █	\$ █
Additional cost to gov. of S85 prescriptions	\$ █	\$ █	\$ █	\$ █	\$ █
Cost offsets from MBS items saved	\$ █	\$ █	\$ █	\$ █	\$ █
Rebate payable under SPA	\$ █	\$ █	\$ █	\$ █	\$ █
Net cost to government	\$ █	\$ █	\$ █	\$ █	\$ █

Source: Tables 1 and 4, p18-19 of the minor submission.

4.6 The minor submission presented 5-year estimates and stated that the expected utilisation for years 1 – 5 are based on the agreed estimates for years 2 – 6 for the September 2017 listing of omalizumab for CSU. However, the minor submission assumed the estimates for years 1 – 5 to be based on listing years (i.e. September 2017 – August 2018, September 2018 – August 2019 and so forth), whereas the original agreed estimates were forecast based on calendar years.

4.7 The minor submission estimated that the net cost to government as a result of a dual S85 listing is \$ █ over five years. The increased cost associated with the proposed S85 listing is due to additional distribution costs (wholesaler mark-up, administration and handling fee and dispensing fees), which are not applicable to S100 drugs. The minor submission also assumed MBS cost offsets, on the claim that

under the current S100 listing, patients whose initial consultation is with a non-hospital affiliated physician must be referred to another doctor eligible to prescribe omalizumab. The minor submission argued that the referral to a physician eligible to prescribe S100 drugs results in an additional MBS consultation, which would not be required if a S85 listing for omalizumab was available.

- 4.8 The PBAC recalled that it previously advised that, where a recommendation is made to move a drug from S100 to S85, the cost of the increased pharmacy remuneration should be borne by the manufacturer. The PBAC therefore considered that the sponsor should reduce the ex-manufacturer price of omalizumab to ensure that the impact to government would remain cost neutral for a dual S85 and S100 listing of omalizumab.
- 4.9 The minor submission stated that it is not expected that a dual S85 listing would increase the number of patients who will gain access to PBS-subsidised omalizumab. The PBAC considered that this is reasonable.

Financial Management – Risk Sharing Arrangements

- 4.10 There is currently a Special Pricing Agreement (SPA) and a Risk Sharing Arrangement (RSA) in place for omalizumab for CSU. [REDACTED]

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

5 PBAC Outcome

- 5.1 The PBAC recommended a Section 85 (S85) Authority Required (Written) and Authority Required (Telephone) listing of omalizumab for the initial and continuing treatment respectively, for patients with severe chronic spontaneous urticaria (CSU), in addition to the existing Section 100 Highly Specialised Drugs (S100 HSD) Authority Required listings for CSU. In making this recommendation, the PBAC noted that it would improve access for patients whose initial consultation is with a non-hospital affiliated physician who cannot prescribe omalizumab under S100, but would be able to do so under S85. The PBAC advised that the sponsor should reduce the ex-manufacturer price of omalizumab to ensure that the impact to government would remain cost neutral for the dual S85 and S100 listings.
- 5.2 The PBAC recalled its advice in consideration of the criteria previously used by the Highly Specialised Drugs Working party at its April 2015 Special PBAC Meeting, that the only criterion that differentiated HSD listings from General Schedule listings was “the drug is highly specialised, making administration outside an institutional environment problematic and the patient target group is clearly identifiable”. The PBAC considered that hospital settings were not required for the administration of omalizumab.

- 5.3 The PBAC recalled that it previously advised that omalizumab is not suitable for prescribing by nurse practitioners, that the Early Supply Rule should not apply and that omalizumab should not be treated as interchangeable on an individual patient basis with any other drugs under Section 101(3BA) of the *National Health Act, 1953* (PSD, November 2015, paragraphs 7.8 – 7.10).
- 5.4 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

6 Recommended listing

- 6.1 Extend the existing listing to include a dual listing in the general schedule as follows:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
OMALIZUMAB 150 mg/mL injection, 1 mL syringe	2	2 (initial) 5 (continuing)	Xolair® Novartis Pharmaceuticals Australia Pty Ltd

Treatment phase: Initial treatment

Category / Program	GENERAL – General Schedule (Code GE)
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
Severity:	Severe
Condition:	Chronic spontaneous urticaria
PBS Indication:	Severe chronic spontaneous urticaria
Treatment phase:	Initial
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 clinical immunologist; OR Must be treated by an allergist; OR Must be treated by a dermatologist; OR Must be treated by a general physician with expertise in the management of chronic spontaneous urticaria (CSU).

Public Summary Document – March 2018 PBAC Meeting

<p>Clinical criteria:</p>	<p>The condition must be based on both physical examination and patient history (to exclude any factors that may be triggering the urticaria), AND Patient must have experienced itch and hives that persist on a daily basis for at least 6 weeks despite treatment with H1 antihistamines, AND Patient must have failed to achieve an adequate response after a minimum of 2 weeks treatment with a standard therapy, AND Patient must not receive more than 12 weeks of treatment under this restriction.</p>
<p>Prescriber Instructions</p>	<p>A standard therapy is defined as a combination of therapies that includes H1 antihistamines at maximally tolerated doses in accordance with clinical guidelines, and one of the following: 1) a H2 receptor antagonist (150 mg twice per day); or 2) a leukotriene receptor antagonist (LTRA) (10 mg per day); or 3) doxepin (up to 25 mg three times a day)</p> <p>If the requirement for treatment with H1 antihistamines and a H2 receptor antagonist, or a leukotriene receptor antagonist or doxepin 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>A failure to achieve an adequate response to standard therapy is defined as a current Urticaria Activity Score 7 (UAS7) score of equal to or greater than 28 with an itch score of greater than 8, as assessed while still on standard 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 Chronic Spontaneous Urticaria Omalizumab Initial PBS Authority Application - Supporting Information Form which must include:</p> <p>(i) demonstration of failure to achieve an adequate response to standard therapy; and</p> <p>(ii) drug names and doses of standard therapies that the patient has failed; and</p> <p>(iii) a signed patient acknowledgment that cessation of therapy should be considered after the patient has demonstrated clinical benefit with omalizumab to re-evaluate the need for continued therapy. Any patient who ceases therapy and whose CSU relapses will need to re-initiate PBS-subsidised omalizumab as a new patient.</p>
<p>Administrative Advice</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). 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>

Treatment phase: Continuing treatment

Category / Program	GENERAL – General Schedule (Code GE)
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
Severity:	Severe
Condition:	Chronic spontaneous urticaria
PBS Indication:	Severe chronic spontaneous urticaria
Treatment phase:	Continuing
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"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined
Treatment criteria:	Must be treated by a clinical immunologist; OR Must be treated by an allergist; OR Must be treated by a dermatologist; OR Must be treated by a general physician with expertise in the management of chronic spontaneous urticaria (CSU).
Clinical criteria:	Patient must have demonstrated a response to the most recent PBS-subsidised treatment with this drug for this condition, AND Patient must not receive more than 24 weeks per authorised course of treatment under this restriction.
Administrative Advice	A proportion of patients respond to 150 mg 4-weekly so where a substantial improvement has been obtained with a 300 mg dose it is reasonable to back-titrate dose after initial treatment. Cessation of therapy should be considered after the patient has demonstrated clinical benefit with omalizumab to re-evaluate the need for continued therapy. Any patient who ceases therapy and whose CSU relapses will need to re-initiate PBS-subsidised omalizumab as a new patient. Applications for authorisation under this criterion may be made 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).

If listed before 1 September 2018, the general schedule listing will also include the grandfather restriction as follows:

Category / Program	GENERAL – General Schedule (Code GE)
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
Episodicity:	-
Severity:	Severe
Condition:	Chronic spontaneous urticaria
PBS Indication:	Severe chronic spontaneous urticaria

Public Summary Document – March 2018 PBAC Meeting

Treatment phase:	Grandfathering treatment
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required - In Writing
Treatment criteria:	<p>Must be treated by a clinical immunologist; OR Must be treated by an allergist; OR Must be treated by a dermatologist; OR Must be treated by a general physician with expertise in the management of chronic spontaneous urticaria (CSU).</p>
Clinical criteria:	<p>Patient must have received non-PBS subsidised treatment with this drug for this condition prior to 1 September 2017, AND Patient must have documented history of itch and hives that persisted on a daily basis for at least 6 weeks despite treatment with H1 antihistamines prior to commencing non-PBS subsidised treatment with this drug for this condition AND Patient must have documented history of failure to achieve an adequate response after a minimum of 2 weeks treatment with a standard therapy prior to commencing non-PBS subsidised treatment with this drug for this condition. AND Patient must not receive more than 24 weeks of treatment under this restriction;</p>
Prescriber Instructions	<p>A standard therapy is defined as a combination of therapies that includes H1 antihistamines at maximally tolerated doses in accordance with clinical guidelines, and one of the following: a/ a H2 receptor antagonist (150 mg twice per day); or b/ a leukotriene receptor antagonist (LTRA)(10 mg per day; or c/ doxepin (up to 25mg three times a day).</p> <p>If the requirement for treatment with H1 antihistamines and a H2 receptor antagonists, or leukotriene receptor antagonists or doxepin 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>A failure to achieve an adequate response to standard therapy is defined as a current Urticaria Activity Score 7 (UAS7) score of ≥ 28 with an itch score of greater than 8, as assessed while still on standard therapy.</p> <p>A patient may qualify for PBS-subsidised treatment under this restriction only once. For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the Continuing treatment criteria.</p> <p>The authority application must be made in writing and must include: (a) a completed authority prescription form; and (b) a completed Chronic Spontaneous Urticaria Omalizumab Initial Grandfather PBS Authority Application - Supporting Information Form which must include: (i) demonstration of failure to achieve an adequate response to standard therapy; and (ii) drug names and doses of standard therapies that the patient has failed; and (iii) a signed patient acknowledgment that cessation of therapy should be considered after the patient has demonstrated clinical benefit with omalizumab to re-evaluate the need for continued therapy. Any patient who ceases therapy and whose CSU relapses will need to re-initiate PBS-subsidised omalizumab as a new patient.</p>

Administrative Advice	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). 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 Applications for authority to prescribe should be forwarded to: Department of Human Services Complex Drugs Reply Paid 9826 HOBART TAS 7001
------------------------------	---

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.