5.23 OMALIZUMAB, Injection 75 mg in 0.5 mL single dose pre-filled syringe, Injection 150 mg in 1 mL single dose pre-filled syringe, Xolair®, Novartis Pharmaceuticals Australia Pty Limited

1 Purpose of Submission

1.1 The Category 4 submission requested to combine the existing listings of the 75 mg and 150 mg strengths of omalizumab (Xolair®) to allow patients requiring a dose of 225 mg or 375 mg to pay a single co-payment.

2 Background

Regulatory status

2.1 Omalizumab was first registered on the Australian Register of Therapeutic Goods (ARTG) on 13 June 2003.

2.2 Omalizumab is ARTG registered as individual packs of the 75 mg or 150 mg strengths in two forms, namely:

- a powder for injection vial with diluent ampoule
- a solution for injection pre-filled syringe (PFS).

2.3 Omalizumab is currently approved for the following indications:

- as add-on therapy to improve asthma control in patients 6 to 12 years of age with severe allergic asthma who have documented exacerbations despite daily high dose inhaled corticosteroids, and who have immunoglobulin E (IgE) levels corresponding to the recommended dosage range (see Figure 1)
- for the management of adult and adolescent patients (≥ 12 years of age) with moderate to severe allergic asthma, who are already being treated with inhaled corticosteroids, and who have serum IgE levels corresponding to the recommended dosage range (see Figure 1)
- as add-on treatment in adult patients (18 years of age and above) with severe chronic rhinosinusitis with nasal polyps (CRSwNP) who have an inadequate response to intranasal corticosteroids, and who have serum IgE levels corresponding to the recommended dosage range

- for adults and adolescents (12 years of age and above) with chronic spontaneous urticaria (CSU) who remain symptomatic despite H1 antihistamine treatment.

Current situation

2.4 Omalizumab 75 mg and 150 mg PFS are currently PBS-listed as Authority Required listings under the Section 100 Highly Specialised Drugs arrangements for:

- Uncontrolled severe asthma in adults and adolescents (aged 12 years and above)
- Uncontrolled severe allergic asthma (USAA) (aged 6 years to less than 12 years)
- CSU.

2.5 Omalizumab is dosed every two to four weeks according to a patient's body weight and total serum IgE level as shown in Figure 1. A patient's total monthly dose can range between 75 mg and 750 mg depending on the combination of their weight and serum IgE. As such, the total monthly dose of omalizumab is achieved with various combinations of the 75 mg and 150 mg PFS. The different strengths and treatment phases have separate PBS item codes.

2.6 Patients who require a monthly dose of 225 mg, 375 mg, 450 mg, or 750 mg currently pay two co-payments per month. Patients who require a monthly dose of 75 mg, 150 mg, 300 mg, or 600 mg pay one co-payment per month. The submission claimed that it was seeking to address concerns raised by both patients and clinicians of considerable financial burden and inequity amongst patients with USAA being treated with omalizumab.

Figure 1: Xolair doses for patients 6 years and older with allergic asthma and for patients 18 years and older with CRSwNP via subcutaneous administration.

Baseline IgE (IU/mL)	Total milligrams of Xolair required per 4-week interval Body Weight (kg)									
	>20–25*	>25-30*	>30–40	>40–50	>50-60	>60–70	>70–80	>80–90	>90–125	>125-150
>30–100	75	75	75	150	150	150	150	150	300	300
>100–200	150	150	150	300	300	300	300	300	450	600
>200–300	150	150	225	300	300	450	450	450	600	750
>300–400	225	225	300	450	450	450	600	600		
>400–500	225	300	450	450	600	600	750	750		
>500–600	300	300	450	600	600	750				
>600–700	300	450	450	600	750					
>700–800	450	450	600	750	Notes:					
>800–900	450	450	600	750	Doses above black line are administered once per 4 weeks.					
>900–1000	450	600	750		Doses below black line are split into 2 equal doses					
>1000–1100	450	600	750		administered every 2 weeks (i.e. 450 total = 225 every 2					
>1100–1200	600	600			weeks; 600 mg total = 300 mg every 2 weeks; 750 total = 375					
>1200–1300	600	750			every 2 weeks).					

Source: p4 of Product Information of Xolair

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

3 Requested listing

3.1 The submission requested to combine the existing listings of the 75 mg and 150 mg PFS of omalizumab for the treatment of USAA into a single listing. The submission proposed two new PBS items as follows:

- A listing of one 150 mg PFS and one 75 mg PFS, allowing patients who require a dose of 225 mg to pay one co-payment and receive two individual products
- A listing of two 150 mg PFS and one 75 mg PFS, allowing patients who require a dose of 375 mg to pay one co-payment and receive three individual products.

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

4 Consideration of evidence

Sponsor hearing

4.1 There was no hearing for this item.

Consumer comments

4.2 The PBAC noted and welcomed the input from health care professionals (3) and organisations (3) via the Consumer Comments facility on the PBS website. The comments described the benefits of allowing patients who require multiple strengths of omalizumab to pay a single co-payment. The comments supported a single co-payment for a combined dose.

4.3 The PBAC noted the comments received from Asthma Australia, the Centre for Community-Driven Research, and the NHMRC Centre of Excellence in Treatable Traits, clarifying the current use of omalizumab in clinical practice. The PBAC specifically noted that the cost burden arises due to omalizumab doses being calculated based on specific combinations of body weight and serum IgE, and the requirement for some patients to pay more than one co-payment in situations where a single pack providing the required dose does not exist.

Estimated PBS utilisation and financial implications

4.4 The submission provided a PBS 10% analysis (based on 2,449 scripts of omalizumab), sourced from a PBS Services Report from 1 January 2020 to 31 December 2020. To determine the doses of omalizumab that were supplied, the analysis specified the quantities of the 75 mg PFS and 150 mg PFS that were supplied with each prescription. The submission claimed that the number of co-payments per patient could be deduced where both strengths of omalizumab were supplied on the same dispensing date for the same Patient ID.

4.5 The PBS 10% analysis indicated that 44.6% of patients have both strengths of omalizumab dispensed together and pay a double patient co-payment, which the submission claimed represented a significant inequity amongst patients and highlights

Quality Use of Medicines (QUM) concerns. While this is evidence that some omalizumab patients require multiple strengths for their treatment, the PBAC considered that the submission did not justify the link between the use of multiple strengths and the QUM. An analysis of 100% PBS data conducted by the Secretariat (herein referred to as "the 100% analysis") showed that 38.1% of omalizumab supplies were that of multiple strengths dispensed on the same day for the same patient, the sum of which amounted to a total dose that would require both the 75 mg and 150 mg strengths (i.e. 225 or 375 mg fortnightly or 225 mg 4-weekly).

4.6 The submission estimated that 93% of patients who are prescribed omalizumab 75 mg are also prescribed the 150 mg strength to make up a total dose of either 225 mg or 375 mg, and that this therefore represents the proportion of 75 mg users paying double patient co-payments for their treatment who under the requested listings would pay only one co-payment. The 100% analysis showed that 98.2% of 75 mg supplies were dispensed on the same day as a 150 mg dispensing for the same patient.

4.7 The table below summarises omalizumab 75 mg PFS usage by patient co-payment level. The submission included the item codes of other indications in its analysis. The fourth column added by the Secretariat shows the proportions for the USAA indication.

Table 1: Omalizumab average co-payment

Co-payment categories	Co-payment (2021)	Proportion of patients (75 mg only for all indications)	Proportion of patients (using both 75 mg and 150 mg data for USAA)
General-Ordinary	$41.30	41.2%	37.6%
General-Safety Net	$6.60	4.7%	6.5%
Concessional-Ordinary	$6.60	34.7%	31.9%
Concessional-Safety Net	$0.00	18.8%	24%
RPBS-Ordinary	$6.60	0.4%	0%
RPBS-Safety Net	$0.00	0.2%	0%
Average co-payment per script	$19.66	-	$18.05

Source: Proportion of patients from PBS/RPBS Services (from Pharmaceutical Benefits Schedule Item Reports website) dispensed for omalizumab 75 mg and 150 mg between Jan-Dec 2020 using the 2021 co-payment amounts.

4.8 The submission claimed that a significant proportion of omalizumab patients are impacted by extra co-payment costs, with 41.2% of omalizumab patients (254 patients) having to pay $82.60 each month instead of $41.30, and 39.8% of omalizumab patients (246 patients) paying $13.20 each month instead of $6.60. The submission's claim assumed that all of the 81% of patients taking the 75 mg strength of omalizumab (500 patients) who paid a co-payment paid more than one co-payment per month, while the remaining 19% of patients paid no co-payment. The PBAC noted that this assumption was inconsistent with the submission's claim that 93% of patients using omalizumab 75 mg pay more than one patient co-payment per month (i.e. 7% paid either one or no co-payment). The PBAC considered it would be reasonable to assume that the distribution across different co-payment categories would remain unchanged between the populations taking a single strength and those taking both

strengths. The PBAC noted, based on the 100% analysis, that 76% of patients taking the 75 mg strength of omalizumab for USAA would pay two co-payments per month.

4.9 The submission estimated that 500 patients per annum would benefit from the requested listing, and estimated using an average co-payment of $19.66 per prescription that the cost to government of reduced patient co-payments due to the requested listing would be $127,871 per annum (see Table 2). The submission noted the annual cost to the PBS/RPBS of omalizumab 75 mg PFS was $2,770,039 using the 2020 PBS Benefits report. The submission requested listings for the USAA indication, but derived the average co-payment and the cost to government using all indications. In calculating the cost to government of reduced patient co-payments, the submission applied the proportion of 75 mg scripts that were dispensed with a 150 mg script to the total cost of omalizumab 75 mg across all indications, and multiplied it by the average co-payment. While the PBAC considered this method appropriate, it considered the input values should be based on the 100% analysis for the USAA indication. An adjusted cost to government based on the 100% analysis for the USAA indication is shown in Table 3.

Table 2: Financial implications of omalizumab 75 mg PFS patient co-payments

Co-payment revenue that would be lost due to the requested listings	$127,871
PBS Benefits associated with 75 mg PFS scripts	$2,770,039
Discount offered on omalizumab 75 mg PFS to remain cost neutral to the PBS/RPBS (co-payment revenue lost as % of PBS Benefits paid)	4.62%

Source: Submission Attachment 3

Table 3: Financial implications of omalizumab 75 mg PFS patient co-payments (adjusted)

Co-payment revenue that would be lost due to the requested listings	$6,282
PBS/RPBS Benefits associated with 75 mg PFS USAA scripts	$133,677
Suggested discount to remain cost neutral (co-payment revenue lost as % of PBS/RPBS Benefits paid)	4.68%

Source: The 100% analysis

4.10 The submission proposed a 4.62% discount on the price of omalizumab 75 mg PFS to offset the financial impact of the reduced patient co-payments should the requested listing be recommended (Table 4). The submission did not offer a discount on the 150 mg PFS stating that only one co-payment would be lost per script dispensed under the requested listings, and that the majority of omalizumab 150 mg/mL usage is not impacted by double co-payments. The 100% analysis showed that 61.2% of omalizumab patients take only the 150 mg strength.

Table 4: Current and proposed DPMQ of omalizumab

Drug name and strength	July 2021		Proposed	
	Published	Effective ($)	Published	Effective ($)
Omalizumab 75mg/0.5mL	$205.00	[redacted]	$205.00	[redacted]
Omalizumab 150mg/mL	$410.00	[redacted]	$410.00	[redacted]
Omalizumab 75mg/0.5mL x 1 and 150mg/mL x 1	$615.00	[redacted]	$615.00	[redacted]
Omalizumab 75mg/0.5mL x 1 and 150mg/mL x 2	$1,025.00	[redacted]	$1,025.00	[redacted]

Source: p17, Table 5 of the main submission

4.11 The submission proposed that the published price of omalizumab 75 mg PFS should stay the same so that it remains proportional to the cost of the 150 mg PFS, and that

the discount should apply to the effective price only. The sponsor proposed an adjustment to the rebate percentage applicable to the 75 mg PFS under the Special Pricing Arrangement, noting that the price offered would apply to all 75 mg PFS scripts in the future, irrespective of whether another strength is prescribed.

Quality Use of Medicines

4.12 The submission noted Section 4.7.1 of the PBAC Guidelines, Activities to Support the QUM, which encourages sponsors to "identify and discuss possible risks to achieving QUM, and offer solutions to mitigate the possibility of inappropriate or potentially harmful use of the proposed medicine". The submission provided a letter from an international respiratory expert to support its claim of QUM issues as a result of the different co-payments required for different total dosages.

4.13 The submission claimed that patients who require a monthly dose of 225 mg, 375 mg, 450 mg, or 750 mg having to pay two co-payments to achieve a fortnightly or 4-weekly dose made up of multiple strengths reflects a QUM concern. The submission considered that requiring patients to pay more than one patient co-payment per month for omalizumab compromises two of the four central objectives of the Australian National Medicines Policy (NMP) 2000, namely:

- "timely access to the medicines that Australians need, at a cost individuals and the community can afford"
- "quality use of medicines".

4.14 The submission claimed that there is evidence of prescribers attempting to prevent patients from paying additional co-payments by prescribing:

- multiple units, e.g. 5 units of 75 mg PFS for a 375 mg total dose
- double the quantity of treatment in a single supply for co-payments to average one fee per month, resulting in patients being dispensed large quantities of their treatment at any one time.

The submission stated that such cases of multiple injections may increase a patient's risk of injection site adverse events. The PBAC considered that the claim of such prescribing behaviour was not reasonably justified. The PBAC noted that the 100% analysis showed three instances (0.017%) out of 16,709 supplies of omalizumab in 2020 where multiple units of the 75 mg were prescribed to make up the total dose of a treatment where a combination of strengths could have been used. These instances may be attributed to patients on a total dose of 75 mg per fortnight or per 4-weeks who received multiple doses at once (e.g. Regulation 24 supply).

4.15 The submission stated that there is a risk of clinicians selecting a dosage that can be dosed with a single strength of omalizumab, which may result in patients being under- or over-dosed for their USAA. The PBAC noted that the submission did not provide any evidence to substantiate this claim.

4.16 The submission claimed that the proposed listing of omalizumab for USAA provides a pragmatic solution for all suitable patients to have equitable, affordable, and safe access to treatment, at no additional cost to the Commonwealth.

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

5 PBAC Outcome

5.1 The PBAC did not recommend combining the existing listings of the 75 mg and 150 mg strengths of omalizumab under the S100 (HSD Program). The PBAC noted that the consumer comments described the financial burden to patients who are currently paying two monthly co-payments for the treatment of USAA. The PBAC noted that the affected patient groups are patients with USAA who require a monthly dose of 225 mg, 375 mg, 450 mg, or 750 mg (hereafter referred to as the "affected patients").

5.2 The PBAC noted that omalizumab is only ARTG registered as individual packs of the 75 mg or 150 mg strengths. The PBAC considered that a solution to allow affected patients to pay a single monthly co-payment instead of two monthly co-payments would be that: i) the sponsor seeks the ARTG registration of a co-pack or other form that provides for the required doses; and ii) seeks PBS listing of this product or products. The PBAC would welcome a submission for a co-pack of omalizumab 75 mg and 150 mg PFS.

5.3 The PBAC noted that when it first recommended omalizumab, as it does with all submissions, it considered any QUM concern, including the requirement for some patients to use a combination of forms to achieve the required dose. The PBAC considered that the QUM concerns the submission raised in relation to prescriber practice were unsubstantiated, and further considered that the way in which omalizumab is listed at present does not contribute to any of the perceived concerns.

5.4 The PBAC noted the pre-PBAC response also proposed to make special arrangements under Section 100(1)(c) of the Act to combine the multiple strengths. The PBAC did not consider such a proposal reasonable given that the sponsor is able to register a combination product on the ARTG and seek PBS subsidy for such a combination product.

5.5 The PBAC noted that this submission is eligible for an Independent Review.

Outcome:
Not recommended

6 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the

merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

7 Sponsor's Comment

Novartis is unable to supply a co-pack for Xolair PFS for reasons outlined in the submission, and is disappointed that the PBAC has not recommended the proposed alternative.