

6.13 MEPOLIZUMAB

**Powder for injection 100 mg;
Injection 100 mg in 1 mL single dose pre-filled pen,
Nucala[®],
GlaxoSmithKline Australia Pty Ltd**

1 Purpose of Submission

1.1 The Category 3 submission requested to amend the restriction level of mepolizumab for the treatment of uncontrolled severe asthma as follows:

- Initiation: Authority Required (Written) to Authority Required (Telephone/Online)
- Continuation: Authority Required (Written) to Authority Required (STREAMLINED)

1.2 The submission also requested to remove the oral corticosteroids (OCSs) requirement within the 'optimised asthma therapy' in the clinical criteria as follows:

- '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'.

2 Background

2.1 Mepolizumab is currently PBS-listed as an:

- Authority Required (Written) listing for initiation and continuation treatment for uncontrolled severe asthma. The balance of supply is PBS-listed as Authority Required (Telephone/Online).
- Authority Required (Written) listing for initiation and Authority Required (Telephone/Online) listing for continuation treatment of chronic rhinosinusitis with nasal polyps (CRSwNP).

Registration status

2.2 Mepolizumab is TGA registered for the following indications:

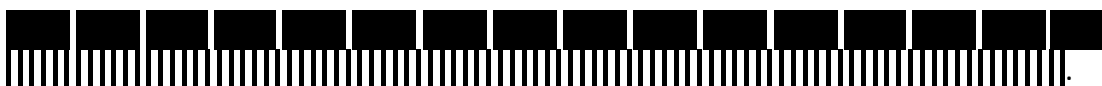
- Severe eosinophilic asthma (SEA)
- Chronic rhinosinusitis with nasal polyps (CRSwNP)
- Relapsed or refractory eosinophilic granulomatosis with polyangiitis (EGPA)

Previous PBAC consideration

- 2.3 At its July 2016 meeting, the PBAC recommended the listing of mepolizumab for the treatment of SEA in patients aged 12 years and over. The PBS listing occurred on 1 January 2017.
- 2.4 On 1 July 2021, the ‘severe eosinophilic asthma’ and ‘severe allergic asthma’ indications for omalizumab, mepolizumab, benralizumab and dupilumab were amended to ‘uncontrolled severe asthma’ for consistency. Omalizumab’s ‘severe allergic asthma’ listings for the population aged 6-12 years were maintained.
- 2.5 At its July 2021 meeting, the PBAC recommended that the authority requirements for continuing treatment with omalizumab for severe allergic asthma (SAA) be amended from Authority Required (Written) to Authority Required (Telephone/Online) to ease administrative burden for prescribers and for consistency with the continuing authority requirements for omalizumab for chronic spontaneous urticaria (CSU) (Review of Authority Required (Written) PBS listings Tranche 3, July 2021 PBAC Meeting outcomes). This has yet to be implemented. See paragraph 4.8 for a summary of the PBAC’s consideration of mepolizumab in its Review of Authority Required (Written) PBS listings.
- 2.6 At its November 2022 meeting, the PBAC recommended the listing of mepolizumab for the treatment of CRSwNP as Authority Required (Written) for initiation and Authority Required (Telephone/Online) for continuation. This indication was PBS-listed on 1 April 2023.
- 2.7 Please see Table 1 for summary of previous PBAC consideration for mepolizumab and other PBS-listed OCSs.

Committee-In-Confidence information

2.8



End Committee-In-Confidence information

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Table 1: Summary of previous PBAC considerations

PBAC Meeting	Item	Mechanism of action – target pathway	Outcome
November 2010	OOS omalizumab for SAA	Anti-IgE	The PBAC recommended the Authority Required (Written) (S100 HSD) listing of omalizumab for SAA on the basis of an acceptable cost-effectiveness ratio in a severe patient group with limited treatment options, whose asthma was uncontrolled while on at least 10mg per day prednisolone equivalent.
July 2016	7.04 mepolizumab for SEA	Anti-IL5	The PBAC recommended the Authority Required (Written) (S100 HSD) listing of mepolizumab for SEA on a cost-minimisation basis with omalizumab. Mepolizumab was listed on the PBS on 1 January 2017.
March 2018	5.01 benralizumab for SEA	Anti-IL5	The PBAC recommended the Authority Required (Written) (S100 HSD) listing of benralizumab for SEA on a cost-minimisation basis with mepolizumab, noting the clinical need for additional treatment options in SEA
December 2018	Severe asthma stakeholder Meeting	N/A	In a meeting with members of the PBAC and DUSC, representatives of the Centre of Excellence in Severe Asthma, Asthma Australia, National Asthma Council Australia, the Department of Health and sponsors in December 2018, stakeholders agreed that the principal objectives are to control asthma and reduce OCS use, and that re-examining some of the PBS initiation criteria for biologic medicines would be beneficial.
November 2020	6.02 dupilumab for uncontrolled severe eosinophilic or allergic asthma	Anti-IL4	The PBAC recommended the listing of dupilumab for uncontrolled severe eosinophilic or allergic asthma under the same authority conditions as benralizumab, mepolizumab and omalizumab.
April 2021 Administrative change with PBAC specialist input	N/A	N/A	The Department considered changes to all indications of omalizumab, mepolizumab, benralizumab and dupilumab to be amended to 'uncontrolled severe asthma'. Implemented 1 July 2021. Omalizumab maintained severe allergic asthma listings for the population aged 6-12.
July 2021	9.02 Tranche 3 DUSC/PBAC review of Authority Required (written) listings	N/A	The PBAC did not recommend an amendment to the authority requirements for benralizumab or mepolizumab for SEA at this time, given that the market is not yet stable. The PBAC recommended that the authority requirements for continuing treatment with omalizumab for SAA be amended from Authority Required (Written) to Authority Required (Telephone/Online) to ease administrative burden for prescribers and for consistency with the continuing authority requirements for omalizumab for CSU.
November 2022	7.04 mepolizumab CRSwNP	Anti-IL5	The PBAC recommended the Authority Required listing of mepolizumab for the treatment of CRSwNP, on the basis that it should be available only under special arrangements under Section 100 (HSD) program.

Abbreviations: CRSwNP chronic rhinosinusitis with nasal polyps; CSU chronic spontaneous urticaria; DUSC drug utilisation sub-committee; HSD highly specialised drugs; OOS out-of-session; PBAC pharmaceutical benefits advisory committee; SAA severe allergic asthma; SEA severe eosinophilic asthma.

3 Requested listing

3.1 The submission requested the following changes to the existing listing for the treatment of uncontrolled severe asthma.

Amendment of Authority Level:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
MEPOLIZUMAB					
mepolizumab 100 mg injection, 1 vial	10966R 11003D	1	1	7	Nucala
mepolizumab 100 mg/mL injection, 1 mL pen device	12007Y 12051G				
Restriction Summary 11843 / Treatment of Concept: 11848					
Concept ID (for internal Dept. use)	Category / Program: Section 100 – Highly Specialised Drugs				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system) <input type="checkbox"/> Authority Required (in writing only via post/HPOS upload)				
Treatment phase: Initial treatment - Initial 1 (New patients; or Recommencement of treatment in a new treatment cycle following a break in PBS subsidised biological medicine therapy) Initial treatment - Initial 2 (Change of treatment)					

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
MEPOLIZUMAB					
mepolizumab 100 mg injection, 1 vial	10908X 11014Q	1	1	5	Nucala
mepolizumab 100 mg/mL injection, 1 mL pen device	12052H 12064Y				
Restriction Summary 11895 / Treatment of Concept: 11842					
Concept ID (for internal Dept. use)	Category / Program: Section 100 – Highly Specialised Drugs				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required (STREAMLINED) <input type="checkbox"/> Authority Required (in writing only via post/HPOS upload)				
Treatment phase: Continuing treatment					

Amendment of clinical criteria:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
MEPOLIZUMAB					
mepolizumab 100 mg injection, 1 vial	10996R 11003D	1	1	7	Nucala
mepolizumab 100 mg/mL injection, 1 mL pen device	12007Y 12051G				
Restriction Summary 11843 / Treatment of Concept: 11848					
	Treatment phase: Initial treatment - Initial 1 (New patients; or Recommencement of treatment in a new treatment cycle following a break in PBS subsidised biological medicine therapy) Initial treatment - Initial 2 (Change of treatment)				
	Prescribing Instructions: 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.				

- 3.2 The Secretariat proposed that the administrative advice ‘No increase in the maximum quantity or number of units may be authorised’ and ‘No increase in the maximum number of repeats may be authorised’ be added to the continuing restriction, based off the dosing in the product information (100 mg administered by subcutaneous injection once every 4 weeks).
- 3.3 The clinical criterion ‘Patient must have received this drug as their most recent course of PBS-subsidised biological agent treatment for this condition in this treatment cycle’ has been added to the continuing restriction for clarity, especially as an Authority Required (STREAMLINED) listing will no longer require approval by Services Australia.
- 3.4 The current definition of optimised asthma therapy was recommended by the PBAC at its July 2014 meeting. In its July 2014 consideration, the PBAC particularly noted the elements of the current restriction referring to OCS use were developed in consultation with the stakeholder group and reflected the best practice guidelines at the time. The PBAC recalled that OCS 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. The PBAC considered that accepting the change to the definition of optimal asthma therapy, with regards to treatment with OCSs, in line with

clinical treatment guidelines was appropriately pragmatic (omalizumab Public Summary Document (PSD) July 2014 PBAC meeting).

- 3.5 At its July 2016 meeting, the PBAC recommended the listing of mepolizumab for SEA on a cost-minimisation basis with omalizumab. The PBAC noted and accepted that the proposed restrictions for mepolizumab was modified to make the listing as consistent as omalizumab restrictions (para 7.4, mepolizumab PSD, July 2016 PBAC meeting).
- 3.6 The submission requested that patient eligibility for each of the treatment phases to remain the same (noting the request relating to the OCS wording within the optimised asthma therapy in the clinical criteria). The submission stated that clinicians would still need to test patients to confirm eligibility and document results appropriately in their medical records. The submission considered that the requested amendment to the Authority level would reduce the burden and administrative complexity for clinicians, thus increasing patient care.

4 Consideration of the evidence

Sponsor hearing

- 4.1 There was no hearing for this item.

Consumer comments

- 4.2 The PBAC noted and welcomed the input from individuals (1), health care professionals (4) and organisations (6) via the Consumer Comments facility on the PBS website. The comments described a range of benefits of the proposed amendments to mepolizumab for uncontrolled severe asthma, including reduced administrative burden and complexity for prescribers. The input stated that while streamlining the process for continuation and switching biologic agent would not increase the number of individuals initiating or continuing on treatment, it would have an impact on improved disease control, as well as reduce the need for OCSs.
- 4.3 The input was also supportive of the removal of the OCS requirement from the clinical criteria. It stated that in order to enable access to mepolizumab, the current threshold may result in unintended exposure to higher doses of corticosteroids beyond what is clinically reasonable. This may lead to long term OCS-related side effects and reduced quality of life.
- 4.4 The PBAC noted the advice received from the National Asthma Council of Australia, the Australasian Society of Clinical Immunology and Allergy, the Thoracic Society of Australia and New Zealand, the National Allergy Council and Allergy and Anaphylaxis Australia, the National Health and Medical Research Council Centres of Research Excellence in Asthma Treatable Traits and Severe Asthma, and Asthma Australia. The organisations were all supportive of the amendment of mepolizumab authority levels to ease administrative burden, and the removal of OCS requirements from the clinical criteria to align current treatment guidelines to improve OCS stewardship and to reduce the incidence and burden of OCS-related side effects.

Authority level amendment

Anti-IL5 market maturation

- 4.5 The submission stated that the annual initiations for the anti-IL5 biologic agents (i.e. mepolizumab and benralizumab) for the treatment of uncontrolled severe asthma have stabilised. In FY2022 and 2023, the growth for anti-IL5 initiation prescriptions was minimal (8% growth in FY 2022 and 3% growth in FY 2023) (see Table 2). The submission stated that the PBS eligibility criteria for the anti-IL5 agents are identical, and clinicians are familiar with identifying patients appropriate for initiating treatment and ensuring treatment is only continued in patients demonstrating benefit.

Table 2: Annual growth in PBS/RPBS services for total Anti-IL5 market (mepolizumab and benralizumab)

Financial Year	2017-2018	2018-2019	2019-2020	2020-2021	2021-2022	2022-2023
Anti-IL5 Initiations	547%	29%	52%	21%	8%	3%
Anti-IL5 Continuations	1469%	230%	90%	56%	26%	16%
Anti-IL5 Total	730%	104%	75%	44%	21%	13%

Source: Submission main body p6

Abbreviations: IL interleukin; PBS pharmaceutical benefits scheme; RPBS repatriation pharmaceutical benefits scheme

- 4.6 The submission stated that while the anti-IL5 agents are part of a broader group of biologic agents for severe asthma (see Table 3), omalizumab and dupilumab are expected to have independent utilisation patterns. The Drug Utilisation Sub-Committee (DUSC) review of biologics for asthma in 2019 (DUSC, 2019) noted that the PBS listing of biologics for the treatment of uncontrolled severe asthma did not create any substantial changes in the use of omalizumab for SAA. The submission further noted that the PBAC consideration of Authority Required (Written) listings in 2021 (PBAC, July 2021 PBAC Meeting outcomes, 2021) separately considered omalizumab and mepolizumab/benralizumab utilisation.
- 4.7 The Secretariat noted that the preference for presenting the PBS/RPBS services is in calendar years, not financial years. This prevents distortions due to seasonality. The pre-PBAC response stated that the analyses for anti-IL-5 initiation PBS/RPBS services were presented according to 2016-2017, 2017-2018, 2018-2019, 2019-2020, 2020-2021, 2021-2022, 2022-23 financial years, incorporating the maximum available data at the time of submission. Given the financial year analyses represent 12 months of PBS/RPBS services for each period (e.g.: July 2022 to June 2023), seasonality is not a factor/distortion that influences the interpretation of the analysis presented in the submission.

Table 3: PBS listing dates for biologics for severe asthma

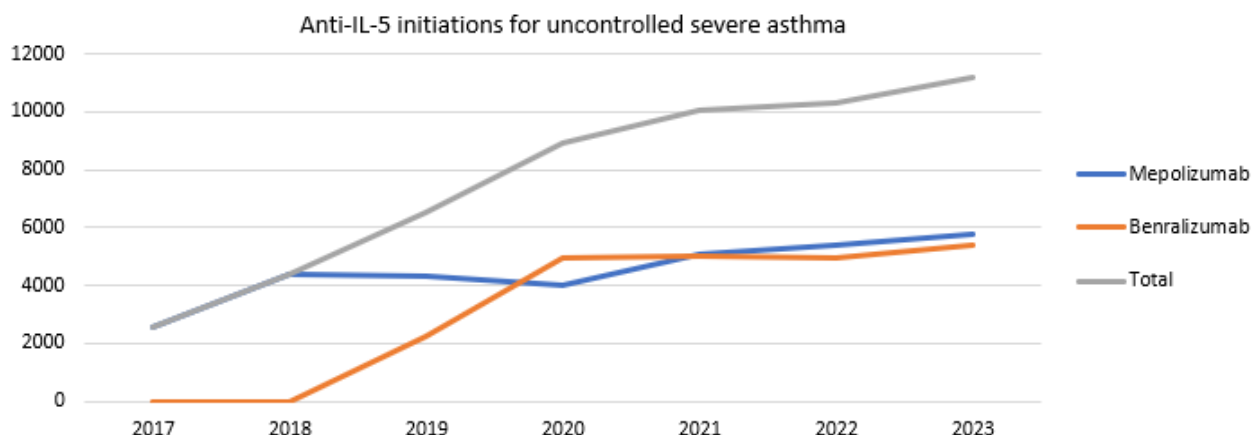
Biologic for severe asthma	Mechanism of action – target pathway	TGA indication*	PBS listing date
Omalizumab	Anti-IgE	Management of moderate to severe allergic asthma in adults and adolescents aged ≥ 12 years already using ICS	1 July 2011
Mepolizumab	Anti-IL5	Add-on treatment for severe eosinophilic asthma in adults and adolescents ≥ 12 years	1 January 2017
Benralizumab	Anti-IL5		1 December 2018
Dupilumab	Anti-IL4	Add-on treatment for moderate to severe asthma with type 2 inflammation (elevated eosinophils \ddagger or elevated FeNO) in adults and adolescents aged ≥ 12 years Maintenance therapy for oral corticosteroid-dependent asthma	1 April 2021

Source: Submission main body p4

*Indications approved by the Therapeutic Goods Administration; PBS restrictions also apply. \ddagger elevated FeNO not included in PBS criteria.

- 4.8 The sponsor stated that it had previously submitted a request to the PBAC to amend the authority level for mepolizumab for uncontrolled severe asthma as part of the sponsor response to the ‘June 2021 DUSC review of PBS Authority Required (Written) listings’. At its July 2021 PBAC meeting, the PBAC noted the sponsor’s suggestion of amending the restriction requirement. However, the PBAC did not recommend an amendment to the authority requirements for benralizumab and mepolizumab at that time, given the anti-IL5 market for SEA was relatively immature and not yet stable (Review of Authority Required (Written) PBS listings Tranche 3, July 2021 PBAC Meeting outcomes).
- 4.9 The submission argued that the PBAC recommended that the authority requirements for continuing treatment with omalizumab for SAA be amended from Authority Required (Written) to Authority Required (Telephone/Online) to ease administrative burden for prescribers and for consistency with the continuing authority requirements for omalizumab for CSU despite the growing number of incident patients and that the treated prevalent population had increased by 196% over the five-year period 2016-2020 (Review of Authority Required (Written) PBS listings Tranche 3, PBAC July 2021).
- 4.10 The PBAC noted there is no risk sharing arrangement (RSA) for omalizumab and commented on the modest special pricing arrangement (SPA), leading to growth in PBS expenditure (Review of Authority Required (Written) PBS listings Tranche 3, July 2021 PBAC Meeting outcomes). The PBAC agreed with DUSC advice and did not recommend an amendment to the authority requirements for initial treatment with omalizumab for SAA, noting the consistent increase in incident and prevalent patient numbers demonstrated the market was not yet stable (Review of Authority Required (Written) PBS listings Tranche 3, July 2021 PBAC Meeting outcomes).
- 4.11 In its pre-PBAC response, the sponsor maintained that the anti-IL-5 market is now sufficiently mature, and provided an additional 6-months of initiation services data from July to December 2023 indicating continued stabilisation of initiations for mepolizumab and benralizumab in uncontrolled severe asthma (Figure 1 and Table 4).

Figure 1: PBS/RPBS anti-IL-5 initiation services by calendar year from 2017 to 2023



Source: Pre-PBAC response - Medicare Statistics, 2024.

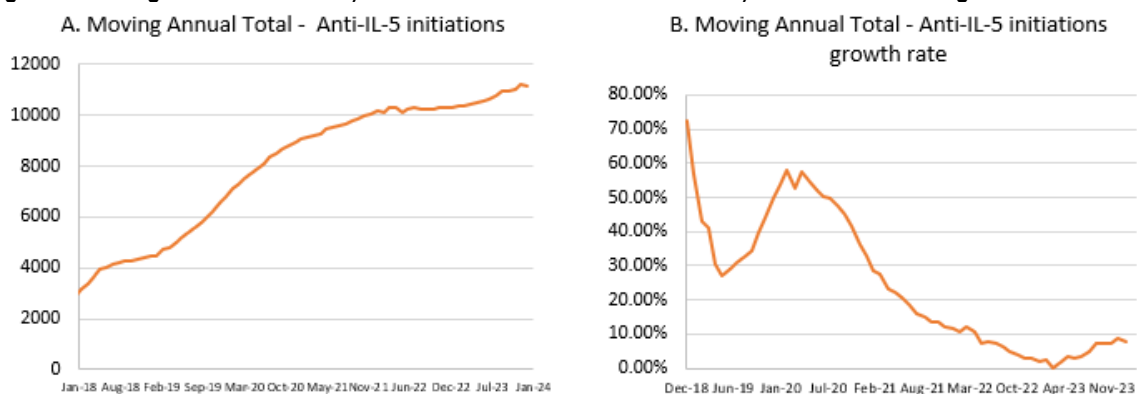
Table 4: Mepolizumab and Benralizumab initiation PBS/RPBS services by calendar year from 2017 to 2023

PBS/RPBS services	2017	2018	2019	2020	2021	2022	2023
Mepolizumab	2,534	4,365	4,340	3,983	5,047	5,367	5,798
Benralizumab	0	5	2,214	4,954	4,982	4,952	5,400
Total Anti-IL-5	2,534	4,370	6,554	8,937	10,029	10,319	11,198
Annual growth		72.5%	50.0%	36.4%	12.2%	2.9%	8.5%

Source: Pre-PBAC response - Medicare Statistics Data (Mepolizumab PBS Items: 10996R,11003D,12007Y,12051G; Benralizumab PBS items: 11523L,11549W,11994G,11997K).

4.12 The pre-PBAC response also provided a review of the 12-month moving annual total (MAT) analysis of the anti-IL5 initiations. The pre-PBAC response stated that the MAT analysis indicated a similar stabilisation trend. MAT growth of less than 10% has been observed since May 2022, with the average from January 2023 to December 2023 being 4.5% (Figure 2).

Figure 2: Moving Annual Total for a) PBS/RPBS anti-IL-5 initiations and b) anti-IL-5 initiations growth rate



Source: Pre-PBAC response - Medicare Statistics, 2024; PBS Data (Anti-IL-5_Initiation Services_MAT).xlsx

Mepolizumab prescribing environment and other biologics

4.13 The submission claimed that clinicians are now far more experienced with prescribing biologics for uncontrolled severe asthma and other conditions. The submission argued

that the following advancements in severe asthma management have ensured the appropriate identification of patients:

- A greater understanding of phenotyping and diagnosis of uncontrolled severe asthma, and evidence supporting biomarkers like eosinophils has grown to help with more targeted treatment of different asthma phenotypes.
 - A number of initiatives from both local Australian professional bodies were established to provide further guidance in the diagnosis and management of severe asthma, including the importance of phenotyping and role of biologics.
- 4.14 The submission stated that since the PBS listing of mepolizumab for uncontrolled severe asthma in January 2017, there have been many PBS listings for biologics in other therapy areas with less restrictive authority levels and changes to other established biologics' authority levels on the PBS.
- 4.15 The submission stated that, at its November 2022 meeting, the PBAC recommended a less restrictive authority level for continuing treatment (i.e., Authority Required (Telephone/Online)) for the listing of mepolizumab for CRSwNP (compared to the uncontrolled severe asthma listing) despite a number of uncertainties.
- 4.16 In its November 2022 consideration, the PBAC considered that due to the limitations of the treatment options currently available, the addition of mepolizumab offered high added therapeutic value. The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of mepolizumab would be acceptable at the price proposed in the pre-PBAC response, and with an RSA to address the uncertainty associated with including patients unsuitable for surgery in the proposed PBS population (para 7.2, mepolizumab PSD, November 2022 PBAC meeting).
- 4.17 The submission further noted that the authority requirements for the Tranche 6 biologic medicines for various PBS rheumatology and dermatology indications were made to be less restrictive (i.e. Authority Required (Written) or Authority Required (Telephone/Online) for initial treatment and Authority Required (STREAMLINED) for continuation treatment) as part of the recommendations from the Review of the PBS Authority Required (Written) listings: Tranche 6 (The Review) at the March 2022 PBAC meeting.
- 4.18 The submission stated that in making the recommendation, the PBAC noted that the market for rheumatoid arthritis (RA) was mature and moderately stable and the administrative burden for prescribers associated with the high volume of written authority applications and the objective initial and continuing treatment PBS restriction criteria for RA (Tranche 6 Review of Written Authority PBS listings, March 2022 PBAC Outcomes). The submission argued that both initial and continuing treatment for mepolizumab in uncontrolled severe asthma have similar issue where 'the administrative burden for prescribers associated with the high volume of written authority applications and the objective initial and continuing treatment PBS

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restriction criteria for RA’ (Tranche 6 Review of Written Authority PBS listings, March 2022 PBAC Outcomes). The amendment for all continuation listings indicated for RA to Authority Required (STREAMLINED) only applied to biosimilar items to support biosimilar uptake drivers. Originator brands remained Authority Required (Written) for first continuing treatment and were lowered to Authority Required (STREAMLINED) for subsequent continuing treatment.

- 4.19 The pre-PBAC response noted the support from the professional and consumer community for changes to the authority level to ensure timely patient access to treatment and to allow more time to be focussed on patient care.

Stabilisation of initiating population

- 4.20 The submission stated that since the Review of Authority Required (Written) PBS listings Tranche 3 July 2021, there is now evidence that initiations for mepolizumab and, more broadly, anti-IL5s, have stabilised, indicating maturity of this class for uncontrolled severe asthma.

- 4.21 Table 5 shows that the estimated total number of patients receiving an anti-IL5 biologic for severe asthma via the PBS was 6,480 in FY2022, based on a prospection report drawing from the 10% PBS sample (Prospection, 2023). Based on Table 2, the submission stated that the total PBS/RPBS services for anti-IL5 agents is still growing (13% in FY2023) and it is primarily driven by continuing prescriptions due to maintenance of response. Table 2 and Figure 3 highlight that PBS/RPBS services for initiation of anti-IL5’s has stabilised with only 8% growth in FY2022 and 3% growth in FY2023 (Illuminate Red, 2023).

Table 5: Patients treated with mepolizumab– estimated vs actual patients treated since PBS listing

Financial Year	2017-2018	2018-2019	2019-2020	2020-2021	2021-2022	2022-2023
Analysis of mepolizumab patient numbers from 2019 DUSC PRD (from 100% PBS sample)	604	1,177				
Patients on treatment (mepolizumab) -Prospection report for GSK (from 10% PBS sample)	■ ¹	■ ²	■ ²	■ ²	■ ²	■ ²
Patients on anti-IL5 treatment (for uncontrolled severe asthma) -Prospection report for GSK (from 10% PBS sample)	■ ¹	■ ²	■ ²	■ ²	■ ³	■ ³

Source: Submission main body p5 (Prospection, 2023)

Abbreviations: DUSC drug utilisation sub-committee; GSK glaxosmithkline; PRD prospection report drawing; PBS pharmaceutical benefits scheme; RPBS repatriation pharmaceutical benefits scheme

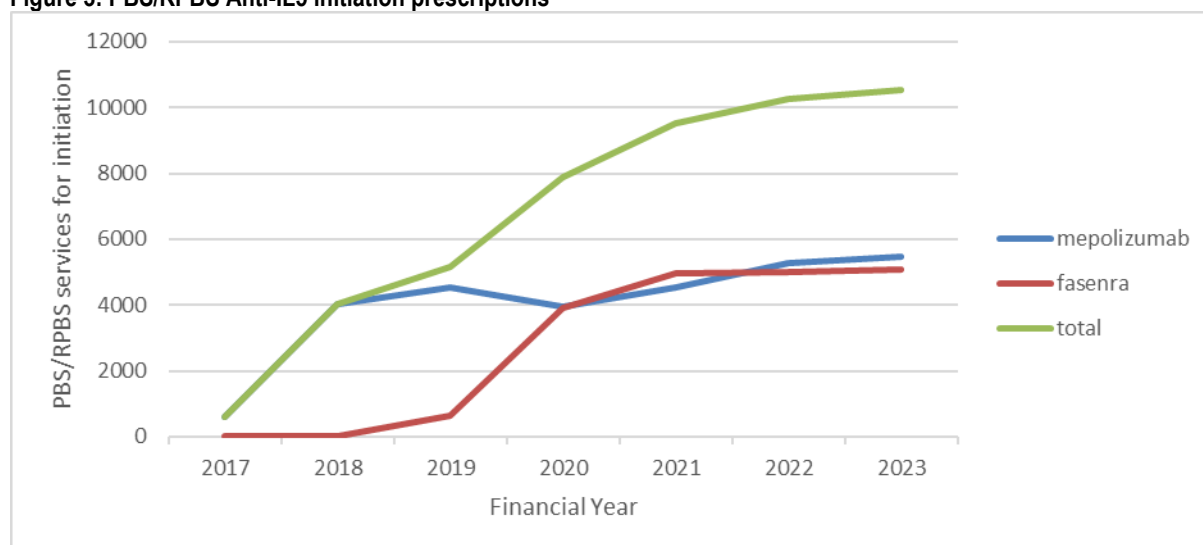
The redacted values correspond to the following ranges

¹<500

² 500 to < 5,000

³ 5,000 to <10,000

Figure 3: PBS/RPBS Anti-IL5 initiation prescriptions



Source: Submission main body p6

4.22 The submission claimed that the growth of anti-IL5 market is consistent and that patient numbers remain below the estimated number of uncontrolled severe asthma patients that may potentially benefit from mepolizumab treatment. The submission argued that, given the eligibility criteria for initiation and continuation in the proposed restriction would remain the same, there is no indication that inappropriate prescribing of mepolizumab would eventuate.

Moderate growth in continuing population

4.23 The submission stated that the moderate growth of mepolizumab in the continuing treatment phase is supported by long-term durability of response in clinical trials. The submission claimed that sustained efficacy of mepolizumab on asthma exacerbation rate, asthma control, lung function, OCS use and blood eosinophil count were evident from the Phase 3 placebo-controlled MENSA, SIRIUS and DREAM studies on patients treated with uncontrolled severe asthma.

4.24 The submission stated that the continuing prescriptions for the anti-IL5 agents showed a moderate growth of 16% in the FY2023 (as per Table 2). The submission claimed that the moderate growth of the continuation prescriptions (26% to 16% for anti-IL5's for uncontrolled severe asthma from FY 2022-2023), is not a function of 'inappropriate use' but of how utilisation has evolved based on clinical experience and long-term studies.

4.25 The submission noted that the PBS continuation response criteria remain relevant but claimed the current Authority Required (Written) is overly burdensome for clinicians and should be amended to Authority Required (STREAMLINED).

4.26 As a category 3 submission, no evaluation of the clinical evidence was undertaken.

Clinical criteria amendment

- 4.27 The submission requested to remove the following OCS clinical criteria within the ‘optimised asthma therapy’ definition for the current initiation therapy of mepolizumab. The submission stated that this criterion may have unintended consequences in encouraging over-utilisation of OCS in patients before qualifying to access mepolizumab on the PBS, contrary to current treatment guidelines.
- (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.
- 4.28 The submission stated that the current Global Initiative for Asthma (GINA) guidelines provide a decision tree regarding the assessment and management of difficult-to-treat asthma in adult and adolescent patients (GINA, 2023). Following the guidelines, patients are not required to be taking OCS currently or in the previous 12 months for determination of a Type 2 airway inflammation to be conducted, and if blood eosinophils ≥ 150 , then a biologic can be added on if the inhaled corticosteroid dose has already been optimised for 3-6 months.
- 4.29 The submission noted that the GINA guidelines for usage of OCS to treat severe exacerbations in adults and adolescents is prednisolone 40-50 mg/day, usually for 5-7 days (tapering is not needed if OCS are prescribed for < 2 weeks) (GINA, 2023). The Australian Asthma Handbook recommendation for treating acute asthma with OCS in adults is a starting dose of prednisolone 37.5–50 mg, then repeat each morning on second and subsequent days (total 5–10 days). It is usually not necessary to taper the dose unless the duration of treatment exceeds 2 weeks (National Asthma Council, 2023).
- 4.30 This submission stated that the current OCS requirement is an unnecessarily high amount of systemic corticosteroid exposure, noting the GINA and Australian Asthma Handbook guidelines. The submission stated that repeated treatment with systemic steroids is associated with increased risk of adverse events including loss of bone density, hypertension, gastrointestinal ulcers/bleeds, and cataracts in addition to serious impacts on mental health (Price, 2020; TSANZ, 2021). The total lifetime exposure of 500-1000 mg of oral prednisolone equivalents are associated with a significantly increased risk of type 2 diabetes mellitus and depression/anxiety (Price, 2018).
- 4.31 The submission also noted that concerns were raised over the high threshold of OCS requirement in the Severe Asthma Stakeholder Meeting in December 2018. Stakeholders highlighted the importance of i) reducing exacerbations and OCS use in the severe asthma population, ii) having a suitable method to assess patients’ response and/or symptom control, iii) re-examining certain aspects of the PBS restriction for biologic medicines to ensure that those most at risk are not excluded.

The PBAC stated the outcomes of the meeting would be used to inform future PBAC considerations on this issue (Severe Asthma Stakeholder Meeting Outcomes, 2018).

- 4.32 The pre-PBAC response reiterated that removal of this OCS criteria ensures alignment with current treatment guidelines and should not broaden patient eligibility, as prior use of systemic corticosteroids (including OCS) for the management of severe exacerbation(s) in the last 12 months remains a criterion defining ‘failure to achieve adequate control’ for initiation of mepolizumab treatment.

Estimated PBS usage and financial implications

- 4.33 The submission stated that the requested amendment to the authority level is not expected to broaden patient eligibility criteria or increase patient uptake, and therefore unlikely to increase the PBS utilisation of mepolizumab.
- 4.34 The submission also stated that the requested amendment to the initiating clinical criteria is not expected to increase eligible patient numbers for mepolizumab as most patients are likely to still receive OCS to manage acute exacerbations prior to treatment initiation, as recommended by guidelines.
- 4.35 The submission did not provide an economic model or financial estimates to support their claim. The Department of Health and Aged Care (the Department) have estimated the extent of use, cost of amending the authority level of mepolizumab for the treatment of uncontrolled severe asthma and the net financial implications to the PBS/RPBS in Table 6.
- 4.36 The number of scripts was estimated using historic dispensing data of mepolizumab and the assumption that a proportion of the rejected authority requests would be reasonably included in the eligible population due to the change to the authority level. The proportion of rejected authority requests was estimated to be 7.57% for initial treatment applications and 3.60% for continuing treatment applications.

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Table 6: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of scripts	1	1	2	2	2	2
Estimated PBS financial implications of the proposed amendment						
Cost to PBS	3	4	4	5	5	5
Patient copayments	6	6	6	6	6	6
Total cost to PBS	3	4	4	5	5	5
Changed listing	6	6	6	6	6	6
Estimated RPBS financial implications of the proposed amendment						
Cost to RPBS	7	7	7	7	7	7
Patient copayments	6	6	6	6	6	6
Total cost to RPBS	7	7	7	7	7	7
Changed listing	6	6	6	6	6	6
Net financial implications						
Total cost to PBS/RPBS	3	4	4	5	5	5
Net cost to PBS	7	7	7	7	7	7
Net cost to RPBS	7	7	7	7	7	7
Net cost to PBS/RPBS	7	7	7	7	7	7

Source: Department utilisation and financial estimates

Abbreviations: PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme.

The redacted values correspond to the following ranges

¹ 20,000 to < 30,000

² 30,000 to < 40,000

³ \$30 million to < \$40 million

⁴ \$40 million to < \$50 million

⁵ \$50 million to < \$60 million

⁶ net cost saving

⁷ \$0 to < \$10 million

- 4.37 The Department estimated that 100,000 to < 200,000 mepolizumab scripts would be supplied to patients over the first six years of amending the listing (20,000 to < 30,000 in Year 1 to 30,000 to < 40,000 in Year 6).
- 4.38 The Department estimated that the cost of amending the listing of mepolizumab to the PBS/RPBS is expected to be \$200 million to < \$300 million over six years (Year 1 \$30 million to < \$40 million to Year 6 \$50 million to < \$60 million) and the net financial impact to the PBS/RPBS to be \$10 million to < \$20 million over six years (Year 1 \$0 to < \$10 million to Year 6 \$0 to < \$10 million).
- 4.39 In its pre-PBAC response, the sponsor stated that the assumption underpinning the financial analyses conducted by the Department (all rejections under the written authority level settings would otherwise be approved under the amended authority level) is unlikely to represent a plausible circumstance. The pre-PBAC response considered that any change in expenditure to PBS is likely to be negligible.
- 4.40 The pre-PBAC response cited a 2010 report conducted by the Department of Health and Ageing, noting the three main reasons for authority application rejections as follows:
- *The patient does not meet the criteria of the restriction, therefore is not eligible for the particular PBS subsidised medicine.* The pre-PBAC response stated that such

rejections would also apply under a telephone/online setting as the clinical criteria dictating patient eligibility remains the same.

- *Another authority prescription for the same item has previously been approved and adequate supplies should still exist for the patient.* The pre-PBAC response stated that rejections related to incorrect timing of application would similarly apply under a telephone/online setting.
- *Prescriber decides during the phone call not to proceed with the authority request.* The pre-PBAC response stated that this situation is not applicable for the Authority Required (Written) restriction for mepolizumab in uncontrolled severe asthma.

- 4.41 The pre-PBAC response further noted input from a Respiratory Clinical Nurse Consultant (RCNC) that stated authority application rejections are primarily related to typographical errors or dates that are incorrectly included in the application, and that most applications are subsequently approved when these errors are corrected. The RCNC also noted that there is a robust assessment in place to ensure patients meet the clinical criteria for biologic treatment, such as mepolizumab and clinicians do not routinely submit for continuation if patients' treatment with mepolizumab are failing.

5 PBAC Outcome

Amendment to authority levels

- 5.1 The PBAC did not recommend amendments to the authority level for mepolizumab for the treatment of uncontrolled severe asthma. The PBAC considered that while the available data suggested that the growth of mepolizumab is gradually stabilising, the overall uncontrolled severe asthma market continues to grow. The PBAC therefore considered that it would not be appropriate to amend the circumstances of mepolizumab in isolation, noting the continued growth of the overall anti-IL5 market for uncontrolled severe asthma.
- 5.2 The PBAC noted that the submission claimed that the annual initiations for the anti-IL5 biologic agents (i.e., mepolizumab and benralizumab) for the treatment of uncontrolled severe asthma have stabilised. The PBAC noted that the pre-PBAC response provided an additional 6-months of initiation services data from July to December 2023, indicating that the annual growth for anti-IL5 initiation prescriptions for Year 2022 and Year 2023 was 2.9% and 8.5%, respectively. The PBAC considered that the available data was insufficient to provide a reliable estimate of the maturity of the anti-IL5 market and considered that the anti-IL5 market was not stable yet.
- 5.3 The PBAC noted the submission's claim that continuing prescriptions for anti-IL5 agents showed moderate growth of 16% in the FY 2023. The PBAC also noted the submission's claim that clinicians are now more experienced with prescribing biologics for uncontrolled severe asthma and other conditions and are familiar with identifying patients appropriate for initiating treatment and ensuring treatment is only continued in patients demonstrating benefit. The PBAC acknowledged the input from health

professionals and organisations in support of the authority level amendment to ease administrative burden.

- 5.4 The PBAC recalled that at its July 2021 meeting, it recommended that the authority requirements for continuing treatment with omalizumab for SAA be amended from Authority Required (Written) to Authority Required (Telephone/Online). The PBAC noted that this amendment has not yet been implemented (Review of Authority Required (Written) PBS listings Tranche 3, July 2021 PBAC Outcomes). The PBAC recalled that it did not recommend an amendment to the authority requirements for initial treatment with omalizumab for SAA, as the consistent increase in incident and prevalent patient numbers demonstrated the market was not yet stable. The PBAC noted that the DUSC could reassess the market utilisation and restriction levels once the listings are mature.
- 5.5 The PBAC noted that the Department had estimated a potential cost to Government of \$10 million to < \$20 million over six years, based on the assumption that a proportion of rejected authority requests would be included in the eligible population due to the change to the authority level of mepolizumab. The PBAC noted the pre-PBAC response stating the common reasons for authority application rejections and considered that the cost to Government may be less than what was estimated by the Department.

Outcome:

Not recommended

Amendment to clinical criteria

- 5.6 The PBAC recommended amending the clinical criteria of mepolizumab for the treatment of uncontrolled severe asthma to remove the OCS requirement within the definition of 'optimised asthma therapy' to align with current treatment guidelines.
- 5.7 The PBAC noted the GINA and Australian Asthma Handbook guidelines and the input from health professionals supporting the removal of the OCS criterion, stating that the current OCS requirement results in an unnecessarily high amount of systemic corticosteroid exposure which does not align with the current treatment guidelines, and that moderate use of corticosteroids over a lifetime can place an individual at risk of significant morbidities. The PBAC also noted input from several health organisations in support of the removal of the current OCS criterion, which stated that the current requirement promotes excessive OCS prescribing and exposure, and that arbitrary OCS requirements to commence treatment do not improve patient outcomes and may incentivise unnecessary treatment of OCS to enable access to mepolizumab.
- 5.8 The PBAC recalled and noted the concerns raised about the high threshold of OCS requirement in the Severe Asthma Stakeholder Meeting (Severe Asthma Stakeholder Meeting Outcome Statement 12-2018).
- 5.9 The PBAC noted the pre-PBAC response reiterated that removal of the OCS criteria ensures alignment with current treatment guidelines and should not broaden patient

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eligibility. The PBAC agreed with the pre-PBAC response and considered the removal of the OCS requirement would not increase the eligible population and therefore considered there to be nil financial impact to the Government.

- 5.10 The PBAC recommended flow-on changes of this amendment to the other PBS-listed biologics for uncontrolled severe asthma.
- 5.11 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met. Specifically, the PBAC found that in the circumstances of its recommendation for the amendment to the clinical criteria for mepolizumab for uncontrolled severe asthma, the removal of OCS requirements is not expected to address a high and urgent unmet clinical need.

Outcome:

Recommended

- 5.12 The PBAC noted that this recommendation is not eligible for an Independent Review as it was not seeking a change to the listing that includes a new indication, objectively subtype of disease or new population, and it received a positive recommendation for the amendment to OCS clinical criteria.

6 Recommended listing

6.1 Amend existing listing as follows:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
MEPOLIZUMAB					
mepolizumab 100 mg injection, 1 vial	10996R 11003D	1	1	7	Nucala
mepolizumab 100 mg/mL injection, 1 mL pen device	12007Y 12051G				
Restriction Summary 11843 / Treatment of Concept: 11848					
Concept ID	Category / Program: Section 100 – Highly Specialised Drugs Program				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required (in writing) – Postal/HPOS upload				
Prescribing rule level	Administrative Advice:				
	<p>TREATMENT OF ADULT AND ADOLESCENT PATIENTS WITH UNCONTROLLED SEVERE ASTHMA</p> <p>The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of the biological medicines benralizumab, dupilumab, mepolizumab and omalizumab for uncontrolled severe asthma. Therefore, where the term 'biological medicine' appears in notes and restrictions, it refers to benralizumab, dupilumab, mepolizumab and omalizumab only.</p> <p>A patient is eligible for PBS-subsidised treatment with only 1 of the above biological medicines at any 1 time.</p> <p>A patient receiving PBS-subsidised treatment for uncontrolled severe asthma is able to commence a treatment cycle where they may trial a biological medicine without having to experience a disease flare when swapping to an alternate biological medicine within the same treatment cycle.</p>				

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	<p>Under these arrangements, within a treatment cycle, a patient may receive long-term treatment with a biological medicine as long as they sustain a response to therapy. A patient currently receiving PBS-subsidised treatment as of 1 April 2021 is considered to have started a cycle of treatment. Within the same treatment cycle, a patient cannot trial and fail, or cease to respond to, the same PBS-subsidised biological medicine more than once. Therefore, once a patient fails to meet the response criteria for a PBS-subsidised biological medicine, they must change to an alternate biological medicine if they wish to continue PBS-subsidised biological treatment. Once a patient has either failed to achieve or sustain a response to treatment 4 times, they are deemed to have completed a single treatment cycle. They must have at least a 12-month break in PBS-subsidised biological medicine therapy before they are eligible to recommence another new treatment cycle [further details are under 'Recommencement of treatment after a treatment break in PBS-subsidised therapy' below]. The length of the break in therapy is measured from the date the most recent treatment with a PBS-subsidised biological medicine is ceased until the date of the first application for recommencement of treatment with a biological medicine under the new treatment cycle. There is no limit to the number of treatment cycles that a patient may undertake in their lifetime. How to prescribe PBS-subsidised biological medicine treatment for uncontrolled severe asthma.</p> <p>(1) Initial treatment: Applications for initial treatment should be made where:</p> <ul style="list-style-type: none">(i) a patient has not received prior PBS-subsidised biological medicine treatment and wishes to commence such therapy (Initial 1 restriction); or(ii) a patient has received prior PBS-subsidised treatment with a biological medicine and wishes to recommence a new treatment cycle with this biological medicine following a treatment break in PBS-subsidised therapy (Initial 1 restriction); or(iii) a patient has received prior PBS-subsidised biological medicine therapy and wishes to trial an alternate biological medicine within the same treatment cycle (Initial 2 restriction) - [further details are under 'Swapping therapy' below]. <p>All applications for initial treatment will be limited to provide for a maximum of up to 32 weeks of therapy of a biological medicine. It is recommended that a patient be reviewed in the month prior to completing their course of initial treatment to ensure uninterrupted biological medicine supply.</p> <p>(2) Continuing treatment: Following the completion of an initial treatment course with a specific biological medicine, a patient may qualify to receive up to 24 weeks of continuing treatment with that biological medicine providing they have demonstrated an adequate response to treatment. The patient remains eligible to receive continuing biological medicine treatment with the same drug in courses of up to 24 weeks providing they continue to sustain the response. It is recommended that a patient be reviewed the month prior to completing their current course of treatment to ensure uninterrupted biological medicine supply.</p> <p>(3) Baseline measurements to determine response: Baseline measurements of the Asthma Control Questionnaire (ACQ; 5 item version) or oral corticosteroid dose submitted with the Initial authority application for a biological medicine must be used to determine whether an adequate response to treatment has been achieved or sustained. For patients transitioned from the paediatric to the 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 these new baseline measurements may be used to assess response.</p> <p>(4) Swapping therapy within the same treatment cycle. Once initial treatment with the first PBS-subsidised biological medicine is approved, a patient may swap to an alternate biological medicine at any time by qualifying under an Initial 2 restriction. However, they cannot swap to a particular biological medicine if they have failed to respond to prior treatment with that drug within the same treatment cycle. Within the same treatment cycle a patient may alternate between therapy with any biological medicine of their choice (1 at a time) providing:</p>
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	<p>(i) they have not received PBS-subsidised treatment with that particular biological medicine previously; or</p> <p>(ii) they have demonstrated an adequate response to that particular biological medicine if they have previously trialled it on the PBS; and</p> <p>(iii) they have not previously failed to respond to treatment with all 4 biological medicines in this treatment cycle.</p> <p>(5) Re-commencement of a new treatment cycle after a treatment break in PBS-subsidised therapy: A patient who wishes to trial a second or subsequent new treatment cycle, following a break in PBS-subsidised therapy of at least 12 months (in patients who have failed to achieve or ceased to sustain a response to treatment 4 times within a treatment cycle), must re-qualify through an Initial 1 restriction.</p> <p>(6) Monitoring of patients: Omalizumab only: 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>Administrative Advice: For copies of the ACQ, please contact GlaxoSmithKline Medical Information on 1800 033 109.</p>
	<p>Administrative Advice: Special Pricing Arrangements apply.</p>
	<p>Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia 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 Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>
	<p>Indication: Uncontrolled severe asthma</p>
	<p>Treatment Phase: Initial treatment – Initial 1 (New patients; or Recommencement of treatment in a new treatment cycle following a break in PBS subsidised biological medicine therapy)</p>
	<p>Treatment criteria:</p>
	<p>Must be treated by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma</p>
	<p>Clinical criteria:</p>
	<p>Patient must be under the care of the same physician for at least 6 months; or</p>
	<p>Patient must have been diagnosed by a multidisciplinary severe asthma clinic team</p>
	<p>AND</p>
	<p>Clinical criteria:</p>
	<p>Patient must not have received PBS-subsidised treatment with a biological medicine for severe asthma; or</p>
	<p>Patient must have had a break in treatment from the most recently approved PBS-subsidised biological medicine for severe asthma</p>
	<p>AND</p>
	<p>Clinical criteria:</p>

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	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; or
	Patient must have a diagnosis of asthma from at least two physicians experienced in the management of patients with severe asthma
	AND
	Clinical criteria:
	Patient must have a duration of asthma of at least 1 year
	AND
	Clinical criteria:
	Patient must have blood eosinophil count greater than or equal to 300 cells per microlitre in the past 12 months; or
	Patient must blood eosinophil count greater than or equal to 150 cells per microlitre while receiving treatment with oral corticosteroids in the last 12 months
	AND
	Clinical criteria:
	Patient must have failed to achieve adequate control with optimised asthma therapy, despite formal assessment of an adherence to correct inhaler technique, which has been documented
	AND
	Clinical criteria:
	Patient must not receive more than 32 weeks of treatment under this restriction
	AND
	Clinical criteria:
	The treatment must not be used in combination with and within 4 weeks of another PBS-subsidised biological medicine prescribed for severe asthma
	Population criteria:
	Patient must be aged 12 years or older
	Prescribing Instructions: 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.
	Prescribing Instructions: The following initiation criteria indicate failure to achieve adequate control and must be demonstrated in all patients at the time of 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

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	<p>of systemic corticosteroids (oral corticosteroids initiated or increased for at least 3 day, 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, should be made at around 28 weeks after the first PBS-subsidised dose of this drug under this restriction so that there is adequate time for a response to be demonstrated and for the application for the first continuing therapy to be processed.</p> <p>This assessment, which will be used to determine eligibility for the first continuing treatment, should be conducted within 4 weeks of the date of assessment. To avoid an interruption of supply for the first continuing treatment, the assessment should be submitted no later than 2 weeks prior to the patient completing their current treatment course, unless the patient is currently on a treatment break. Where a response assessment is not undertaken and submitted, the patient will be deemed to have failed to respond to treatment with this drug.</p> <p>If a patient fails to demonstrate a response to treatment with this drug they will not be eligible to receive further PBS-subsidised treatment with this drug for this condition within the same treatment cycle.</p> <p>A treatment break in PBS-subsidised biological medicine therapy of at least 12 months must be observed in a patient who has either failed to achieve or sustain a response to treatment with 4 biological medicines within the same treatment cycle.</p> <p>The length of the break in therapy is measured from the date the most recent treatment with a PBS-subsidised biological medicine was administered until the date of the first application for commencement of treatment with a biological medicine under the new treatment cycle.</p> <p>There is no limit to the number of treatment cycles that a patient may undertake in their lifetime.</p> <p>At the time of the authority application, medical practitioners should request up to 7 repeats to provide for an initial course of mepolizumab sufficient for up to 32 weeks of therapy.</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>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 <i>authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice)</i>, which includes: Severe Asthma Initial PBS Authority Application – Supporting Information Form, 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 eosinophil count and date; and</p> <p>(iv) Asthma Control Questionnaire (ACQ-5) score.</p>
	<p>Administrative Advice:</p> <p>The Services Australia website (www.servicesaustralia.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>Administrative Advice:</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.servicesaustralia.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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Restriction Summary 11896/ Treatment of Concept: 11950	
Concept ID	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required (in writing only via post/HPOS upload)
	Indication: Uncontrolled severe asthma
	Treatment Phase: Initial treatment – Initial 2 (Change of treatment)
	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 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
	Clinical criteria:
	Patient must have received prior PBS-subsidised treatment with a biological medicine for severe asthma in this treatment cycle
	AND
	Clinical criteria:
	Patient must not have failed, or ceased to respond to, PBS-subsidised treatment with this drug for severe asthma during the current treatment cycle
	AND
	Clinical criteria:
	Patient must have had a blood eosinophil count greater than or equal to 300 cells per microlitre and that is no older than 12 months immediately prior to commencing PBS-subsidised biological medicine treatment for severe asthma; or
	Patient must have had a blood eosinophil count greater than or equal to 150 cells per microlitre while receiving treatment with oral corticosteroids and that is no older than 12 months immediately prior to commencing PBS-subsidised biological medicine treatment for severe asthma
	AND
	Clinical criteria:
	Patient must not receive more than 32 weeks of treatment under this restriction
	AND
	Clinical criteria:
	The treatment must not be used in combination with and within 4 weeks of another PBS-subsidised biological medicine prescribed for severe asthma
	Population criteria:
	Patient must be aged 12 years or older

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	<p>Prescribing Instructions:</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 <i>authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice), which includes: Severe Asthma (mepolizumab/benralizumab) Initial PBS Authority Application – Supporting Information Form, which includes the following:</i></p> <p>(i) Asthma Control Questionnaire (ACQ-5 item version) score (where a new baseline is being submitted or where the patient has responded to prior treatment); and</p> <p>(ii) the details of prior biological medicine treatment including the details of date and duration of treatment; and</p> <p>(iii) eosinophil count and date; and</p> <p>(iv) the dose of the maintenance oral corticosteroid (where the response criteria or baseline is based on corticosteroid dose); and</p> <p>(v) the reason for switching therapy (e.g. failure of prior therapy, partial response to prior therapy, adverse event to prior therapy).</p> <p>An application for a patient who has received PBS-subsidised biological medicine treatment for severe asthma who wishes to change therapy to this biological medicine, must be accompanied by the results of an ACQ-5 assessment of the patient's most recent course of PBS-subsidised biological medicine treatment. The assessment must have been made not more than 4 weeks after the last dose of biological medicine. Where a response assessment was not undertaken, the patient will be deemed to have failed to respond to treatment with that previous biological medicine.</p> <p>An ACQ-5 assessment of the patient may be made at the time of application for treatment (to establish a new baseline score) but should be made again around 28 weeks after the first PBS-subsidised dose of this biological medicine under this restriction so that there is adequate time for a response to be demonstrated and for the application for the first continuing therapy to be processed.</p> <p>This assessment, which will be used to determine eligibility for the first continuing treatment, should be conducted within 4 weeks of the <i>last dose of biological medicine</i> date of assessment. To avoid an interruption of supply for the first continuing treatment, the assessment should be submitted no later than 2 weeks prior to the patient completing their current treatment course, unless the patient is currently on a treatment break. Where a response assessment is not undertaken and submitted, the patient will be deemed to have failed to respond to treatment with this drug.</p> <p>At the time of the authority application, medical practitioners should request up to 7 repeats to provide for an initial course sufficient for up to 32 weeks of therapy.</p> <p>A multidisciplinary severe asthma clinic team comprises of:</p> <ul style="list-style-type: none"> • A respiratory physician; and <p>A pharmacist, nurse or asthma educator.</p>
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6.2 Flow-on changes to the optimised asthma therapy definition as shown above to the following item codes:

MEDICINAL PRODUCT medicinal product pack	PBS item code
OMALIZUMAB	
omalizumab 75 mg/0.5 mL injection, 0.5 mL syringe	10118M
	10110D
omalizumab 150 mg/mL injection, 1 mL syringe	10109C
	10122R
BENRALIZUMAB	
benralizumab 30 mg/mL injection, 1 mL pen device	11997K

	11994G
DUPILUMAB	
dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes	12309W
	12313C

These restrictions may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

7 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.

8 Sponsor's Comment

GSK welcomes the PBAC's recommendation to remove the oral corticosteroid requirement within the definition of 'optimised asthma therapy' from the clinical criteria of mepolizumab for the treatment of uncontrolled severe asthma to align with current treatment guidelines.

GSK notes the PBAC's decision not to recommend changes to the authority level for prescribing. With healthcare professionals and patient organisations highlighting the benefits of such changes through efficient access and increased opportunity for patient care, GSK would appreciate that this matter is addressed by the DUSC and PBAC in a timely manner.