# 5.15 TEZEPELUMAB, Solution for injection 210 mg in 1.91 mL single dose pre-filled pen (110 mg per mL), Tezspire®, ASTRAZENECA PTY LTD.

## 1 Purpose of submission

1.1 The Category 1 submission requested Section 100 (Highly Specialised Drugs [HSD] Program), Authority Required (Written), listing for tezepelumab for the treatment of patients aged 12 years and older with severe uncontrolled asthma (SUA) that are 1) non-eosinophilic and non-allergic, 2) eosinophilic or allergic.

1.2 Listing for the severe uncontrolled non-eosinophilic and non-allergic asthma population was requested on the basis of a cost-effectiveness analysis versus standard of care (SoC). Listing for the severe uncontrolled eosinophilic or allergic asthma population was requested on the basis of a cost-minimisation approach versus dupilumab.

1.3 The key components of the clinical issue addressed by the submission are summarised in Table 1.

**Table 1: Key components of the clinical issue addressed by the submission (as stated in the submission)**

| Component | EOSic or allergic SUA | Non-EOSic and non-allergic SUA |
|---|---|---|
| Population | Patients aged ≥12 years with severe uncontrolled eosinophilic or allergic asthma for 1 year. | Patients aged ≥12 years with severe uncontrolled asthma that is not eosinophilic or allergic for 1 year. |
| Intervention | Tezepelumab 210 mg SC injection Q4W | Tezepelumab 210 mg SC injection Q4W |
| Comparator | Primary: dupilumab<br>Secondary: benralizumab, mepolizumab, omalizumab | Standard of care (SoC) |
| Outcomes | AAER, any AEs, serious AEs, withdrawals due to AEs, deaths | AAER, change in daily OCS, FEV1, change in ACQ-6 score, change in AQLQ(S)+12 total score; change in SGRQ total score; change in HRQoL any AEs, serious AEs, withdrawals due to AEs, deaths |
| Clinical claim | Non-inferior effectiveness<br>Non-inferior safety | Superior effectiveness<br>Non-inferior safety |

Source: Table 1-2, p9 of the submission.

AAER = annualised asthma exacerbation rate; ACQ-6 = 6 question Asthma Control Questionnaire; AE = adverse event; AQLQ(S)+12 = Standardised Asthma Quality of Life Questionnaire for patients 12 years and older; EOSic = eosinophilic; FEV1 = forced expiratory volume; HRQoL=health related quality of life; OCS = oral corticosteroids; Q4W = every 4 weeks; SC = subcutaneous; SGRQ = St. George's Respiratory Questionnaire; SUA = severe uncontrolled asthma

# 2 Background

## *Registration status*

2.1 Tezepelumab was TGA registered on 24 March 2025 as an 'add-on maintenance treatment in patients aged 12 years and older with severe asthma who are inadequately controlled despite optimal therapy including medium or high-dose inhaled corticosteroids plus another non-steroidal medicinal product for maintenance treatment'.

## *Previous PBAC consideration*

2.2 A Category 1 submission for the consideration of a PBAC listing of tezepelumab for the treatment of severe uncontrolled eosinophilic or allergic asthma population was submitted in July 2022. The July 2022 submission was considered by ESC and DUSC but was withdrawn prior to the PBAC meeting. The submission stated the decision to withdraw was made to allow tezepelumab to proceed completely through the TGA registration process rather than continue through a TGA/PBAC parallel process. The July 2022 submission did not request a listing for the severe uncontrolled non-eosinophilic and non-allergic asthma population.

# 3 Requested listing

3.1 The submission proposed separate restrictions for the severe uncontrolled non-eosinophilic and non-allergic asthma population and the severe uncontrolled eosinophilic or allergic asthma population. An abridged version of the restrictions is presented below. The submission noted that it would also be supportive of a single restriction across both proposed populations.

**Non-eosinophilic and non-allergic SUA**

| MEDICINAL PRODUCT medicinal product pack | Dispensed Price for Max. Qty | Max. qty packs | Max. qty units | №.of Rpts | Available brands |
|---|---|---|---|---|---|
| TEZEPELUMAB | | | | | |
| Tezepelumab, 210 mg in 1.91 mL (110 mg/mL) in a prefilled pen | Published<br>$1,671.78 Public<br>$1,720.45 Private<br>Effective<br>$[redacted] Public[a]<br>$[redacted] Private | 1 | 1 | 7 | Tezspire |
| **Category / Program:** General Schedule/Section 100 | | | | | |
| **Prescriber type:** ☒ Medical Practitioners | | | | | |
| **Restriction type:** ☒Authority Required (in writing only via post/HPOS upload) | | | | | |
| **Episodicity:** Active | | | | | |
| **Severity:** Uncontrolled Severe | | | | | |
| **Condition:** Uncontrolled severe asthma | | | | | |

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| **Indication:** Uncontrolled severe asthma |
| **Treatment Phase:** Initial treatment – New patients |
| **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** |
| Patient must not have received PBS-subsidised treatment with a biological medicine for severe asthma; or |
| Patient must have had a break in treatment from a PBS-subsidised biological medicine for severe asthma. |
| **AND** |
| Patient must have a diagnosis of asthma confirmed and documented by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma, defined by the following standard clinical features: (i) forced expiratory volume ($FEV_1$) 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 $FEV_1$ 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** |
| Patient must have a duration of asthma of at least 1 year. |
| **AND** |
| Patient must have blood eosinophil count less than 300 cells per microlitre in the last 12 months while not receiving treatment with oral corticosteroids, or |
| Patient must have blood eosinophil count less than 150 cells per microlitre while receiving treatment with oral corticosteroids in the last 12 months |
| **AND** |
| Patient must have total serum human immunoglobulin E less than 30 IU/mL, measured in the last 12 months and no past or current evidence of atopy, documented by either: (i) skin prick testing; (ii) an in vitro measure of specific IgE |
| **AND** |
| Patient must have failed to achieve adequate control with optimised asthma therapy, despite formal assessment of and adherence to correct inhaler technique, which has been documented. |
| **AND** |
| Patient must not receive more than 32 weeks of treatment under this restriction. |
| **Treatment criteria:** |
| Must be treated by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma. |
| **Population criteria:** |
| Patients must be aged 12 years or older. |

| MEDICINAL PRODUCT medicinal product pack | Dispensed Price for Max. Qty | Max. qty packs | Max. qty units | №.of Rpts | Available brands |
|---|---|---|---|---|---|
| TEZEPELUMAB | | | | | |
| Tezepelumab, 210 mg in 1.91 mL (110 mg/mL) in a prefilled pen | Published<br>$1,671.78 Public<br>$1,720.45 Private<br>Effective<br>$[redacted][a] Public<br>$[redacted] Private | 1 | 1 | 5 | Tezspire |
| **Category / Program:** General Schedule/Section 100 | | | | | |
| **Prescriber type:** ☒ Medical Practitioners | | | | | |
| **Restriction type:** ☒Authority Required (in writing only via post/HPOS upload) | | | | | |
| **Episodicity:** Active | | | | | |
| **Severity:** Uncontrolled Severe | | | | | |
| **Condition:** Uncontrolled severe asthma | | | | | |
| **Indication:** Uncontrolled severe asthma | | | | | |
| **Treatment Phase:** Continuing treatment | | | | | |
| **Clinical criteria:** | | | | | |
| Patient must have demonstrated or sustained an adequate response to PBS-subsidised treatment with this drug for this condition. | | | | | |
| **Treatment criteria:** | | | | | |
| Must be treated by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma. | | | | | |
| **Population criteria:** | | | | | |
| Patient must be aged 12 years or older. | | | | | |

a AEMP, also public hospital DPMQ

## Eosinophilic or allergic SUA

| MEDICINAL PRODUCT medicinal product pack | Dispensed Price for Max. Qty | Max. qty packs | Max. qty units | №.of Rpts | Available brands |
|---|---|---|---|---|---|
| TEZEPELUMAB | | | | | |
| Tezepelumab, 210 mg in 1.91 mL (110 mg/mL) in a prefilled pen | Published<br>$1,671.78 Public<br>$1,720.45 Private<br>Effective<br>$TBD | 1 | 1 | 7 | Tezspire |
| | | | | | |
| **Category / Program:** General Schedule/Section 100 | | | | | |
| **Prescriber type:** ☒ Medical Practitioners | | | | | |
| **Restriction type:** ☒Authority Required (in writing only via post/HPOS upload) | | | | | |
| **Episodicity:** Active | | | | | |
| **Severity:** Uncontrolled Severe | | | | | |
| **Condition:** Uncontrolled severe asthma | | | | | |
| **Indication:** Uncontrolled severe asthma | | | | | |
| **Treatment Phase:** Initial treatment 1– New patients (New patients; or Recommencement of treatment in a new treatment cycle following a break in PBS-subsidised biological medicine therapy) | | | | | |

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| **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** |
| Patient must not have received PBS-subsidised treatment with a biological medicine for severe asthma; or |
| Patient must have had a break in treatment from a PBS-subsidised biological medicine for severe asthma. |
| **AND** |
| And have had asthma for 1 year 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 ($FEV_1$) 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 $FEV_1$ 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** |
| Patient must have a duration of asthma of at least 1 year. |
| **AND** |
| Patient must have blood eosinophil count at least 300 cells per microlitre in the last 12 months, or |
| Patient must have blood eosinophil count at least 150 cells per microlitre while receiving treatment with oral corticosteroids in the last 12 months |
| **OR** |
| Patient must have total serum human immunoglobulin E of at least 30 IU/mL, measured in the last 12 months that has past or current evidence of atopy, documented by either: (i) skin prick testing; (ii) an in vitro measure of specific IgE |
| **AND** |
| Patient must have failed to achieve adequate control with optimised asthma therapy, despite formal assessment of and adherence to correct inhaler technique, which has been documented. |
| **AND** |
| Patient must not receive more than 32 weeks of treatment under this restriction. |
| **Treatment criteria:** |
| Must be treated by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma. |
| **Population criteria:** |
| Patients must be aged 12 years or older. |

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| **Treatment Phase:** Initial treatment 2 – (Change of treatment) |
| **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** |
| Patient must have received prior PBS-subsidised treatment with a biological medicine for severe asthma in this treatment cycle. |
| **AND** |
| 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** |

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| 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; or |
| Patient must have each of: i) total serum human immunoglobulin E greater than or equal to 30 IU/mL measured no more than 12 months prior to initiating PBS-subsidised treatment with a biological medicine for severe asthma, ii) past or current evidence of atopy, documented by skin prick testing or an in vitro measure of specific IgE in the past 12 months or in the 12 months prior to initiating PBS-subsidised treatment with a biological medicine for severe asthma. |
| **AND** |
| The treatment must not be used in combination with and within 4 weeks of another PBS-subsidised biological medicine prescribed for severe asthma. |
| **Treatment criteria:** |
| Must be treated by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma. |
| **Population criteria:** |
| Patients must be aged 12 years or older. |

| **MEDICINAL PRODUCT medicinal product pack** | **Dispensed Price for Max. Qty** | **Max. qty packs** | **Max. qty units** | **№.of Rpts** | **Available brands** |
|---|---|---|---|---|---|
| TEZEPELUMAB | | | | | |
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| **Episodicity:** Active |
| **Severity:** Uncontrolled Severe |
| **Condition:** Uncontrolled severe asthma |
| **Indication:** Uncontrolled severe asthma |
| **Treatment Phase:** Continuing treatment |
| **Clinical criteria:** |
| Patient must have demonstrated or sustained an adequate response to PBS-subsidised treatment with this drug for this condition. |
| **Treatment criteria:** |
| Must be treated by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma. |
| **Population criteria:** |
| Patients must be aged 12 years or older. |

3.2 The submission proposed a Special Pricing Arrangement (SPA) with a published ex-manufacturer price (EMP) of $1,671.78 per prefilled pen (110 mg/mL) for both populations. For the non-eosinophilic and non-allergic SUA population the submission proposed an effective EMP of $[redacted] per prefilled pen (110 mg/mL). The submission

did not propose an effective price for the eosinophilic or allergic SUA population as the effective price of dupilumab was not known.

3.3 The recommended dose of tezepelumab is 210 mg by subcutaneous (SC) injection every 4 weeks. The submission requested a maximum quantity of 1 single dose and 7 repeats for the initial restrictions, which provides 32 weeks of treatment. The submission stated that this duration corresponds with the typical timeframe required to assess a response to treatment, which is approximately 28 weeks, and aligns with other biologics for SUA. The submission requested 5 repeats for the continuing restrictions, which corresponds to 24 weeks of treatment. The durations of therapy allowed by the number of repeats for initial and continuing therapy were consistent with existing PBS listings of other biologics for SUA.

3.4 The submission requested a second initial restriction for the eosinophilic or allergic population to allow patients to switch biologic treatment. This is consistent with existing PBS listings for biologics. As there are no other biologic agents PBS-listed for the non-eosinophilic or non-allergic population, a second initial restriction was not requested.

3.5 The TGA indication specifies that tezepelumab is an 'add on' maintenance treatment in those who are inadequately controlled despite 'optimal therapy including medium or high-dose inhaled corticosteroids plus another non-steroidal medicinal product for maintenance treatment'. The proposed PBS restriction defines optimised asthma therapy as high-dose inhaled corticosteroid (ICS) plus long-acting beta-2 agonist (LABA) therapy for at least 12 months, unless contraindicated or not tolerated, despite formal assessment of and adherence to correct inhaler technique. The ESC noted that the proposed PBS restriction was narrower than the TGA indication, as it specifies optimal therapy as only high-dose ICS and the TGA indication includes both medium or high-dose ICS.

3.6 The submission stated that, while there are currently no patients receiving tezepelumab in Australia, a patient access program is planned to commence in November 2025. However, no grandfathering restriction was proposed in the submission. The Pre-Sub-Committee Response (PSCR) clarified that the patient access program is planned for the eosinophilic or allergic SUA population and will include 250 patients. The pre-PBAC Response noted that a separate grandfathering restriction would be required for eosinophilic or allergic SUA patients accessing tezepelumab under the sponsors proposed patient access program.

*For more detail on PBAC's view, see section 7 PBAC outcome.*

# 4 Population and disease

4.1 Asthma is a heterogeneous disease, characterised by chronic airway inflammation, and defined by the history of respiratory symptoms, such as wheeze, shortness of breath, chest tightness and cough, that vary over time and in intensity, together with

variable expiratory airflow limitation. Around 2.8 million Australians (11% of the total population) were estimated to be living with asthma in 2022.

4.2 The overall patient population considered in this submission are those with SUA. The 2024 GINA guidance for adolescents and adults with difficult-to-treat and severe asthma[1] defines uncontrolled asthma as including one or both of the following:

- poor symptom control (frequent symptoms or reliever use, activity limited by asthma, night waking due to asthma);
- frequent exacerbations (≥2 per year) requiring oral corticosteroids (OCS), or serious exacerbations (≥1 per year) requiring hospitalisation.

The 2024 GINA guidance defines severe asthma as that which is uncontrolled despite adherence with maximal optimised high-dose ICS-LABA treatment and management of contributory factors, or that worsens when high-dose treatment is decreased.

4.3 Given the high symptom burden, SUA has a major impact on health-related quality of life (HRQoL). Asthma that remains uncontrolled despite high-dose ICS and LABA, irrespective of asthma associated biomarkers such as blood eosinophil counts and allergy status, is associated with significant burden on patients, carers and the healthcare system.

4.4 Currently, there are 4 biologic therapies on the PBS for the treatment of eosinophilic or allergic SUA: dupilumab, benralizumab, mepolizumab and omalizumab. Dupilumab is listed for both eosinophilic and allergic SUA. Benralizumab and mepolizumab are listed for eosinophilic SUA and omalizumab is listed for allergic SUA. There are currently no PBS-listed therapies for non-eosinophilic and non-allergic SUA.

4.5 Tezepelumab has a novel mechanism of action that suppresses multiple downstream inflammatory pathways. Thymic stromal lymphopoietin (TSLP) is an epithelial cytokine that has broad and multifaceted effects on the initiation and persistence of asthma airway inflammation. Tezepelumab is a first-in-class monoclonal antibody that blocks the activity of TSLP. The ESC noted the TSLP blocking action of tezepelumab means that it reduces eosinophilic inflammation, allergic inflammation and also neutrophilic inflammation. The ESC noted that Type 2 inflammation is often characterised by elevated eosinophils or increased fractional exhaled nitric oxide (FeNO), and it may be accompanied by atopy and elevated IgE.[1] Whereas non-Type 2 inflammation is often characterised by increased neutrophils.[1] The ESC advised that it is tezepelumab's

[1] Global Initiative for Asthma. Difficult-To-Treat & Severe Asthma in Adolescent and Adult Patients, v5.0, 2024. Available from: www.ginasthma.org/reports

impact on neutrophilic inflammation that allows it to be considered for use in the non-eosinophilic and non-allergic SUA population.

*For more detail on PBAC's view, see section 7 PBAC outcome.*

# 5 Comparator

5.1 The submission nominated SoC as the comparator for the non-eosinophilic and non-allergic SUA population. SoC was stated to include optimised asthma therapy with high-dose ICS combined with LABA as the primary treatment, with optional add-ons (e.g. OCS, long-acting muscarinic antagonist [LAMA] or short-acting beta-agonist [SABA] inhalers, or azithromycin). The submission stated that available biologic therapies for SUA were not considered to be appropriate comparators as there is no overlap between the proposed new population (non-eosinophilic and non-allergic) and the existing reimbursed population (eosinophilic or allergic). The ESC considered that SoC, as defined by the submission, was the appropriate comparator for the non-eosinophilic and non-allergic SUA population.

5.2 The submission nominated dupilumab as the main comparator for the eosinophilic or allergic SUA population. The submission noted that dupilumab is the only biologic that is PBS listed with a restriction that aligns with that being sought for tezepelumab (i.e. it is listed for both eosinophilic or allergic SUA) and hence it was the medicine most likely to be replaced. The submission noted that dupilumab was the most recently recommended biologic for SUA by the PBAC and that the consideration was based on a clinical comparison with benralizumab, mepolizumab and omalizumab. The submission nominated benralizumab, mepolizumab and omalizumab as secondary comparators. The ESC considered that this was appropriate.

5.3 In the context of the cost-minimisation approach taken by the submission for the eosinophilic or allergic SUA population, a further consideration for PBAC is that, under Section 101(3B) of the National Health Act 1953, when the proposed medicine is substantially more costly than an alternative therapy, the committee cannot make a positive recommendation unless it is satisfied that, for some patients, the proposed medicine provides a significant improvement in efficacy and/or reduction of toxicity over the alternative therapy. If the committee is so satisfied, it must make a statement to this effect. For the requested population, the following PBS-listed medicines may be considered alternative therapies because they could be replaced in practice: dupilumab, benralizumab, mepolizumab and omalizumab. Some of these alternative therapies may be less costly than tezepelumab.

*For more detail on PBAC's view, see section 7 PBAC outcome.*

# 6 Consideration of the evidence

## *Sponsor hearing*

6.1 The sponsor requested a hearing for this item. The clinician discussed the natural history of the disease and how the drug would be used in practice. The clinician emphasised that for patients with SUA, exacerbations can have a significant impact on the quality of life of patients and lead to long-term airway damage. The clinician noted that monoclonal antibodies approved in Australia have led to substantial clinical improvements for many patients with SUA, though some individuals experience only partial benefit. The clinician noted that tezepelumab has a unique mechanism of action, acting upstream in the inflammatory cascade, which the clinician considered was clinically important given that phenotypic expression in SUA can shift over time in individual patients. The clinician also noted that individuals with SUA and type 2 low inflammation (non-eosinophilic and non-allergic) currently have limited treatment options and are often treated with repeated courses of OCS, which carries significant cumulative risk of multi-system harm. The clinician considered these patients would benefit from treatment with tezepelumab. The PBAC considered that the clinician presentation was informative. In addition to the clinician presentation, the PBAC noted that the sponsor reiterated points previously made regarding the appropriate clinical and pricing comparator for eosinophilic or allergic SUA patients.

## *Consumer comments*

6.2 The PBAC noted and welcomed input from health care professionals (2), a medical organisation (1) and a consumer group/organisation (1) via the Office of Health Technology Assessment Consultation Hub. Health care professional input emphasised that there is a clinical need for patients with T2-low biomarkers (non-eosinophilic and non-allergic) as they are ineligible, and not suitable, for biologics currently subsidised through the PBS. Comments highlighted that monoclonal antibodies generally have a favourable side effect profile, especially when compared to the cumulative harms associated with long-term OCS use. Comments also noted the high cost of tezepelumab and considered that the listing of tezepelumab on the PBS would ensure equitable access to treatment.

6.3 The comments from The Centre of Excellence in Severe Asthma/The Centre of Excellence in Asthma Treatable Traits along with Asthma Australia expressed support for the proposed PBS listing of tezepelumab. The organisations noted the clinical trial evidence for tezepelumab demonstrated a clinical benefit for both type 2-low and type 2-high SUA patients, showing improvements in exacerbation rates, lung function, and quality of life, with the potential to achieve clinical remission. The organisations emphasised the importance of optimising asthma management in all patients, and to reduce the need for OCS, which are associated with adverse effects to multiple body systems and include diabetes, dyspepsia, renal impairment, obesity, cataracts, mood

disorders, cardiovascular disease and decreased bone density leading to fractures. The organisations highlighted that tezepelumab provides a steroid-sparing option for individuals who remain dependent on OCS despite high-dose inhaled therapy, while preserving asthma control.

### *Clinical trials*

6.4 The submission was based on 3 randomised, double-blind, placebo-controlled trials comparing tezepelumab to placebo:

- NAVIGATOR (N=1,061) was a Phase III randomised controlled trial (RCT) comparing tezepelumab (210 mg once every 4 weeks [Q4W] SC) to placebo in adults and adolescents aged 12 to 80 years with SUA.
- PATHWAY (N=550) was a Phase II dose-ranging RCT comparing tezepelumab (70mg Q4W SC, 210mg Q4W SC, 280mg once every 2 weeks [Q2W] SC) to placebo in adults aged 18 to 75 years with SUA.
- SOURCE (N=150) was a Phase III RCT comparing tezepelumab (210 mg Q4W SC) to placebo in adults aged 18 to 80 years with OCS dependent SUA.

6.5 The submission also presented the DESTINATION study which was a Phase III, double-blind, randomised and placebo-controlled extension study. It evaluated the safety and tolerability of tezepelumab (210 mg Q4W SC) in adults and adolescents completing the NAVIGATOR and SOURCE trials for up to 2 continuous years of treatment, including 1 year of treatment in predecessor studies. Efficacy analyses were performed using the full analysis set (FAS) which consisted of all patients who were randomised and received at least 1 dose of the investigational product in either parent study, irrespective of their protocol adherence and continued participation in either of the studies or their enrolment in the extension study. Efficacy analyses were also performed using the FAS-long term extension (LTE) set consisting of patients who were randomised and received at least 1 dose of the investigational product in the DESTINATION study. The FAS-LTE results of the DESTINATION study are presented in the comparative effectiveness section.

6.6 To support the clinical claim of superiority of tezepelumab versus SoC in the non-eosinophilic and non-allergic SUA population, the submission presented post-hoc subgroup analyses of this population who were on high-dose ICS from the NAVIGATOR and PATHWAY clinical trials. The data used to inform the clinical claim for this population were different to that used to inform the economic evaluation. The economic evaluation for this population was informed by data from a subgroup of pooled patients from the SOURCE and NAVIGATOR trials who were on high-dose ICS and were classified as either non-eosinophilic or non-allergic.

6.7 No head-to-head trials comparing tezepelumab to dupilumab or the secondary comparators (benralizumab, mepolizumab, and omalizumab) were identified for the

eosinophilic or allergic SUA patient population. As such, the submission conducted a series of indirect treatment comparisons, based on meta-analysed outcomes from post-hoc subgroups from the tezepelumab trials (NAVIGATOR, PATHWAY and SOURCE) and 14 comparator trials of dupilumab (QUEST, DRI12544, VENTURE), benralizumab (CALIMA, SIROCCO, ZONDA, ANDHI, MIRACLE), mepolizumab (MENSA, MUSCA, SIRIUS, 201536) and omalizumab (EXTRA, INNOVATE) with placebo as the common reference.

6.8 The evaluation noted a number of issues related to the tezepelumab versus dupilumab indirect treatment comparisons. The publicly available dupilumab data used for the subgroup + high-dose ICS analysis were available only for the intention to treat (ITT) population and the eosinophilic subgroup (not the allergic subgroup). Therefore, patients on both medium-dose ICS and high-dose ICS were included to compare tezepelumab and dupilumab for the allergic population. Furthermore, the SOURCE and VENTURE trials did not report results for an allergic subgroup, so an indirect treatment comparison could not be performed for an allergic subgroup on OCS.

6.9 There were also key differences in trial and patient baseline characteristics that may have influenced the transitivity of the indirect treatment comparisons. In July 2022, the ESC noted that patients in the NAVIGATOR trial of tezepelumab appeared to have more severe asthma than those included in the other trials based on differences in event rates in the placebo groups and higher number of exacerbations and portion on high ICS. The ESC previously noted that transitivity concerns were also raised during the PBAC consideration of dupilumab in November 2020, and at that time, the dupilumab populations were noted to have relatively less severe asthma than the comparator populations (para. 6.57, tezepelumab ESC advice, July 2022 PBAC Meeting) (further discussed in paragraphs 6.13−6.14).

6.10 Details of the trials presented in the submission are provided in Table 2.

**Table 2: Trials and associated reports presented in the submission**

| Trial ID | Protocol title/ Publication title | Publication citation |
|---|---|---|
| **Tezepelumab** | | |
| NAVIGATOR | A Multicentre, Randomised, Double-Blind, Placebo Controlled, Parallel Group, Phase 3 Study to Evaluate the Efficacy and Safety of Tezepelumab in Adults and Adolescents with Severe Uncontrolled Asthma (NAVIGATOR)<br>Menzies-Gow A, Corren J et al. Tezepelumab in adults and adolescents with SUA. | 26 February 2021<br><br>*NEJM* 2021;384(19):1800-1809. |
| PATHWAY | A Phase 2 Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of MEDI9929 in Adult Subjects with Inadequately Controlled, Severe Asthma<br>Corren J, Parnes J. R et al. Tezepelumab in adults with uncontrolled asthma. | 05 April 2018<br><br>*NEJM* 2017;377(10): 936-946. |
| SOURCE | A Multicentre, Randomized, Double-Blind, Placebo Controlled, Phase 3 Study to Evaluate the Efficacy and Safety of Tezepelumab in Reducing Oral Corticosteroid Use in Adults with Oral Corticosteroid Dependent Asthma (SOURCE)<br>Wechsler ME, Menzies-Gow A, et al. SOURCE study group. Evaluation of the oral corticosteroid-sparing effect of tezepelumab in adults with oral corticosteroid-dependent asthma (SOURCE): a randomised, placebo-controlled, phase 3 study. | 22 March 2021<br><br>*Lancet Respir Med*. 2022 Jul;10(7):650-660. |
| DESTINATION | A Multicentre, Double-blind, Randomised, Placebo Controlled, Parallel Group, Phase 3, Safety Extension Study to Evaluate the Safety and Tolerability of Tezepelumab in Adults and Adolescents with Severe Uncontrolled Asthma (DESTINATION) | 08 April 2022 |
| | Menzies-Gow A, Wechsler ME et al; DESTINATION study investigators. Long-term safety and efficacy of tezepelumab in people with severe, uncontrolled asthma (DESTINATION): a randomised, placebo-controlled extension study. | *Lancet Respir Med*. 2023 May;11(5):425-438. |
| **Dupilumab** | | |
| QUEST<br>EFC13579<br>NCT02528214 | A randomised, double blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of dupilumab in patients with persistent asthma. Clinical study report.<br>Busse W, Maspero J, Rabe K, et al. Liberty asthma QUEST: Phase 3 randomised, double-blind, placebo-controlled, parallel-group study to evaluate dupilumab efficacy/safety in patients with uncontrolled, moderate-to-severe asthma.<br>Corren J, Castro M, O'Riordan T, et al. Dupilumab efficacy in patients with uncontrolled, moderate-to-severe allergic asthma. | November 2017<br><br>*Adv Ther* 2018; 35(5):737-748<br><br>*J Allergy Clin Immunol Pract* 2020; 8(2):516-526. |
| DRI2544 | A randomised, double blind, placebo-controlled, dose-ranging study to evaluate dupilumab in patients with moderate to severe uncontrolled asthma. Clinical study report.<br>Wenzel S, Castro M, Corren J, et al. Dupilumab efficacy and safety in adults with uncontrolled persistent asthma despite use of medium-to-high-dose inhaled corticosteroids plus a long-acting ß$_2$ agonist: a randomised double-blind placebo-controlled pivotal phase 2b dose-ranging trial. | February 2016<br><br>*Lancet* 2016; 388:31-44. |
| VENTURE<br>EFC13691 | A randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of dupilumab in patients with severe steroid dependent asthma. Clinical study report. | December 2017 |

| Trial ID | Protocol title/ Publication title | Publication citation |
|---|---|---|
| | Rabe K, Nair P, Brusselle G, et al. Efficacy and safety of dupilumab in glucocorticoid-dependent severe asthma. | *N Engl J Med* 2018; 378:2475-85. |
| **Benralizumab** | | |
| SIROCCO | Bleecker E, FitzGerald J, Chanez P, et al. Efficacy and safety of benralizumab for patients with severe asthma uncontrolled with high-dosage inhaled corticosteroids and long-acting β2-agonists (SIROCCO): a randomised, multicentre, placebo-controlled phase 3 trial. | *Lancet* 2016*; 388*:2115-27. |
| CALIMA | FitzGerald J, Bleecker E, Nair, P, et al. Benralizumab, an anti-interleukin-5 receptor α monoclonal antibody, as add-on treatment for patients with severe, uncontrolled, eosinophilic asthma (CALIMA): a randomised, double-blind, placebo-controlled phase 3 trial. | *Lancet* 2016*; 388*:2128-41 |
| ZONDA | Nair P, Wenzel S, Rabe K, et al. Oral glucocorticoid–sparing effect of benralizumab in severe asthma. | *N Engl J Med* 2017; 376:2448-58 |
| ANDHI | Harrison TW, Chanez P, Menzella F et al. Onset of effect and impact on health-related quality of life, exacerbation rate, lung function, and nasal polyposis symptoms for patients with severe eosinophilic asthma treated with benralizumab (ANDHI): a randomised, controlled, phase 3b trial. | *The Lancet Respiratory Medicine* 2021;9(3):260-274. |
| MIRACLE | Lai K, Sun D, Dai R et al. Benralizumab efficacy and safety in severe asthma: A randomized trial in Asia. | *Respir Med.* 2024;229(1):107611. |
| **Mepolizumab** | | |
| MENSA | Ortega H, Liu M, Pavord I, et al. Mepolizumab Treatment in Patients with Severe Eosinophilic Asthma. | *N Engl J Med* 2014; 371:1198-207. |
| MUSCA | Chupp G, Bradford E, Albers F, et al. Efficacy of mepolizumab add-on therapy on health-related quality of life and markers of asthma control in severe eosinophilic asthma (MUSCA): a randomised, double-blind, placebo-controlled, parallel-group, multicentre, phase 3b trial. | *Lancet Respir Med 2017; 5:390-400.* |
| SIRIUS | Bel E, Wenzel S, Thompson P, et al. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. | *N Engl J Med* 2014*;* 371:1189-97. |
| 201536 | Chen R, Wei L, Dai Y et al. Efficacy and safety of mepolizumab in a Chinese population with severe asthma: a phase III, randomised, double-blind, placebo-controlled trial. | *ERJ Open Res.* 2024;10(3):1:14. |
| **Omalizumab** | | |
| EXTRA | Hanania N, Alpan O, Hamilos D, et al. Omalizumab in severe allergic asthma inadequately controlled with standard therapy. | *Ann Intern Med* 2011; 154:573-582. |
| INNOVATE | Humbert M, Beasley R, Ayres J, et al. Benefits of omalizumab as add-on therapy in patients with severe persistent asthma who are inadequately controlled despite best available therapy (GINA 2002 step 4 treatment): INNOVATE | *Allergy* 2005; 60:309-16. |

Source: Table 2-9, pp42-43; Table 2-11, p45 of the submission and Table 1, p1; Table 3, p3; Table 5, p4 of the Attachment 2.9 TEZE submission_Section 2 Additional Comparators_May 2025 and para., 6.3, dupilumab PSD, November 2020 PBAC Meeting.
Blue shading indicates previously seen by the PBAC.

6.11 The key features of the tezepelumab and the primary comparator dupilumab direct randomised trials are summarised in Table 3.

**Table 3: Key features of the included evidence**

| Trial | N | Design / Duration | Risk of bias | Patient population | Outcomes | Use in modelled evaluation |
|---|---|---|---|---|---|---|
| **Tezepelumab versus placebo** | | | | | | |
| NAVIGATOR | 1,061 | R, DB, MC 52 weeks | Low | Adults and adolescents with moderate-to-severe uncontrolled asthma | Primary: AAER Secondary: FEV1 AQLQ(S)+12 ACQ-6 | AAER ACQ-6 EQ-5D-5L |
| PATHWAY | 550 (275) [a] | R, DB, MC 52 weeks | Low | Adults and adolescents with moderate-to-severe uncontrolled asthma | Primary: AAER Secondary: FEV1 AQLQ(S)+12 ACQ-6 | Not used |
| SOURCE | 150 | R, DB, MC 48 weeks | Low | Adults with OCS-dependent, severe asthma | Primary: Categorised % reduction in daily OCS dose while not losing asthma control Secondary: AAER FEV1 AQLQ(S)+ | AAER ACQ-6 EQ-5D-5L |
| DESTINATION (NAVIGATOR) | 1059 | R, DB, MC 104 weeks | Moderate | Adult and adolescent subjects with moderate-to-severe uncontrolled asthma who were included in the NAVIGATOR trial | Primary: Exposure-adjusted incidence rates of AEs/SAEs over 104 weeks Secondary: AAER over 104 weeks | AEs |
| DESTINATION (SOURCE) | 150 | R, DB, MC 104 weeks | Moderate | Adults with OCS dependent, severe asthma who were included in the SOURCE trial | | |
| **Dupilumab versus placebo** | | | | | | |
| QUEST | 1902 (938) [b] | R, DB, MC 52 weeks | Low | Adults and adolescents with moderate-to-severe uncontrolled asthma | AASER [d] FEV1 change from baseline at week 12 | AAER |
| DRI12544 | 308 (315) | R, DB, MC 24 weeks | Low | Adults with moderate-to-severe uncontrolled asthma | FEV1 (L) change from baseline at week 12 (AASER [d] was a secondary outcome) | AAER |

| Trial | N | Design / Duration | Risk of bias | Patient population | Outcomes | Use in modelled evaluation |
|---|---|---|---|---|---|---|
| VENTURE | 210 | R, DB, MC<br>24 weeks | Low | Adults with OCS-dependent, severe asthma | Percentage reduction in OCS dose at week 24 (AASER [d] was a secondary outcome) | AAER |

Source: Based on Table 2-19, pp59-60 of the submission and adapted from 6.02, dupilumab PSD – November 2020 PBAC meeting.
AAER = annual asthma exacerbation rate; AASER = annual asthma severe exacerbation rate; AER = asthma exacerbation rate; DB = Double blind; DUPI = dupilumab; EOSic = eosinophilic; FEV1 = forced expiratory volume in 1 second; IV = intravenous; MC = multicentre; NA = Not Applicable; OCS = oral corticosteroid; PBO = placebo; Q2W = every 2 weeks; Q4W = every 4 weeks; Q8W = every 8 weeks; R = randomised; SC = subcutaneous; TEZE = tezepelumab
Blue shading indicates previously seen by the PBAC.
[a] Excludes patients from the TEZE 70 mg Q4W and TEZE 280 mg Q2W arms because they are not relevant to this submission.
[b] Excludes patients from the DUPI 300 mg Q2W and PBO 2.00 mL arms because they are not relevant to this submission
[c] Excludes patients from the DUPI 200 mg Q4W, DUPI 300 mg Q4W and DUPI 300 mg Q2W arms because they are not relevant to this submission.
[d] While called annual severe asthma exacerbation rate (AASER) the definition of this outcome was the same as AAER in the other studies.

6.12 The evaluator considered the risk of bias in the randomised tezepelumab trials was low and risk of bias in the extension study was moderate due to selection and reporting bias.

6.13 Key differences in trial and patient baseline characteristics that might influence the transitivity of the indirect treatment comparisons are summarised for the relevant subgroups in Table 4. All indirect treatment comparisons were based on post hoc subgroups.

**Table 4: Differences that might influence the transitivity of the indirect comparisons**

| | Tezepelumab vs placebo | Dupilumab versus placebo |
|---|---|---|
| **EOSic (EOS ≥300 cells/µL) + High ICS with no OCS subgroup** | | |
| Trials or relevant subgroups | NAVIGATOR: N=152 vs 166<br>PATHWAY: N=29 vs 22 | QUEST: N=128 vs N=80<br>DRI12544: N=37 vs 35 |
| Exacerbations in previous 12 months (mean) | NAVIGATOR: 3.07 vs 3.00<br>PATHWAY: 2.66 vs 2.55 | QUEST: 2.3 vs 2.4<br>DRI12544: 0.7 vs 1.1 |
| Pre-BD FEV1 % Predicted Normal | NAVIGATOR: 57.9% vs 60.1%<br>PATHWAY: 57.3% vs 59.6% | QUEST: 55.6% vs 57.8%<br>DRI12544: 58.0% vs 57.4% |
| FEV1 reversibility % | NAVIGATOR: 17.6% vs 16.0%<br>PATHWAY: 22.5% vs 22.5% | QUEST: 27.0% vs 25.0%<br>DRI12544: 21.2% vs 22.1% |
| **Allergic + medium and high ICS** | | |
| Trials or relevant subgroups | NAVIGATOR: N=339 vs N=341<br>PATHWAY: N=77 vs 80 | QUEST: N=360 vs 183 |
| Allergic definition | NAVIGATOR: positive serum IgE result specific to a panel of perennial aeroallergens in the fluorescent enzyme immunoassay<br>PATHWAY: positive IgE FEIA level to one or more region-specific allergens | QUEST: total serum IgE ≥30 IU/mL and ≥1 perennial aeroallergen-specific IgE≥0.35 kU/L |
| Proportion receiving high-dose ICS | NAVIGATOR: NR (75.2% vs 75.0% in FAS)<br>PATHWAY: NR (48.9% vs 47.1% in ITT) | QUEST: NR (50.2% vs 54.3% in ITT) |
| Exacerbations in previous 12 months (mean) | NAVIGATOR: NR (2.8 vs 2.7 in FAS)<br>PATHWAY: NR (2.4 vs 2.5 in ITT) | QUEST: 1.98 vs 1.89 |
| Proportion receiving OCS | NAVIGATOR: NR (9.3% vs 9.6% in FAS)<br>PATHWAY: NR (6.6% vs 9.4% in ITT) | QUEST: 0% |
| Pre-BD FEV1 % Predicted Normal | NAVIGATOR: 60.0% vs 60.8%<br>PATHWAY: NR (59.0% vs 59.4% in ITT) | QUEST: NR (58.4% vs 58.4% in ITT) |
| FEV1 reversibility % | NAVIGATOR: 17.1% vs 15.2%<br>PATHWAY: NR (20.9% vs 22.7% in ITT) | QUEST: NR (27.4% vs 25.1% in ITT) |
| **EOSic (EOS ≥150 cells/µL) + High ICS and OCS** | | |
| Trials or relevant subgroups | SOURCE: N=47 vs 52 | VENTURE: N=81 vs 69 |
| Exacerbations in previous 12 months (mean) | SOURCE: NR (2.0 vs 2.0 in FAS) | VENTURE: NR (2.01 vs 2.17 in ITT) |
| Pre-BD FEV1 % Predicted Normal | SOURCE: NR (54.3% vs 53.3% in FAS) | VENTURE: NR (51.6% vs 52.7% in ITT) |
| FEV1 reversibility % | SOURCE: NR (16.5% vs 13.9% in FAS) | VENTURE: NR |

Source; Table 2-142, p213; Table 2-144, pp215-216; Table 2-146, pp218-219 of the submission.
BD = bronchodilator; FAS = full analysis set; EOSic = eosinophilic; FEV1 = forced expiratory volume in 1 second; ICS = inhaled corticosteroids; ITT = intention-to-treat; NR = not reported; OCS = oral corticosteroid; PN = predicted normal.

6.14 Overall, the tezepelumab trial subgroups generally had patients with more severe asthma as indicated by the higher mean number of exacerbations in the previous 12 months. The proportion of patients receiving high-dose ICS was also higher in the NAVIGATOR trial (75.2% vs 75.0% for the tezepelumab and placebo arms respectively in FAS) compared to the QUEST trial (50.2% vs 54.3% for the dupilumab and placebo arms respectively in the ITT population). Differences in the duration of the trials was also evident with two of the three dupilumab studies conducted over 24 weeks (DRI12544 and VENTURE) compared to at least 48 weeks for the tezepelumab studies.

6.15 The submission proposed a non-inferiority margin (NIM) of 28% (upper confidence interval [CI] of 1.28 rate ratio) for the analysis of annualised asthma exacerbation rate

(AAER). This NIM was consistent with that used in the consideration of dupilumab in November 2020 (para. 6.6, dupilumab Public Summary Document [PSD], November 2020 PBAC Meeting) and for the consideration of benralizumab in March 2018 (paras. 6.13, 6.36, benralizumab PSD, March 2018 PBAC Meeting). The submission nominated a minimal clinically important difference (MCID) of 0.5 points for the Asthma Control Questionnaire (ACQ)-6 and the Asthma Quality of Life Questionnaire (AQLQ)(S)+12. A ≥ 0.5 reduction in ACQ-6 score and a ≥ 0.5 increase in AQLQ(S)+12 score from baseline was considered clinically meaningful with these values used as the basis of the responder analyses. A decrease of 4 points or more in the total score was nominated as the MCID and used as the basis of the responder analysis for the St George's Respiratory Questionnaire (SGRQ).

## *Comparative effectiveness*

6.16 Table 5 presents the whole of trial evidence for the primary outcomes: AAER (NAVIGATOR and PATHWAY) and OCS reduction (SOURCE trial only). AAER was a secondary outcome in the SOURCE trial and in the DESTINATION extension study.

**Table 5: Results of AAER and change from baseline daily OCS while maintaining asthma control**

| Trial ID | Tezepelumab Rate (95% CI) | Placebo Rate (95% CI) | Rate Ratio (95% CI) | Risk difference (95% CI, p-value) |
|---|---|---|---|---|
| **AAER** | | | | |
| NAVIGATOR AAER, 52 wks | 0.93 (0.80, 1.07) | 2.10 (1.84, 2.39) | **0.44 (0.37, 0.53)** | **-1.17 (-1.47, -0.88); <0.001** |
| PATHWAY AAER, 52 wks | 0.20 (0.13, 0.30) | 0.72 (0.59, 0.88) | **0.29 (0.16, 0.51)** | **NR; <0.001** |
| SOURCE AAER, 48 wks | 1.38 (0.98, 1.95) | 2.00 (1.46, 2.74) | 0.69 (0.44, 1.09) | -0.62 (-1.40, 0.15); 0.111 |
| DESTINATION [a] (NAVIGATOR) AAER over 104 wks | 0.72 (0.62, 0.83) | 1.43 (1.18, 1.72) | **0.50 (0.40, 0.63)** | **-0.71 (-1.00, -0.43)** |
| DESTINATION [b] (SOURCE) AAER over 104 wks | 0.88 (0.61, 1.27) | 1.34 (0.84, 2.15) | 0.66 (0.37, 1.19) | -0.46 (-1.16, 0.25) |
| **Change from baseline daily OCS while maintaining asthma control (categorical)** | | | | |
| SOURCE | - | - | COR 1.28 (0.69, 2.35) | - |

Source: Constructed during the evaluation from Table 2-54, p118; Table 2-55, p122 &Table 2-56, p124

AAER = annual asthma exacerbation rate; CI = confidence interval; COR = Cumulative odds ratio; FAS = full analysis set; LTE = long-term extension; n = number of patients with event; N = total patients in group, NR = not reported; OCS = oral corticosteroids; PBO = placebo; wks = weeks.

**Bold** indicates statistically significant results.

[a] Tezepelumab plus Tezepelumab (N= 415) versus placebo plus placebo (N=206) (FAS-LTE)

[b] Tezepelumab plus tezepelumab (N= 60) versus placebo plus placebo (N=32) (FAS-LTE)

6.17 In the NAVIGATOR and PATHWAY trials there was a statistically significant greater reduction in AAER to 52 weeks for tezepelumab compared to placebo: rate ratio (RR) 0.44 (95% CI 0.37, 0.53) and RR 0.29 (95% CI: 0.16, 0.51), respectively. In the SOURCE trial, the reduction in asthma exacerbation rate (not annualised) was not statistically

significant. Among patients enrolled in the DESTINATION extension study from the NAVIGATOR study, tezepelumab resulted in a reduction in the rate of asthma exacerbation compared to placebo (RR 0.50, 95% CI 0.40, 0.63). In patients enrolled in the DESTINATION extension study from the SOURCE study, the AAER for asthma exacerbations between tezepelumab and placebo was 0.66 (95% CI 0.37, 1.19).

6.18 In the SOURCE trial, there was not a statistically significant change from baseline daily OCS while maintaining asthma control (categorical) to 48 weeks for tezepelumab 210 mg every 4 weeks compared to placebo (cumulative odds ratio (OR) 1.28, 95% CI: 0.69,2.35).

6.19 Table 6 presents key patient reported and QOL outcomes. The Asthma Control Questionnaire (ACQ)-6 responders and Asthma Quality of Life Questionnaire (AQLQ)(S)+12 responders were used in the economic model.

**Table 6: Key patient reported and QOL outcomes**

| Trial ID | Tezepelumab Responders (%) | Placebo Responders (%) | Odds Ratio (95% CI) | p-value |
|---|---|---|---|---|
| **ACQ-6 Responders** [a] | | | | |
| NAVIGATOR | 418 (86.2) | 361 (76.5) | 1.99 (1.43, 2.76) | **<0.001** |
| PATHWAY | 103 (76.3) | 83 (63.4) | NR [b] | **0.0** |
| SOURCE | 43 (65.2) | 31 (45.6) | 2.30 (1.10, 4.81) | **0.03** |
| **AQLQ(S)+12 Responders** [c] | | | | |
| NAVIGATOR | 372 (77.5) | 335 (71.7) | 1.36 (1.02, 1.82) | **0.04** |
| PATHWAY | 87 (73.1) | 74 (61.7) | NR | NR |
| SOURCE | 41 (62.1) | 35 (52.2) | 1.66 (0.81, 3.43) | 0.17 |
| **SGRQ Responders** [d] | | | | |
| NAVIGATOR | 318 (81.7) | 273 (72.6) | 1.66 (1.17, 2.36) | **0.005** |
| PATHWAY | NA | NA | NA | NA |
| SOURCE | 48 (72.2) | 32 (49.2) | 3.12 (1.44, 6.77) | **0.004** |

Source: Table 2-53, pp116-117; Table 2-61, p133; Table 2-65, p138; Table 2-67, p140; Table 2-71, p143; Table 2-73, p145; Table 2-75, p146 of the submission.

ACQ-6 = Asthma Control Questionnaire-6; AQLQ(S)+12 = Standardised Asthma Quality of Life Questionnaire for 12 Years and Older; CI = confidence interval; NA = Not assessed; NR = Not reported; SGRQ = St. George's Respiratory Questionnaire.

[a] Subject is classified as a responder if change from baseline in ACQ-6 score ≥ 0.5 point reduction

[b] Unable to be verified from the CSR, therefore NR. 2 were missing and CIs were not provided (reference: PATHWAY CSR: Table 11.4.1.2-6, p100 (Summary of Improvement from Baseline in ACQ-6 at Week 52 – LOCF (ITT Population))

[c] Subject is classified as a responder if change from baseline in AQLQ(S)+12 score is ≥ 0.5 point increase

[d] Subject is classified as responder if change from baseline in SGRQ score is a ≥ 4 point decrease

### Subgroup analyses of tezepelumab trials

6.20 The results of subgroup analyses for the AAER by biomarker subgroup are presented in Table 7 for tezepelumab versus placebo. The results shaded grey refer to the non-eosinophilic and non-allergic SUA population. The unshaded results refer to the eosinophilic and allergic SUA population.

**Table 7: Results of subgroup analyses for AAER by biomarker subgroup for tezepelumab versus placebo**

| Population | Trial ID | Tezepelumab Annual exacerbation rate (95% CI) | Placebo Annual exacerbation rate (95% CI) | RR or OR (95% CI) | AD (95% CI) |
|---|---|---|---|---|---|
| **EOSic or allergic SUA subgroup** | | | | | |
| **EOSic subgroup (EOS ≥300 cells/µL)** | | | | | |
| Medium + high ICS | NAVIGATOR | N=219<br>0.79 (NR) | N=222<br>2.66 (NR) | **0.30**<br>**(0.22, 0.40)** | **NA** |
| | PATHWAY | N=68<br>0.26 (NR) | N=71<br>0.65 (NR) | **0.40**<br>**(0.19, 0.85)** | **NR** |
| High ICS | NAVIGATOR | N=171<br>0.76 (0.58, 0.99) | N=181<br>2.84 (2.27, 3.54) | **0.27**<br>**(0.19, 0.37)** | **-2.08**<br>**(-2.73, -1.43)** |
| | PATHWAY | N=33<br>0.27 (0.12, 0.54) | N=30<br>0.99 (0.66, 1.42) | **0.27**<br>**(0.10, 0.77)** | **NR** |
| High ICS with no OCS | NAVIGATOR | N=152<br>0.69 (0.52, 0.91) | N=166<br>2.83 (2.26, 3.54) | **0.24**<br>**(0.17, 0.35)** | **-2.14**<br>**(-2.80, -1.49)** |
| | PATHWAY | N=29<br>0.19 (0.06, 0.45) | N=22<br>0.91 (0.56, 1.40) | **0.21**<br>**(0.06, 0.72)** | **NR** |
| **Allergic subgroup (any perennial specific IgA positive)** | | | | | |
| Medium + high ICS | NAVIGATOR | N=339<br>0.85 (NR) | N=341<br>2.03 (NR) | **0.42**<br>**(0.33, 0.53)** | **NA** |
| | PATHWAY | N=77<br>0.14 (NR) | N=80<br>0.75 (NR) | **0.18**<br>**(0.07, 0.44)** | **NR** |
| High ICS | NAVIGATOR | N=255<br>0.83 (0.67, 1.04) | N=258<br>2.47 (2.04, 2.99) | **0.34**<br>**(0.25, 0.45)** | **-1.64**<br>**(-2.13, -1.14)** |
| | PATHWAY | N=36<br>0.24 (0.10, 0.48) | N=41<br>1.10 (0.79, 1.48) | **0.18**<br>**(0.05, 0.67)** | **NR** |
| High ICS with no OCS | NAVIGATOR | N=232<br>0.74 (0.58, 0.93) | N=235<br>2.34 (1.92, 2.86) | **0.32**<br>**(0.23, 0.43)** | **-1.60**<br>**(-2.09, -1.11)** |
| | PATHWAY | N=31<br>0.18 (0.06, 0.41) | N=32<br>0.83 (0.54, 1.22) | **0.16**<br>**(0.03, 0.90)** | **NR** |
| **EOSic subgroup (EOS ≥150 cells/µL)** | | | | | |
| High ICS and OCS | SOURCE | N=47<br>0.92 (0.58,1.44) | N=52<br>2.15 (1.49,3.09) | **0.43**<br>**(0.24, 0.76)** | **-1.23**<br>**(-2.10,-0.35)** |
| **Non-EOSic and non-allergic SUA subgroup [a]** | | | | | |
| **Non-EOSic (<300cells/µl) + non-allergic (perennial specific IgE status negative)** | | | | | |
| High ICS | NAVIGATOR | N=86<br>1.41 (1.04, 1.91) | N=83<br>2.15 (1.60, 2.89) | **0.66**<br>**(0.43, 0.99)** | **-0.74**<br>**(-1.49, 0.01)** |
| | PATHWAY | N=18<br>0.29 (0.09, 0.68) | N=13<br>0.81 (0.39, 1.48) | 0.33<br>(0.09, 1.18) | NR |

Source: Constructed during the evaluation from Table 2-119, p190; Table 2-122, p194; Table 2-124, pp195-196; Table 2-127, p198; Table 2-130, p202 of the submission.

AAER = annual asthma exacerbation rate; AD = absolute difference; CI = confidence interval; EFAS = full analysis set; EOSic = eosinophilic; ICS = inhaled corticosteroids; N = total patients in group; NR = not reported; OCS = oral corticosteroids; PBO = placebo; RR = rate ratio

[a] The submission did not present AAER results for the non-EOSic and non-Allergic subgroup of the SOURCE study.

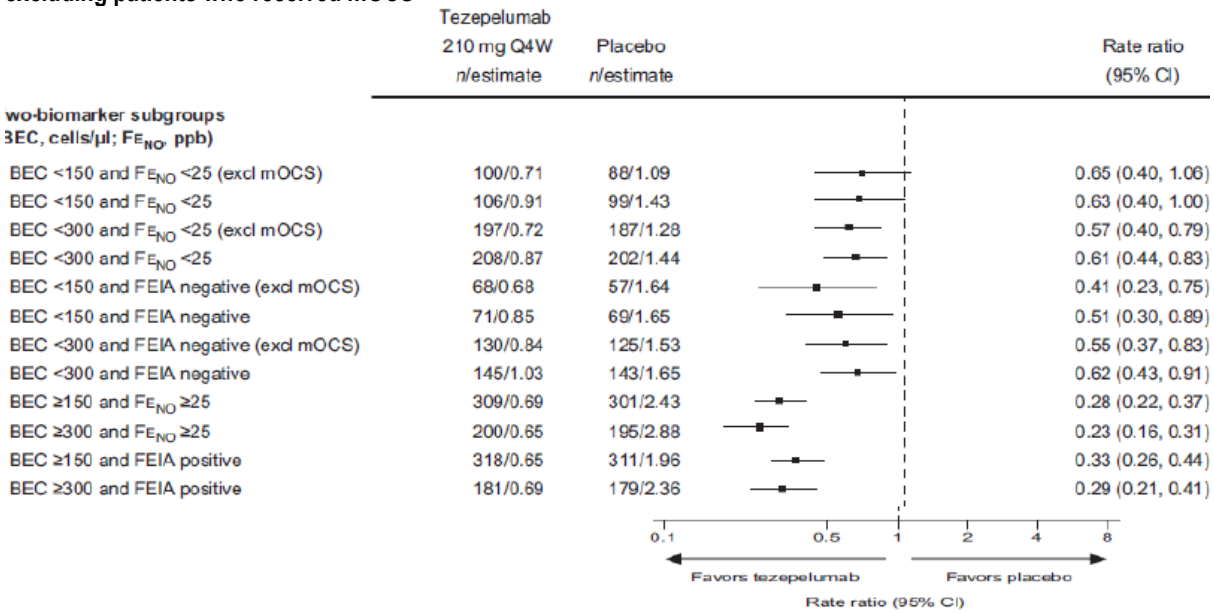
**Non-eosinophilic and non-allergic SUA**

6.21 The results presented for the non-eosinophilic and non-allergic subgroups in Table 7 (shaded in grey) were used to inform the submission claim of superior effectiveness of tezepelumab compared to placebo. In the NAVIGATOR trial, there was a statistically significant greater reduction in AAER to 52 weeks for tezepelumab 210 mg Q4W compared to placebo (absolute difference (AD) -0.74, 95% CI: -1.49, 0.01 and RR 0.66, 95% CI: 0.43, 0.99). The upper bound of the AD 95% CI crosses 0, and the rate ratio almost crossed 1 (0.99). In the non-eosinophilic and non-allergic subgroup in the PATHWAY trial, there was no statistically significant reduction in AAER to 52 weeks for tezepelumab 210 mg every 4 weeks compared to placebo (RR 0.33, 95% CI: 0.09, 1.18). The submission did not present AAER results for the non-eosinophilic and non-allergic subgroup of the SOURCE study.

6.22 The PSCR provided a meta-analysis conducted using AAER data from the NAVIGATOR and PATHWAY trials (odds ratio [OR] 0.62, 95% CI 0.42–0.92; p = 0.02). The ESC noted the meta-analysis indicated a statistically significant reduction in AAER with tezepelumab versus placebo but noted that the sample size was not provided to assist with confirming the population and that it had not been evaluated. The ESC also noted the PSCR highlighted a published pooled analysis of the PATHWAY and NAVIGATOR trials (Corren et al. 2023[2]) which demonstrated that tezepelumab reduced exacerbations compared with placebo across subgroups stratified by IgE and eosinophil levels (Figure 1). The ESC noted that while a reduction in AAER was evident across all subgroups the level of reduction was consistently higher for the subgroups with patients who were both higher eosinophil levels (i.e. BEC ≥ 150 cells/µL) and either FeNO or IgE positive.

[2] Corren J, Menzies-Gow A, Chupp G, Israel E, Korn S, Cook B, Ambrose CS, Hellqvist Å, Roseti SL, Molfino NA, Llanos JP, Martin N, Bowen K, Griffiths JM, Parnes JR, Colice G. Efficacy of Tezepelumab in Severe, Uncontrolled Asthma: Pooled Analysis of the PATHWAY and NAVIGATOR Clinical Trials. Am J Respir Crit Care Med. 2023 Jul 1;208(1):13-24

**Figure 1: Annualised asthma exacerbation rate over 52 weeks compared with placebo in biomarker subgroups excluding patients who received mOCS**




Source: Corren et al. 2023; PSCR (p2)

Notes: Rate ratio is displayed on a log scale. Data are from a negative binomial regression analysis with treatment, study (PATHWAY and NAVIGATOR), history of exacerbations (two or fewer or more than two in the previous 12 months) subgroup, and treatment-by-subgroup interaction as covariates.

BEC= blood eosinophil count; CI =confidence interval; excl= excluding; FEIA=fluorescence enzyme immunoassay; FENO= fractional exhaled nitric oxide; mOCS= maintenance oral corticosteroid; OCS=oral corticosteroid; NAVIGATOR= Study to Evaluate TEZE in Adults & Adolescents With Severe Uncontrolled Asthma; Q4W=every 4 weeks.

### Eosinophilic or allergic SUA

6.23 The results presented for the eosinophilic and allergic subgroups in Table 7 (unshaded) along with the AAER results in Table 8 for dupilumab were used to inform the indirect treatment comparisons for this population. Indirect treatment comparisons of the secondary comparators benralizumab, mepolizumab and omalizumab are not discussed in this document.

**Table 8: AAER - dupilumab trials (ITT and subgroups)**

| | Dupilumab Rate (95% CI) [N] | Placebo Rate (95% CI) [N] | RR (95% CI) |
|---|---|---|---|
| **AAER (ITT)** | | | |
| QUEST (DUPI 200 Q2W) | 0.46 (0.39, 0.53) [631] | 0.87 (0.72, 1.05) [317] | **0.52 (0.41, 0.66)** |
| DRI12544 (DUPI 200 Q2W) | 0.27 (0.16, 0.46) [158] | 0.90 (0.62, 1.30) [158] | **0.30 (0.16, 0.57)** |
| VENTURE (DUPI 300 Q2W) | 0.65 (0.44, 0.96) [103] | 1.60 (1.25, 2.04) [107] | **0.41 (0.26, 0.63)** |
| **AAER (EOS ≥300 cells/µL)** | | | |
| QUEST (DUPI 200 Q2W) | 0.37 (0.29, 0.48) [264] | 1.08 (0.85, 1.38) [148] | **0.34 (0.24, 0.48)** |
| DRI12544 (DUPI 200 Q2W) | 0.30 (0.13, 0.68) [66] | 1.04 (0.57, 1.90) [68] | **0.29 (0.10, 0.76)** |
| **AAER (EOS ≥150 cells/µL)** | | | |
| VENTURE (DUPI 300 Q2W) | 0.64 (0.43, 0.97) [81] | 1.54 (1.14, 2.07) [69] | **0.42 (0.25, 0.69)** |
| **AAER (Allergic)** [a] | | | |
| QUEST (DUPI 200 Q2W) | 0.47 (0.38, 0.57) [360] | 0.74 (0.57, 0.95) [183] | **0.63 (0.46, 0.87)** |

Source: Table 2-131, p203; Table 2-132, p203 and Table 2-133, p204 of the submission.
CI = confidence interval; DUPI = dupilumab; EOS+ = eosinophilic; ITT = intention-to-treat; N = Number; NR = not reported; OCS = oral corticosteroid; Q2W = every 2 weeks.
[a] Results for the allergic population were available only for the QUEST trial in the submission.
**Bold** indicates statistically significant results.

6.24 Table 9 presents the indirect comparison and summary of comparative benefits for tezepelumab and dupilumab via placebo.

**Table 9: AAER ITC: Summary of comparative benefits for tezepelumab versus dupilumab via placebo**

| Trial | TEZE vs PBO RR (95% CI) | TEZE rate (exacerbation /year) | PBO rate (exacerbation /year) | DUPI 200 rate (exacerbation /year) | DUPI 200 vs PBO RR (95% CI) | TEZE vs DUPI 200 via PBO RR (95% CI) |
|---|---|---|---|---|---|---|
| **EOSic (EOS ≥300 cells/μL) + High ICS with no OCS** | | | | | | |
| **Tezepelumab 210 mg SC Q4W** | | | | | | |
| NAVIGATOR | 0.24 (0.17, 0.35) | 0.69 (0.52, 0.91) | 2.83 (2.26, 3.54) | - | - | - |
| PATHWAY | 0.21 (0.06, 0.72) | 0.19 (0.06, 0.45) | 0.91 (0.56, 1.40) | - | - | - |
| **Pooled** | **0.24 (0.17, 0.34)** | - | - | - | - | - |
| **Dupilumab 200 mg Q2W** | | | | | | |
| QUEST | - | - | 1.35 (0.98, 1.84) | 0.55 (0.40, 0.75) | 0.41 (0.26, 0.64) | - |
| DRI12544 | - | - | 1.28 (0.71, 2.32) | 0.97 (0.51, 1.84) | 0.76 (0.32, 1.81) | - |
| **Pooled** | **-** | **-** | **-** | **-** | **0.46 (0.31, 0.69)** | - |
| Indirect treatment comparison | | | | | | **0.52 (0.31, 0.89) p=0.02** |
| **Allergic + Medium or High ICS** | | | | | | |
| **Tezepelumab 210 mg SC Q4W** | | | | | | |
| NAVIGATOR | 0.42 (0.33, 0.53) | 0.85 | 2.03 | - | - | - |
| PATHWAY | 0.18 (0.07, 0.46) | 0.14 | 0.75 | - | - | - |
| Pooled | 0.31 (0.14, 0.69) | - | - | - | - | - |
| **Dupilumab 200 mg Q2W** | | | | | | |
| QUEST | - | - | 0.74 (0.57. 0.95) | 0.47 (0.38, 0.57) | 0.63 (0.46, 0.87) | - |
| Indirect treatment comparison (all trials): | | | | | | 0.49 (0.21, 1.16) |
| Indirect treatment comparison (NAVIGATOR and QUEST trials only): | | | | | | **0.67 (0.45, 0.99) p=0.045** |
| **EOSic (EOS ≥150 cells/μL) + High ICS and OCS** | | | | | | |
| **Tezepelumab 210 mg SC Q4W** | | | | | | |
| SOURCE | 0.43 (0.24, 0.76) | 0.92 (0.58, 1.44) | 2.15 (1.49, 3.09) | - | - | - |
| **Dupilumab 300 mg Q2W** | | | | | | |
| VENTURE | - | - | 1.54 (1.14, 2.07) | 0.64 (0.43, 0.97) | 0.42 (0.25, 0.69) | - |
| Indirect treatment comparison: | | | | | | 1.03 (0.48, 2.21) p=0.94 |

Source: Table 2-143, p214; Table 2-145, p217; Table 2-147, p219 of the submission.

AAER = annual asthma exacerbation rate; CI = confidence interval; DUPI = dupilumab; EOSic = eosinophilic; ICS = inhaled corticosteroids; ITC = indirect treatment comparison; OCS = oral corticosteroid; PBO = placebo; Q4W= once every 4 weeks; RR = rate ratio; SC = subcutaneous; TEZE = tezepelumab
**Bold** indicates statistically significant result.

6.25 For patients with an eosinophil count of 300 cells/µL on high-dose ICS and no OSC, tezepelumab showed a statistically significant greater reduction in AAER compared with dupilumab (RR 0.52, 95%CI: 0.31, 0.89; p=0.02).

6.26 For patients with allergic asthma on moderate or high-dose ICS, there was no statistically significant difference in AAER for tezepelumab compared with dupilumab (RR 0.49, 95%CI: 0.21, 1.16; p=NR). The upper 95% CI did not exceed the proposed NIM of 1.28. Due to substantial heterogeneity caused by including data from the small phase II PATHWAY trial, the analysis was repeated using only the phase III NAVIGATOR trial. This analysis showed a marginally statistically significant result favouring tezepelumab over dupilumab (RR 0.67; 95% CI 0.45, 0.99; p=0.045).

6.27 For patients with an eosinophil count of 150 cells/µL on high-dose ICS and taking OSC, there was no statistically significant difference in AAER for tezepelumab compared with dupilumab (RR 1.03, 95%CI: 0.48, 2.21; p=0.94). The upper 95% CI exceeded the NIM of 1.28.

6.28 The PSCR argued additional data supporting the non-inferiority efficacy claim in the eosinophilic or allergic SUA population included the non-randomised WAYFINDER study (N=298) and a retrospective study by Biener et al. 2024[3] (N=129). The PSCR argued that these studies provided evidence of tezepelumab efficacy in OCS-dependent populations. The Response stated that Biener et al. 2024 reported that tezepelumab was associated with a reduction in annual exacerbations and OCS use in a cohort where 37.2% received long-term OCS therapy.

## *Comparative harms*

6.29 An overview of the adverse events from the tezepelumab trials is summarised in Table 10.

[3] Biener L, Mümmler C, Hinze CA, Suhling H, Korn S, Fisser C, Biener A, Pizarro C, Lenoir A, Hackl C, Skowasch D, Milger K. Real-World Data on Tezepelumab in Patients With Severe Asthma in Germany. J Allergy Clin Immunol Pract. 2024 Sep;12(9):2399-2407.e5.

**Table 10: Summary of AEs in the tezepelumab trials**

| Trial ID | Tezepelumab 210 mg n/N (%) | Placebo n/N (%) | RR (95% CI) |
|---|---|---|---|
| **NAVIGATOR (52 weeks)** | | | |
| ≥1 AE | 407/528 (77.1) | 422/531 (79.5) | 0.97 (0.91, 1.03) |
| ≥1 SAE | 46/528 (8.7) | 70/531 (13.2) | 0.66 (0.46, 0.94) |
| asthma | 12/528 (2.3) | 40/531 (7.5) | NR |
| AE leading to discontinuation | 11/528 (2.1) | 19/531 (3.6) | 0.58 (0.28, 1.21) |
| Deaths | 0/528 | 2/531[a] | NR |
| Severe infections | 46/528 (8.7) | 44/531 (8.3) | NR |
| **PATHWAY (52 weeks)** | | | |
| ≥1 AE | 90/137 (65.7) | 91/138 (65.9) | 1.00 (0.84, 1.18) |
| ≥1 SAE | 13/137 (9.5) | 18/138 (13.0) | 0.73 (0.37, 1.43) |
| asthma | 4/137 (2.9) | 10/138 (7.2) | NR |
| AE leading to discontinuation | 2/137 (1.5) | 1/138 (0.7) | 2.01 (0.18, 22.0) |
| Deaths | 0/137 | 0/138 | NR |
| Severe infections | 1/137 (0.7) | 4/138 (2.9) | NR |
| **SOURCE (48 weeks)** | | | |
| ≥1 AE | 53/74 (71.6) | 65/76 (85.5) | 0.84 (0.71, 0.99) |
| ≥1 SAE | 11/74 (14.9) | 16/76 (21.1) | 0.71 (0.35, 1.42) |
| asthma | 2/74 (2.7) | 8/76 (10.5) | NR |
| AE leading to discontinuation | 2/74 (2.7) | 2/76 (2.6) | 1.03 (0.15, 7.10) |
| Deaths | 1/74 | 0/76 | NR |
| Severe infections | 4/74 (5.4) | 7/76 (9.2) | NR |
| **DESTINATION (NAVIGATOR)** [b] | | | |
| ≥1 AE | 359 (86.5) | 178 (86.4) | NR |
| ≥1 SAE | 58 (14.0) | 37 (18.0) | NR |
| AE leading to discontinuation | 4 (1.0) | 2 (1.0) | NR |
| Deaths | 7 (1.7) | 1 (0.5) | NR |
| **DESTINATION (SOURCE)** [c] | | | |
| ≥1 AE | 52 (86.7) | 31 (96.9) | NR |
| ≥1 SAE | 14 (23.3) | 7 (21.9) | NR |
| AE leading to discontinuation | 0 | 0 | NR |
| Deaths | 1 (1.7) | 0 (0.0) | NR |

Source: Table 2-84, 153; Table 2-154, p246; Table 2-86, p155; Table 2-98, p164; Table 2-103, Table 2-104 p170 of the submission. NAVIGATOR CSR – Table 40, p205 and post-hoc calculations using https://www.medcalc.org/calc/relative_risk.php

AE = adverse event; CI = confidence interval; q4w = every 4 weeks; q8w = every 8 weeks; RR = rate ratio; SAE = Serious adverse event; NR= not reported.

[a] The submission stated that 2 deaths occurred during the on study period, both of which occurred in the placebo group (one due to an unknown cause and one due to cardiac failure). Neither death was considered by the investigator to be related to the investigational product (p158 of the submission)

[b] Tezepelumab plus Tezepelumab (N= 415) versus placebo plus placebo (N=206) (FAS-LTE)

[c] Tezepelumab plus tezepelumab (N= 60) versus placebo plus placebo (N=32) (FAS-LTE)

6.30 Adverse events in the tezepelumab versus placebo groups occurred in 77% versus 80% of patients, respectively, in the NAVIGATOR study; 72% versus 86%, respectively, in the SOURCE study; and 66% of patients in each group in the PATHWAY study.

6.31 The frequency of adverse events in the DESTINATION study was generally balanced between the tezepelumab and placebo groups. However, a numerical imbalance in both the deaths and cardiac disorder System Organ Class (SOC) serious adverse events were noted by the sponsor when considering the FAS and were subject to further evaluation (Table 11). Investigator assessment and blinded Independent Adjudication Committee review reported that none of the deaths were considered related to tezepelumab. In terms of the cardiac disorder SOC serious adverse events, the tezepelumab TGA product information states 'In a long-term clinical study, there were more numerically serious cardiac adverse events observed in patients treated with tezepelumab compared to those treated with placebo. No causal relationship between tezepelumab and these events has been established, nor has a patient population at risk of these events been identified.' The product information notes the figures in Table 11 and states 'The difference in events compared with placebo was present despite a similar spread of cardiovascular risk factors and diagnoses between the drug and the placebo groups at baseline. All patients who experienced a serious cardiac adverse event had an existing cardiovascular disorder or at least two cardiovascular risk factors at baseline. The types of serious cardiac adverse events were heterogeneous.' The product information states that patients should be advised of signs or symptoms suggestive of a cardiac event and to seek immediate medical attention if such symptoms occur.

**Table 11: Summary of deaths and cardiac disorder SOC SAEs in DESTINATION (NAVIGATOR and SOURCE)**

| | All TEZE (N=839) [a] Total time at risk on treatment = 1282.9 y Total time at risk on study = 1379.6 y | | Rand placebo (N=607) [a] Total time at risk on treatment = 799.0 y Total time at risk on study = 868.3 y | |
|---|---|---|---|---|
| | N | IR (95% CI)/100 py | N | IR (95% CI)/100py |
| **Death** | | | | |
| On treatment | 10 | 0.78 (0.37, 1.43) | 1 | 0.13 (0.00, 0.7) |
| On study | 11 | 0.80 (0.40, 1.43) | 5 | 0.58 (0.19, 1.34) |
| **Cardiac disorder SOC SAEs** | | | | |
| On treatment | 17 | 1.33 (0.77, 2.12) | 0 | 0.00 (0.00, 0.37) |
| On study | 18 | 1.30 (0.77, 2.06) | 2 | 0.23 (0.03, 0.83) |

Source: Table 2-111, p178.

CI = confidence interval; IR = incidence rate; PBO = placebo; py = person years; Rand = randomised; SAE = serious adverse event; SOC = System Organ Class; TEZE = tezepelumab; y = years

Note: Incidence rate = Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100. The 95% CI for the incidence rate is calculated using a chi-square distribution and for the 0 rate a (0, 1-sided 95% CI) is included.

[a] All TEZE includes subjects randomised to TEZE in the predecessor studies NAVIGATOR and SOURCE and subjects re-randomised from PBO to TEZE in DESTINATION (and as such the N includes the 1 subject randomised to TEZE in DESTINATION with a fatal AE prior to receiving TEZE, however the fatal AE is counted under the Rand PBO group). Rand PBO includes subjects randomised to placebo in the predecessor studies.

6.32 The PSCR noted that the tezepelumab cumulative global post-marketing patient exposure (January 2022−30 November 2024) includes an estimated 73,425 patient-years and reports 131 serious cardiac events with 75 medically confirmed. The

Response noted that no causal relationship between tezepelumab and these events has been established.

6.33 Table 12 presents the results of the safety indirect comparison (tezepelumab vs dupilumab). All indirect comparisons favoured tezepelumab. Indirect comparisons of the additional comparators benralizumab, mepolizumab and omalizumab are not discussed in this document.

**Table 12: Eosinophilic or allergic SUA results of the safety indirect comparison (tezepelumab vs dupilumab)**

| Analysis | Comparison (n) | RR (95% CI) |
|---|---|---|
| **Safety** | | |
| AEs | TEZE vs DUPI 200/300 (4372) | 0.96 (0.87, 1.05) |
| SAEs | TEZE vs DUPI 200/300 (4372) | 0.64 (0.43, 0.95) |
| Withdrawals due to AEs | TEZE vs DUPI 200/300 (4372) | 0.68 (0.32, 1.44) |

Source: Table 2-156, p247 of the submission

AE= adverse event; CI = confidence interval; DUPI = dupilumab; ITC = indirect treatment comparison; RR = rate ratio; SAE = serious adverse event; TEZE = tezepelumab

RR <1 favours TEZE over the comparator.

## *Benefits/harms*

6.34 A benefits and harms table is not presented for the eosinophilic or allergic SUA population, as the submission made a claim of non-inferiority to dupilumab.

6.35 For the non-eosinophilic and non-allergic SUA population, on the basis of the direct evidence presented in the NAVIGATOR[4] trial, patients treated with tezepelumab in comparison with placebo over 52 weeks experienced approximately 34% fewer asthma exacerbations. In the extended follow up data, for all patients, based on the evidence presented in DESTINATION[5] study, a higher incidence of cardiac disorder SOC serious adverse events were noted for tezepelumab treated patients compared to placebo.

## *Clinical claim*

### Non-eosinophilic and non-allergic SUA

6.36 For the non-eosinophilic and non-allergic SUA population, the submission described tezepelumab as superior in terms of effectiveness compared to placebo. The ESC noted the following uncertainties regarding the data presented in the submission:

[4] Results from the SUA subgroup of patients with non-EOSic (<300cells/µl) + non-allergic (perennial specific IgE status negative) + high ICS

[5] Patients randomised to tezepelumab in the predecessor studies NAVIGATOR and SOURCE and patients re-randomised from placebo to tezepelumab in DESTINATION

- The rate ratios observed in the subgroup analyses showed marked variation for the primary outcome of AAER (NAVIGATOR: RR 0.66, 95% CI: 0.43, 0.99; PATHWAY: RR 0.33, 95% CI: 0.09, 1.18), with statistical significance in only one study with the upper bound of the CI almost crossing 1 (0.99). While the direction of effect was consistent, the inconsistency in statistical significance increased uncertainty.
- The non-eosinophilic and non-allergic SUA subgroup represented a small proportion of the participants in both the NAVIGATOR trial (tezepelumab 86/528= 16%; placebo 83/531 = 16%) and PATHWAY trial (tezepelumab 18/137 = 13%; placebo 13/138 = 9%). Data from the SOURCE trial for this subgroup was not presented. The reduced sample size increased uncertainty.

The ESC noted additional supportive data presented in the PSCR , including a meta-analysis and published pooled analyses (see paragraph 6.22) and considered that overall, despite some uncertainty in the overall evidence, the clinical claim appeared to be supported.

6.37 The submission described tezepelumab as non-inferior in terms of safety in the non-eosinophilic and non-allergic SUA subgroup compared to placebo. The ESC noted that no direct evidence on safety was provided for this population, as no subgroup analysis on safety was reported, with the comparison including all participants in the NAVIGATOR and PATHWAY trials. However, the ESC noted that disease phenotype is not likely to affect safety and a claim of non-inferior safety being reasonable for eosinophilic or allergic SUA (paragraph 6.42).

6.38 The PBAC considered that the claim of superior comparative effectiveness was adequately supported by the data.

6.39 The PBAC considered that the claim of non-inferior comparative safety was reasonable.

**Eosinophilic or allergic SUA**

6.40 For the eosinophilic or allergic SUA population, the submission described tezepelumab as non-inferior in terms of effectiveness compared to dupilumab (primary comparator) and additional comparators (benralizumab, mepolizumab and omalizumab). The ESC noted the key issues were:

- All indirect comparisons of efficacy were based on post hoc subgroups. This reduced the sample size and thus increased uncertainty in the results.
- There were transitivity issues between the trials included in the indirect comparisons, which may have introduced bias (as described in paragraphs 6.13−6.14).

6.41 The ESC noted that the evidence presented for the eosinophilic or allergic SUA population was the same as previously considered by ESC at their June 2022 meeting.

The ESC recalled it had previously considered that the evidence for tezepelumab was less robust for the OCS dependent population and that overall, the strength of evidence to support a conclusion of non-inferior effectiveness was consistent with the evidence that was considered for dupilumab in November 2020. (paragraph 6.61, tezepelumab ESC advice, July 2022 PBAC Meeting). The ESC noted the additional supportive data provided in the PSCR (paragraph 6.28). Overall, the ESC considered the efficacy claim was generally supported.

6.42 The submission described tezepelumab as non-inferior in terms of safety compared to dupilumab (primary comparator) and additional comparators (benralizumab, mepolizumab and omalizumab). Overall, the ESC considered this was reasonable.

6.43 The PBAC considered that the claim of non-inferior comparative effectiveness was adequately supported by the data.

6.44 The PBAC considered that the claim of non-inferior comparative safety was reasonable.

## *Economic analysis*

### Non-eosinophilic and non-allergic SUA

6.45 The submission presented a stepped economic evaluation of tezepelumab compared to SoC in patients with non-eosinophilic and non-allergic SUA who require high-dose ICS.

6.46 The type of economic evaluation presented was a cost-utility analysis and cost-effectiveness approach. The cost-utility analysis was consistent with the clinical claim of superior effectiveness and non-inferior safety of tezepelumab compared to SoC for the population.

6.47 The key features of the economic evaluation are presented in Table 13.

**Table 13: Summary of model structure, key inputs and rationale**

| Component | Description |
|---|---|
| Population | Patients with non-eosinophilic and non-allergic SUA, aged 56 years. 32.9% assumed to be men. |
| Treatments | Tezepelumab + SoC compared to SoC |
| Type of analysis | Cost-utility analysis / cost-effectiveness analysis |
| Outcomes | Number of exacerbations.<br>Change in the rate of asthma exacerbations.<br>Change in the proportion of exacerbations requiring hospitalisation.<br>Change in the proportion of exacerbations leading to emergency department admission and OCS burst.<br>Change in the quality of life.<br>OCS sparing and associated OCS adverse event avoidance. |
| Time horizon | 40 years in the model base case compared to 52 weeks in the key trials. Age at model entrance was assumed to be 56 years based on the mean baseline age of patients in the NAVIGATOR and SOURCE trials. |
| Methods used to generate results | Markov cohort model. The evaluation considered that this was likely reasonable. |

| Component | Description |
|---|---|
| Health states | 5 core health states each for OCS users and OCS non-users:<br>- Controlled asthma: ACQ-6 <1.5 without exacerbation.<br>- Uncontrolled asthma: ACQ-6 ≥1.5 without exacerbation.<br>- Exacerbation (from the controlled health state).<br>- Exacerbation (from the uncontrolled health state).<br>- Dead: Includes asthma-related mortality and all-cause mortality.<br>The evaluation considered that the use of these health states was reasonable and consistent with published evidence. |
| Cycle length | 4 weeks. Aligned with the dosing regimen of tezepelumab. |
| Population and source data | Derived from subgroups within the NAVIGATOR and SOURCE trials.<br>All analyses were based on a subgroup of patients with non-eosinophilic ([EOS ≤ 150 cells/μL and OCS] or [EOS ≤ 300 cells/μL no OCS]) **OR** non-allergic (IgE<30) SUA using high-dose ICS. This did not align with the proposed PBS population non-eosinophilic ([EOS ≤ 150 cells/μL and OCS] or [EOS ≤ 300 cells/μL no OCS]) **AND** non-allergic (IgE<30) SUA using high-dose ICS. There was a lack of transparency and missing trial data which introduced uncertainty in the model. |
| Time on treatment | The economic model considered two types of treatment discontinuation: ongoing discontinuation based on observed data from the trials (probability per month [with OCS = 1.299%; without OCS = 0.648%]), and discontinuation based on a stopping rule and response assessment at 32 weeks. This restricted continued treatment to patients with controlled disease (defined as ACQ-6 < 1.5) and therefore discontinued patients with uncontrolled disease (ACQ-6 ≥ 1.5).<br>The discontinuation probabilities could not be verified during the evaluation and were not consistent with those reported in the full analysis set of the NAVIGATOR and SOURCE trials (discontinuation rates of 6.8% at week 52 and 10.8% at week 48, respectively). |
| Definition of response rate | Controlled asthma was defined as ACQ-6 score <1.5. Uncontrolled asthma was defined as ACQ-6≥1.5. The evaluation considered that this was not reasonable. It was not consistent with the current guidelines and published studies, which suggest that ACQ-6 <0.75 indicated well-controlled asthma. |
| Rate of exacerbations | Annual event rates of controlled and uncontrolled asthma used in the submission were:<br>- Tezepelumab + OCS and SoC + OCS: Controlled= 1.15, Uncontrolled =1.88<br>- Tezepelumab - OCS: Controlled= 0.49, Uncontrolled =1.12<br>- SoC - OCS: Controlled = 0.98, Uncontrolled 2.20 per year<br>The submission assumed that compared to SoC, tezepelumab did not lower the risk of exacerbation in patients on OCS, and that tezepelumab decreased the risk by 50% among patients not on OCS. |
| Transition probabilities for death | Asthma-related deaths:<br>- Exacerbation with OCS burst = 1.13% (Mepolizumab PSD, March 2016 PBAC meeting)<br>- Exacerbation with ED visit = 1.8% (Bacharier 2018)<br>- Exacerbation with hospitalisation = 2.5% (De Vries 2010)<br>- Age based all-cause mortality was based on ABS life tables (2021-2023).<br>A mortality benefit of tezepelumab versus SoC was modelled indirectly as fewer exacerbation events were assumed to occur for tezepelumab vs SoC. However, a mortality benefit was not demonstrated in the clinical trials. The evaluation considered that the magnitude of difference between these mortality estimates also appeared infeasible. The evaluation also considered that the sources of the estimates for exacerbation with ED visit or with hospitalisation were also not reliable. |
| Probability of adverse events | The economic evaluation did not model a difference in AEs based on the clinical claim that tezepelumab was non-inferior to SoC in terms of safety. |

| Component | Description |
|---|---|
| Health state utility values | Based on the NAVIGATOR and SOURCE trials:<br>- Controlled asthma = 0.875<br>- Uncontrolled asthma = 0.631<br>Disutilities:<br>- Exacerbation requiring OCS burst = 0.100 (Lloyd 2006)<br>- Exacerbation requiring ED visit = 0.150 (assumption)<br>- Exacerbation requiring hospitalisation = 0.200 (Lloyd 2006).<br>The economic model also applied disutilities for AEs associated with OCS use; based on marginal disutilities corresponding to different chronic conditions (categorised by Complex Chronic Conditions codes) reported in a UK-based catalogue of EQ-5D index scores (Sullivan 2011). This was consistent with disutilities used in published studies and the evaluation considered that this was appropriate. |
| Costs | Tezepelumab cost: Weighted DPMQ= $[redacted]/dose; Effective DPMQ= $[redacted]/dose<br>Administration costs: $88.90 (one-off application of MBS item 82215)<br>SoC costs: $48.26/pack [a]<br>OCS cost: $18.18/pack [b]<br>Disease management costs:<br>- GP Visit (Outpatient), GP visit (Home) $43.90 (MBS item 23)<br>- Respiratory specialist visit (outpatient) Initial=$178.70 (MBS item 110)<br>- Respiratory specialist visit (outpatient) Subsequent= $89.40 (MBS item 116)<br>- Spirometry=$48.05 (MBS item 11505)<br>- Desensitisation of asthma= $92.95 [c]<br>- ED visit= $883.94 [d]<br>- Hospital admission= $5,322<br>For GP Visit (Home). MBS item 24 would have been more appropriate. The cost of an ED admission for Australian Emergency Care Classification (AECC) E0430B 'Asthma Complexity level B' was $1,033. The ICER was not sensitive to the disease management costs. |
| Software package | Microsoft Office 365 Excel. |

Source: Compiled during the evaluation from Table 2-127, p198; Table 3-5, pp256-257; pp274-276, p278, Table 3-14, p283, p285 of the submission.

ACQ-6 = asthma control questionnaire 6-question version, CDA, Canadian Drug Agency; ; DPMQ= dispensed price for maximum quantity; ED= emergency department; ICER = incremental cost-effectiveness ratio, NICE = National Institute of Health Care and Excellence, OCS = oral corticosteroid, QALY = quality-adjusted life-year, SoC = standard of care.

[a] The cost of fluticasone propionate was $48.26 per pack (as of 1 August 2025).

[b] The submission calculated the cost of 1 milligram based on Jan 2025 PBS DPMQ of $17.85 per pack (30 tablets, 25 mg each) = 17.85/750. The cost of prednisolone was $18.18 per pack (as of 1 August 2025).

[c] Desensitisation using Actair: sold privately. Cost derived from https://www.healthylife.com.au/products/actair-continuation-300ir-subl.

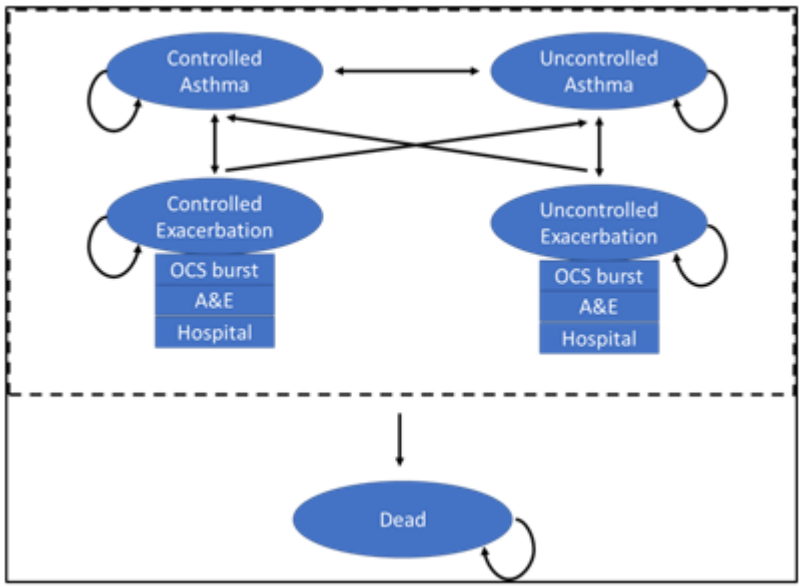
[d] Source not reported.

[e] Updated AR-DRG cost for E69A 'Bronchitis and Asthma, Major Complexity' costs based on rates as of 1 August 2025.

6.48 The submission presented a Markov model with 5 core health states: uncontrolled asthma; controlled asthma; previously uncontrolled asthma with exacerbation (uncontrolled exacerbation); previously controlled asthma with exacerbation (controlled exacerbation); and dead (Figure 2). Health states were further stratified by OCS use. The asthma control health states were defined based on ACQ-6 scores (controlled asthma: ACQ-6 score <1.5 without exacerbation; uncontrolled asthma: ACQ-6 score ≥ 1.5 without exacerbation). The exacerbation health states were defined as a worsening of asthma symptoms that causes 1 of 3 events: a burst of OCS for at least 3 consecutive days, an emergency department visit, or hospitalisation.

6.49 Individuals entered the model with uncontrolled asthma and could transition to other health states from the first model cycle. The starting proportion of OCS used to distribute patients among OCS and no OCS health state variants was defined by baseline characteristics and did not differ by treatment arm. The evaluation considered that the model structure was reasonable and consistent with the published literature.

**Figure 2: Model structure for the 5-state Markov model**




Source: Figure 3-1, p 269
A&E = Accident and emergency department; OCS= Oral corticosteroids; SoC= standard of care

6.50 Individuals could transition from 'with OCS' states to 'without OCS' states through OCS discontinuation. Individuals receiving OCS were further stratified into dosing categories, where the risk of adverse events was a function of the dose of OCS received. Individuals on tezepelumab transitioned to SoC (discontinued treatment) through natural attrition (probability per month [with OCS = 1.299%; without OCS = 0.648%]) or via a response assessment at 32 weeks. This response assessment or 'stopping rule' meant that individuals who responded to tezepelumab treatment (i.e. those in 'controlled state', with ACQ-6 < 1.5) at week 32 qualified for continued treatment, whereas those who did not respond discontinued treatment and were assumed to have the same efficacy profile and costs of SoC. Week 32 was selected based on the PBS restrictions for dupilumab, omalizumab, benralizumab and mepolizumab. It is also consistent with the proposed PBS restriction. The evaluation noted that it is possible that for some patients the effect of tezepelumab at 32 weeks would not be sustained at week 52, in which case the response estimated may have been overestimated. Conversely, it is possible that response to tezepelumab at 32 week was less than that at week 52, in which case response may have been underestimated. This introduced uncertainty in the economic model. Furthermore, for

the consideration of mepolizumab for the treatment of severe eosinophilic asthma, the ESC recalled it had previously noted that if this continuation criterion (of 32 weeks) was not effectively applied in practice, the ICER would be higher than estimated in the submission (assuming that patients not meeting this criterion have higher exacerbation rates than patients who do meet this criterion) (para. 6.33, mepolizumab PSD, March 2016 PBAC Meeting). The ESC noted that due to the model setup, the impact of patients with a lower response remaining on treatment post-32 weeks could not be directly tested in a sensitivity analysis, and considered that this was not appropriate, and led to uncertainty in the economic model. The pre-PBAC Response (p1) stated that the stopping rule could be removed in the Excel workbook by overwriting a reference to a named range for discontinuation parameters in the non-user facing Markov trace for tezepelumab. The PBAC considered that this method for changing a key input was likely inappropriate and overly complex. The PBAC also noted that this change resulted in the uncontrolled discontinuation rate to equal the controlled discontinuation rate and does not change the one-off OCS-related discontinuation at 32 weeks (54.3%) in the tezepelumab arm.

6.51 The submission applied a lifetime time horizon of 40 years to capture the costs and benefits of tezepelumab. The age of initiating patients in the model was 56 years, based on the mean age in the NAVIGATOR and SOURCE trials. The ESC considered that the lifetime time horizon in the model (40 years) was long compared to the duration of follow-up in the NAVIGATOR trial (52 weeks) and the SOURCE trial (48 weeks). It is likely that using a long time horizon overestimated the effects of tezepelumab. The model assumed that after the 32 week response assessment, the treatment effect of tezepelumab would be maintained over a lifetime. No treatment waning was assumed. The ESC agreed with the evaluation that this was likely not reasonable. The PBAC previously considered that extrapolation to 50 years may not be reasonable and was highly uncertain for the consideration of omalizumab for the treatment of patients with allergic SUA (para. 12, omalizumab PSD, November 2010 PBAC Meeting). The ESC considered that a 20-year time horizon would be more reasonable and noted that this change to the model increased the incremental cost-effectiveness ratio (ICER) from $75,000 to < $95,000 to $75,000 to < $95,000 (+[redacted]%) per quality adjusted life year (QALY) gained.

6.52 The submission stated that the economic model inputs were derived from pooled clinical trial data from the SOURCE and NAVIGATOR trials. It could not be verified if relevant subgroup data were used from the 2 trials during the evaluation. The economic model was developed using individual patient data that differed from the data presented in the clinical section of the submission and assumed an assessment at 32 weeks using an outcome definition of controlled asthma (ACQ threshold of 1.5) which was not consistent with that in the trials. It was also not consistent with the continuation criterion in the proposed restriction (an adequate response to treatment

defined as a reduction in the ACQ-5 score of at least 0.5 points from baseline). The ESC agreed with the evaluation that this lack of data transparency and difference in outcome definitions used in the model compared to in the trials and proposed PBS population introduced significant uncertainty in the model. The pre-PBAC Response (p1) argued that an ACQ-6 <1.5 threshold was conservative and consistent with real-world data showing higher exacerbations and poorer quality of life for patients above a score of 1.5.

6.53 The ESC noted that the model did not use data from the PATHWAY trial and did not justify excluding this data from the economic model. The PATHWAY trial included patients with SUA who may or may not have received maintenance OCS and were non-eosinophilic and non-allergic on high-dose ICS. The ESC considered that the exclusion of these data was not reasonable and introduced uncertainty in the economic model.

6.54 The proposed population is patients with non-eosinophilic **AND** non-allergic SUA using high-dose ICS. However, the economic model used trial data for subgroup of patients with non-eosinophilic **OR** non-allergic SUA using high-dose ICS (see Table 13). The submission stated that this difference was necessary because there was insufficient information available for the non-eosinophilic and non-allergic SUA subgroup. This was not appropriate as the trial data used in the model did not align with the proposed PBS population. Therefore, the model likely included allergic or eosinophilic populations, which introduced significant uncertainty in the ICER. Including these populations likely favoured tezepelumab because the NAVIGATOR and the PATHWAY trials demonstrated a statistically significant reduction in AAER in their full analysis sets (see Table 5) but only a borderline significant reduction for the non-eosinophilic and non-allergic subgroup, with the other failing to reach statistical significance (NAVIGATOR, PATHWAY trials, respectively; see Table 7). Furthermore, AAER data for the non-eosinophilic and non-allergic population of the SOURCE trial were not provided in the submission. The PSCR acknowledged there was a discrepancy between the modelled and proposed PBS population, however maintained that this was unavoidable due to data scarcity. The ESC noted that the PSCR stated that the data included in the model were consistent with the published data and the observed effect of tezepelumab to reduce exacerbations across biomarker-defined subgroups, including different combinations of IgE and EOS levels (Corren et al. 2023, discussed in paragraph 6.22), however considered that this remained a primary uncertainty in the model and likely favoured tezepelumab.

6.55 There was a distinct drop in patients on treatment in the model due to the stopping rule at week 32. The model showed that at 32 weeks, 94.4% of the cohort was on tezepelumab, and at 36 weeks, 45.1% were on tezepelumab. This indicated that 49.3% of patients on tezepelumab discontinued after the week 32 assessment, either because they did not respond or they switched to SoC. This assumed discontinuation was not consistent with the trial data; it was however consistent with the proposed PBS population. For the full analysis set, the NAVIGATOR and SOURCE trials reported

a lower discontinuation rate in the tezepelumab arm than that used in the economic model — 6.8% at week 52 (NAVIGATOR) and 10.8% at week 48 (SOURCE). For the full analysis set, the long-term extension study of the NAVIGATOR and SOURCE trials— the DESTINATION trial also reported a lower discontinuation rate in the tezepelumab arm than that used in the economic model— 21.4% in the tezepelumab arm of the NAVIGATOR trial and 19.1% in the SOURCE trial. The raw data for transition probabilities, pre- or post-32-week assessment, could not be verified for the subgroups of interest during the evaluation. These data were not reported in the trial CSRs or the trial publications for either the NAVIGATOR or SOURCE trials. Also, the trials' definition of controlled disease was not consistent with that of the submission (as described in the subsequent paragraphs). Therefore, the trial's effect estimates of AAER and proportion of patients considered controlled or uncontrolled were likely different from the model's inputs. The evaluation considered this introduced uncertainty in the model.

6.56 The ACQ-6 threshold of 1.5 used in the submission and economic model was not consistent with the definitions used in the trials or published data, or previous PBAC considerations of biologics in SUA and introduced uncertainty in the model. The SOURCE trial described lower ACQ-6 to indicate better disease control: scores higher than 1.5 indicate inadequately controlled asthma and scores lower than 0.75 indicate well-controlled asthma (Wechsler 2022). In the PBAC's consideration of omalizumab for SUA, failure to achieve adequate control was defined as an ACQ-5 score of at least 2.0, as assessed in the previous month (para. 4, p1, omalizumab PSD, November 2010 PBAC Meeting), and an adequate response to omalizumab treatment was a reduction in the ACQ-5 score of at least 0.5 from baseline (para. 4, p2, omalizumab PSD, November 2010 PBAC Meeting). A reduction of at least 0.5 points from baseline is consistent with the proposed continuing restriction for tezepelumab. Similar restrictions to the omalizumab assessment were listed for benralizumab (para. 8, benralizumab PSD, March 2018 PBAC Meeting), dupilumab (para. 8, dupilumab PSD, November 2020 PBAC Meeting) and mepolizumab (para. 6, mepolizumab PSD, March 2024 PBAC Meeting). The PSCR argued that applying a threshold of 1.5 ACQ-5 points provides a meaningful marker for assessing treatment effectiveness which aligns with real-world outcomes and was methodologically conservative. However, the ESC noted that it was unclear whether this stratification would be representative of the proposed PBS population (individuals who obtain a reduction of at least 0.5 ACQ-5 points from baseline).

6.57 The economic model assumed that tezepelumab did not lower the risk of exacerbation in individuals on OCS (i.e. the rates of exacerbations for tezepelumab + OCS and SoC + OCS both equalled 1.15/1.88 for each controlled/uncontrolled patient per year). However, the model assumed that tezepelumab reduced exacerbation risk by 50% compared with SoC in individuals not on OCS (i.e. the rates of exacerbations for tezepelumab-OCS and SoC-OCS were 0.49/1.12 and 0.98/2.20 for each

controlled/uncontrolled patient per year). However, the supporting evidence for a benefit in AAER for tezepelumab patients relative to SoC was uncertain in this population (see paragraph 6.36). Assuming the exacerbation rate to be equal for tezepelumab and SoC in the non-OCS dependent group increased the ICER by [redacted]% to $135,000 to < $155,000 per QALY gained. The PSCR argued that modelling no difference in risk between tezepelumab and SoC in the non-OCS group would be inconsistent with the clinical evidence. The Response noted that the 50% reduction in exacerbation risk assumed for tezepelumab treated patients (not receiving OCS) had been informed by subgroup analyses of IPD from the NAVIGATOR trial, where patients with uncontrolled disease experienced a decrease in annual exacerbation rate from 2.2 to 1.1, and those with controlled disease from 1.0 to 0.5. The Response also noted this reduction had been supported by a meta-analysis of AAER data from the NAVIGATOR and PATHWAY trials (OR 0.62, 95% CI 0.42–0.92; p = 0.02; paragraph 6.22). The ESC noted that the PSCR included a sensitivity analysis with a reduced effect on exacerbation rates (from a 50% to 37.5% reduction [RR 0.625]) and noted that this increased the base case ICER to $75,000 to < $95,000 per QALY gained. The ESC agreed with the PSCR that this would be more consistent with the supporting pooled analysis (OR 0.62) and noted it was also consistent with the NAVIGATOR trial evidence for this population (34% reduction). The ESC considered that a smaller reduction in exacerbation risk (from 50% to 38%) would be appropriate to include in a respecified base case.

6.58 The economic model included exacerbation-related mortality for OCS bursts (1.13% per month); emergency department (ED) visits (1.8% per month); and hospitalisation (2.5% per month), and general population mortality to estimate mortality risk in non-exacerbation health states. A mortality benefit was indirectly modelled for tezepelumab versus SoC because tezepelumab was assumed to reduce the rate of severe exacerbations. The evaluation considered that applying exacerbation-related mortality to the economic model was not appropriate given that asthma-related deaths are rare. Furthermore, a mortality benefit associated with tezepelumab was not demonstrated in the trials.

6.59 The evaluation considered that the sources used to derive the probabilities of mortality after exacerbation requiring an ED visit or hospital admission were not reliable. The 1.8% mortality rate assumed for an exacerbation requiring an ED visit was

sourced from an abstract by Bacharier (2018)[6]. However, it did not contain any information on mortality rates from asthma exacerbation for patients on tezepelumab. The 2.5% mortality rate assumed for an exacerbation requiring hospitalisation was sourced from a study by De Vries (2010)[7]. This study was based on a UK General Practice Research Database (GPRD), which did not include any patients receiving a biologic medicine. The study reported rates based on an analysis of a prescription database and did not consider confounding factors such as comorbidities or other factors that could result in death. Therefore, using this study as a source in the economic model introduced uncertainty. The economic model used for the mepolizumab submission (severe eosinophilic asthma) included similar mortality probabilities. In considering mepolizumab, the ESC considered that the magnitude of difference between these mortality estimates (i.e. risk of mortality is more than doubled if an exacerbation requires hospitalisation compared to exacerbation without hospitalisation) appeared infeasible, and a review of similar parameter estimates from published asthma cost-effectiveness models should have been presented to demonstrate feasibility (para. 6.37, mepolizumab PSD, March 2016 PBAC Meeting). In the current submission, mortality was a driver of the ICER. Removing exacerbation-related mortality resulted in an ICER of $155,000 to < $255,000 per QALY gained, an increase of [redacted]% from the base case. The PSCR maintained that the inclusion of exacerbation-related mortality in the economic evaluation was appropriate. The PSCR noted that published studies report mortality rates among hospitalised asthma patients that range between 0.43−0.9% (Watson et al., 2007[8]; Krishnan et al., 2006[9]; Roberts et al., 2013[10]) and highlighted that this risk increases with age. The PSCR noted that in the UK, patients over 45 experience a mortality rate of 2.4% (Roberts et al., 2013; Watson et al., 2007). The PSCR also noted that a French retrospective observational study of 467,716 individuals which reported 739 (4.5%) patients with severe uncontrolled disease had a 2-year survival probability of 92.0% compared to

[6] Bacharier, L., Casale, T., Holden, M., Rajput, Y., Dang, J., Li, Q., ... & Karabis, A. (2018). Differences in eligibility criteria and baseline patient characteristics amongst trials of biologic therapies in asthma. Annals of Allergy, Asthma & Immunology, 121(5), S45-S46.

[7] De Vries, F., Setakis, E., Zhang, B., & Van Staa, T. P. (2010). Long-acting β2-agonists in adult asthma and the pattern of risk of death and severe asthma outcomes: a study using the GPRD. European Respiratory Journal, 36(3), 494-502.

[8] Watson L, Turk F, James P, Holgate ST (2007) Factors associated with mortality after an asthma admission: a national United Kingdom database analysis. Respiratory medicine 101 (8): 1659-1664.

[9] Krishnan V, Diette GB, Rand CS, Bilderback AL, Merriman B et al. (2006) Mortality in patients hospitalized for asthma exacerbations in the United States. American journal of respiratory and critical care medicine 174 (6): 633-638.

[10] Roberts NJ, Lewsey JD, Gillies M, Briggs AH, Belozeroff V et al. (2013) Time trends in 30 day case-fatality following hospitalisation for asthma in adults in Scotland: a retrospective cohort study from 1981 to 2009. Respiratory medicine 107 (8): 1172-1177

96.6% in the general population (relative risk of death: 2.35; 95% CI: 1.70 to 3.29; p<0.0001). This group also exhibited higher rates of emergency department visits and hospitalisations (64.7% vs. 34.9%; p<0.0001)[11].

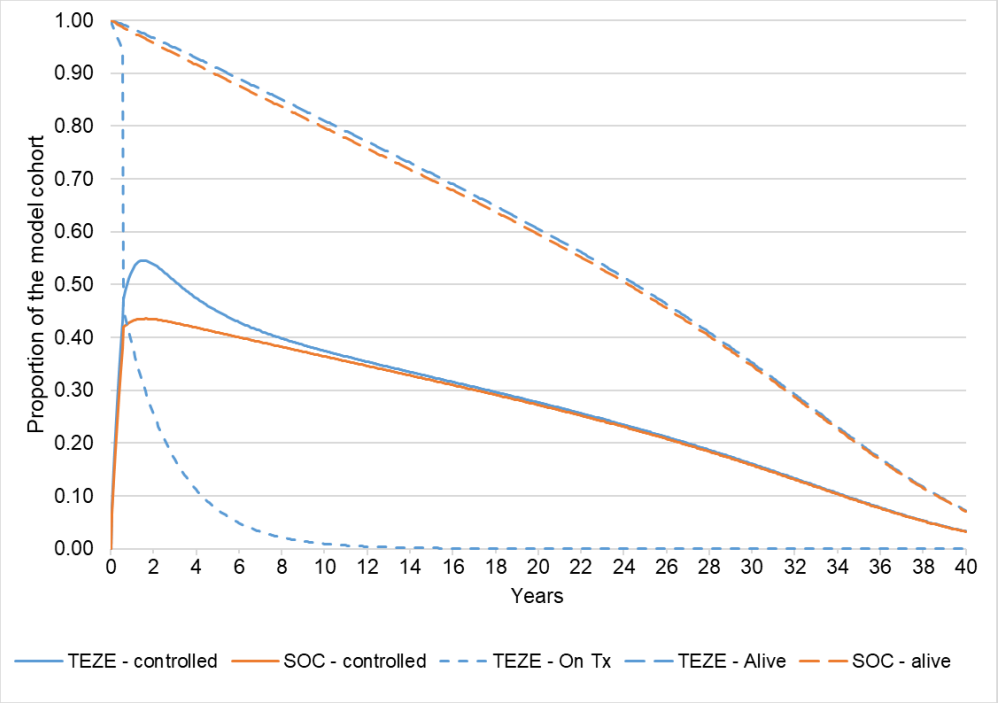
6.60 The ESC noted the additional studies referenced in the PSCR as supportive evidence for the mortality assumptions in the economic model. Overall, the ESC considered that the submission had likely overestimated the mortality benefit in the economic model and considered that reduced exacerbation-related mortality rates consistent with the mepolizumab economic model case (OCS burst: 0.43%; with ED or hospitalisation: 1.13%) would be appropriate to include in a revised base. The pre-PBAC Response noted that the ESC had previously considered 'that the magnitude of difference between these mortality estimates (i.e. risk of mortality is more than doubled if an exacerbation requires hospitalisation compared to exacerbation without hospitalisation) appeared infeasible, and a review of similar parameter estimates from published asthma cost-effectiveness models should have been presented to demonstrate feasibility' (paragraph 6.37, mepolizumab PSD, March 2016). The pre-PBAC Response therefore proposed a revised base case which applied a probably of 1.13% across all exacerbations (paragraph 6.67). However, the PBAC previously considered that the model could not be relied upon given the substantial variation in the outputs (paragraph 6.37, mepolizumab PSD, March 2016).

6.61 The economic model applied utility inputs of 0.875 for controlled asthma and 0.631 for uncontrolled asthma (difference in utility 0.244). The submission derived the inputs using Australian health state values using the mapping value set from the trial utilities: 0.877 for controlled asthma and 0.683 for uncontrolled asthma (difference in utility of 0.194). The ICER was moderately sensitive to the difference in utilities. Using the difference in utility of 0.194 increased the ICER by [redacted]% to $75,000 to < $95,000/QALY gained.

6.62 Figure 3 presents the Markov traces of the economic model. The submission noted that a difference in mortality was evident between tezepelumab and SoC from the 10-year mark, reflective of the modelled difference in fatal incident exacerbations. However, similar mortality would be more consistent with complete treatment discontinuation of tezepelumab by this time, while surviving patients in both treatment arms were on SoC and dying at an equal rate.

[11] Roche N, Garcia G, de Larrard A, Cancalon C, Bénard S, Perez V, Mahieu A, Vieu L, Demoly P. Real-life impact of uncontrolled severe asthma on mortality and healthcare use in adolescents and adults: findings from the retrospective, observational RESONANCE study in France. BMJ Open. 2022 Aug 24;12(8):e060160.

**Figure 3 Model trace: Proportion of cohort with controlled disease proportion alive and proportion on tezepelumab treatment**




Source: Figure 3-3, p302 of the submission.
TEZE= tezepelumab; SoC= standard of care

6.63 Table 14 presents the key drivers of the model.

**Table 14: Key drivers of the model**

| Description | Method/Value | Impact<br>Base case: $[redacted][1]/QALY gained. |
|---|---|---|
| Time horizon | The lifetime time horizon in the model (40 years) was long compared to the duration of follow-up in the NAVIGATOR trial (52 weeks) and the SOURCE trial (48 weeks). | Moderate, favours tezepelumab.<br>Reducing the time horizon to 20 years increased the ICER to $[redacted][1]/QALY gained. |
| Stopping rule at 32 weeks | A 32-week stopping rule was introduced so individuals who achieved a response on tezepelumab continued treatment in the model, and others switched to SoC. If this continuation criterion is not effectively applied in practice, the ICER would be higher than estimated in the submission. | High, favours tezepelumab. However, this could not be directly changed in the model.<br>Removing this 32-week assessment by assuming the same control probability before and after 32 weeks increased the ICER to $[redacted][1]/QALY gained. |
| Response definition | Controlled asthma: ACQ-6 score <1.5, and uncontrolled asthma: ACQ-6 score ≥1.5. This was not consistent with the published definitions and definitions used in the trials. | Likely moderate, favours tezepelumab. It could not be tested due to the model setup. |
| Exacerbation risk | Tezepelumab reduced exacerbation risk by 50% in individuals not on OCS. However, there were uncertainties related to the observed benefit in AAER in this population. | High, favours tezepelumab.<br>Removing this benefit increased the ICER to $[redacted][2]/QALY gained. |
| Exacerbation-related mortality | Risk of exacerbation-related mortality was 1.13% following OCS bursts; 1.8% following emergency department visits; and 2.5% following hospitalisation. The evaluation considered that sources used to derive exacerbation-related mortality requiring ED visit or hospitalisation were unreliable. | High, favours tezepelumab.<br>Using a mortality rate of 0% for all types of exacerbations increased the ICER to $[redacted][3]/QALY gained. |
| Patient population composition | The model had a high discontinuation rate in the tezepelumab arm (60.7%) at 32 weeks and retained only controlled asthma in the treatment arm, while others switched to SoC for the remainder of the time horizon. Therefore, only responders contributed to the tezepelumab arm in the model. | Likely high, favours tezepelumab. It could not be tested in sensitivity analysis due to the model setup. |

Source: Compiled during the evaluation from Table 2-127, p198; Table 3-5, pp256-257; pp274-276, p278, Table 3-14, p283, p285 of the submission.

ACQ-6 = asthma control questionnaire 6 question version, EQ-5D-5L= EuroQol 5 dimension 5 level; ICER = incremental cost-effectiveness ratio, QALY= Quality-Adjusted Life Years.

*The redacted values correspond to the following ranges:*

[1] *$75,000 to < $95,000*

[2] *$135,000 to < $155,000*

[3] *$155,000 to < $255,000*

6.64 The submission reported a base case ICER of $75,000 to < $95,000/QALY gained. The submission presented a stepped economic evaluation showing the transformation of exacerbation rates and ACQ response rates. However, the inputs for this stepped evaluation could not be verified or mapped to the trial reports because the model used individual patient data, with outcomes assessed at 32 weeks using a response definition of ACQ threshold of 1.5. The stepped economic evaluation developed during the evaluation is presented in Table 15.

**Table 15: Results of the stepped economic evaluation developed during the evaluation**

| Step and component | Tezepelumab | Standard of care | Increment |
|---|---|---|---|
| **Step 1: Trial-based costs and outcomes (Discount rate 0%, Time horizon 1 year)[a]** | | | |
| Costs[b] | $[redacted] | $581 | $[redacted] |
| LY[c] | 0.993 | 0.989 | 0.004 |
| Incremental cost/ LYG | | | $[redacted][1] |
| **Step 2: Time horizon extended to lifetime (40 years) horizon[d]** | | | |
| Costs[b] | $[redacted] | $13,258 | $[redacted] |
| LY[c] | 23.082 | 22.728 | 0.354 |
| Incremental cost/ LYG | | | $[redacted][2] |
| **Step 3: Discounting (5%) included** | | | |
| Costs | $[redacted] | $7,241 | $[redacted] |
| LY[c] | 12.590 | 12.410 | 0.180 |
| Incremental cost/ LYG | | | $[redacted][3] |
| **Step 4: Incorporation of medical resource costs** | | | |
| Costs[e] | $[redacted] | $31,957 | $[redacted] |
| LY[c] | 12.590 | 12.410 | 0.180 |
| Incremental cost/ LYG | | | $[redacted][3] |
| **Step 5: Incorporation of utilities** | | | |
| Costs | $[redacted] | $31,957 | $[redacted] |
| QALYs | 9.255 | 9.025 | 0.230 |
| Incremental cost/ QALY gained | | | $[redacted][4] |

Source: Developed during the evaluation from 'Attachment 3 2 CEA model Teze SUA July 2025.xlm', Tab 'Deterministic results'
LY= Life Years; LYG = life years gained; QALY = Quality adjusted life-years

[a] Calculated during the evaluation by setting the time horizon to 1 year to reflect the NAVIGATOR trial duration, although it was 4 weeks longer than the SOURCE trial. To replicate trial-based costs, the values of these cells were changed in 'Attachment 3 2 CEA model Teze SUA July 2025.xlm', Tab 'Summary': Cell D5 set to 1 for time horizon and Cell D10 set to 0 for discount rate. Trial-based costs were then calculated as described in footnote 'b'.

[b] Cost of tezepelumab was calculated as cost of tezepelumab + administration costs + cost of SoC + cost of OCS derived from 'Attachment 3 2 CEA model Teze SUA July 2025.xlm', Tab 'Deterministic Results' Cells J22, K22, L22 and M22 and the cost of SoC was calculated as cost of SoC + cost of OCS derived from 'Attachment 3 2 CEA model Teze SUA July 2025.xlm', Tab 'Deterministic Results' Cells J28, and M28.

[c] Derived from 'Attachment 3 2 CEA model Teze SUA July 2025.xlm', Tab 'Tezepelumab Trace' Cell HX8, and Tab 'SoC Trace' Cell JC8.

[d] Calculated by resetting the time horizon to 40 years used in the submission's model, 'Attachment 3 2 CEA model Teze SUA July 2025.xlm', Tab 'Summary': Cell D5 set to blank to reset the time horizon.

[e] Derived from 'Attachment 3 2 CEA model Teze SUA July 2025.xlm', Tab 'Deterministic Results': Cells E95 and F95.

*The redacted values correspond to the following ranges:*

[1] *> $1,055,000*

[2] *$55,000 to < $75,000*

[3] *$95,000 to < $115,000*

[4] *$75,000 to < $95,000*

6.65 The results of key univariate sensitivity analyses are summarised in Table 16.

**Table 16: Sensitivity analyses for the economic model for the non-eosinophilic and non-allergic subgroup**

| Analyses | Incremental cost | Incremental QALY | ICER ($/QALY gained) | % change from base case ICER |
|---|---|---|---|---|
| **Base case** | **$** [redacted] | **0.230** | **$** [redacted][1] | **0%** |
| **Discount rate (Base case 5%)** | | | | |
| 3.5% | $ [redacted] | 0.260 | $ [redacted][2] | - [redacted]% |
| 0% | $ [redacted] | 0.374 | $ [redacted][3] | - [redacted]% |
| **Time horizon (Base case 40 years)** | | | | |
| 10 years | $ [redacted] | 0.162 | $ [redacted][4] | [redacted]% |
| 20 years **#1** | $ [redacted] | 0.207 | $ [redacted][1] | [redacted]% |
| 25 years | $ [redacted] | 0.218 | $ [redacted][1] | [redacted]% |
| **Response probability in the SoC arm between 32-52 weeks (Base case: 0.721)** | | | | |
| Same as tezepelumab arm (0.886) | $ [redacted] | 0.134 | $ [redacted][5] | [redacted]% |
| **Exacerbation mortality (Base case: OCS burst, 1.13%; ED visit, 1.8%; Hospitalisation 2.5%)** | | | | |
| Mortality = 0% | $ [redacted] | 0.097 | $ [redacted][6] | [redacted]% |
| OCS burst: 0.43%; ED visit: 1.13%; Hospitalisation: 1.13% (based on mepolizumab PSD) **#2** | $ [redacted] | 0.159 | $ [redacted][4] | [redacted]% |
| Rate=1.13% for all exacerbation scenarios | $ [redacted] | 0.214 | $ [redacted][1] | [redacted]% |
| **Utility gain from controlled disease (Base case: 0.244)** | | | | |
| 0.00 (no utility gain)[a] | $ [redacted] | 0.121 | $ [redacted][7] | [redacted]% |
| 0.194 (Trial data)[b] | $ [redacted] | 0.208 | $ [redacted][1] | [redacted]% |
| **Effect on risk of exacerbation in the non-OCS population = 50%. (Base case: tezepelumab controlled: 0.49, uncontrolled: 1.12; SoC controlled: 0.98, uncontrolled 2.20 per year)** | | | | |
| Removal of effect. Rates for SoC equal to the rates for tezepelumab [c] | $ [redacted] | 0.119 | $ [redacted][7] | [redacted]% |
| Reduced effect on risk of exacerbation to 20%: annual rate of exacerbation, tezepelumab controlled: 0.784, uncontrolled 1.760; SoC controlled: 0.98, uncontrolled 2.20 [d] | $ [redacted] | 0.172 | $ [redacted][4] | [redacted]% |
| Reduced effect on risk of exacerbation to 38%: annual rate of exacerbation, tezepelumab controlled: 0.607, uncontrolled 1.364; SoC controlled: 0.98, uncontrolled 2.20[d] **#3** | $ [redacted] | 0.206 | $ [redacted][1] | [redacted]% |
| **Health state utility for controlled disease (Base case: 0.875)** | | | | |
| 0.74[e] | $ [redacted] | 0.170 | $ [redacted][4] | [redacted]% |
| **Health state utility for uncontrolled disease (Base case: 0.631)** | | | | |
| 0.812[f] | $ [redacted] | 0.149 | $ [redacted][5] | [redacted]% |
| **Probability of achieving control after 32 weeks (Base Case: tezepelumab OCS/no OCS:0.0, SoC with OCS 8.8%, SoC no OCS:24.7%)** | | | | |
| Probability equal to pre-32-week assessment [g] | $ [redacted] | 0.201 | $ [redacted][1] | [redacted]% |
| **ESC respecified base case** | | | | |
| **1# + 2# + 3#** | $ [redacted] | 0.137 | $ [redacted][5] | [redacted]% |

Source: Based on Table 3-36, pp309-311 of the submission. Analyses presented in italics were added during the evaluation.
CV= cardiovascular; ED= emergency department; ICER= incremental cost-effectiveness ratio; OCS= oral corticosteroids; PSD= public summary document; QALY= quality adjusted life years; RR= risk ratio; SoC= standard of care; Teze = tezepelumab.
All analyses were conducted by making the following changes in "Attachment 3 2 CEA model Teze SUA July 2025.xlm"

[a] Input on tab "Summary" Cell M14= 0.0 (User input cells for sensitivity analysis). Assuming no difference in health state utility between controlled and uncontrolled.
[b] Input on tab "Summary" Cell M14= 0.194 Using the utility values as reported in the NAVIGATOR and SOURCE trials without applying Australian values.
[c] Input on Tab 'Summary': M32=0.49, M33=1.12. Base case: Tezepelumab did not lower the risk of exacerbation in individuals on OCS but reduced exacerbation risk by 50% in individuals not on OCS. But the NAVIGATOR trial results (individuals with and without OCS) indicated a relative effect that was not statistically significant.
[d] Input tab 'Summary' L32=H32*(1-0.20/0.38); L33 =H33*(1-0.20/0.38)
[e] Input on tab "Summary" Cell M14= 0.109 (User input cells for sensitivity analysis). Input from Buendía, J. A., & Zuluaga, A. F. (2024). Exploratory analysis of the economically justifiable price of tezepelumab for severe asthma in Colombia. Journal of Asthma, 62(4), 684–693.
[f] Input on tab "Summary" Cell M14= 0.063 (User input cells for sensitivity analysis). Input from Habash, M., Guiang, H et al (2023). Cost-effectiveness of tezepelumab in Canada for severe asthma. Journal of Medical Economics, 26(1), 902-914.
[g] Input on tab "Summary" Cell J27=E23, K27=F23, L27=G23 and M27=H23 assuming no difference in efficacy of tezepelumab after 32 weeks assessment.
*The redacted values correspond to the following ranges:*
[1] *$75,000 to < $95,000*
[2] *$55,000 to < $75,000*
[3] *$45,000 to < $55,000*
[4] *$95,000 to < $115,000*
[5] *$115,000 to < $135,000*
[6] *$155,000 to < $255,000*
[7] *$135,000 to < $155,000*

6.66 The ESC noted the model contained substantial uncertainty and considered the assumptions adopted in the base case to be overly optimistic. The ESC advised that a respecified base case would be required to improve certainty in the model, including changes to the following:

- a shorter time horizon (from lifetime [40 years] to a 20-year time horizon);
- a smaller reduction in exacerbation risk in the non-OCS tezepelumab group relative to SoC (from 50% to 38%); and
- reduced exacerbation-related mortality rates consistent with the mepolizumab economic model (OCS burst: 0.43%; ED or hospitalisation: 1.13%).

6.67 The pre-PBAC Response accepted the smaller reduction in exacerbation risk in the non-OCS tezepelumab group proposed by the ESC. However, the pre-PBAC Response argued that the probability of exacerbation-related mortality should be 1.13% across all types and that a lifetime time horizon should remain. The Response noted that with these assumptions the ICER is $75,000 to < $95,000 per QALY gained.

**Eosinophilic or allergic SUA**

6.68 The submission presented a cost-minimisation approach of tezepelumab versus dupilumab, the primary comparator in the eosinophilic or allergic SUA population. The cost-minimisation approach was consistent with the submission's claim of non-inferiority of tezepelumab versus dupilumab. The ESC considered that this was reasonable.

6.69 In patients with eosinophilic SUA, the proposed equi-effective doses were estimated as:

- Tezepelumab 210 mg by SC injection every 4 weeks over 1 year (13 doses).
- Dupilumab 400 mg (non-OCS dependent) or 600mg (OCS dependent) by SC injection (2 injections consecutively in 2 different injection sites) followed by 200 mg (non-OCS dependent) or 300 mg (OCS dependent) SC given every 2 weeks over 1 year (27 doses).
- Benralizumab 30 mg by SC injection every 4 weeks for the first 3 doses, then every 8 weeks over 1 year (7.5 doses).
- Mepolizumab 100 mg by SC injection every 4 weeks over 1 year (13 doses).

6.70 In patients with allergic SUA, the proposed equi-effective doses were estimated as:

- Tezepelumab 210 mg by SC injection every 4 weeks over 1 year (13 doses).
- Dupilumab 400 mg (non-OCS dependent) or 600mg (OCS dependent) by SC injection (2 injections consecutively in 2 different injection sites) followed by 200 mg (non-OCS dependent) or 300 mg (OCS dependent) given every 2 weeks over 1 year (27 doses).
- Omalizumab 398 mg by SC injection every 4 weeks over 1 year (dosed at 2 or 4 weeks depending on patient weight and immunoglobulin E levels; 13 doses).

6.71 The proposed equi-effective doses for tezepelumab were based on the fixed-dose regimen used in the NAVIGATOR and SOURCE trials and the relevant 210 mg every 4 weeks treatment group in the dose-ranging PATHWAY trial. The ESC considered that this was reasonable. The proposed equi-effective doses for dupilumab, benralizumab, mepolizumab and omalizumab were the same as the equi-effective doses accepted by the PBAC at its November 2020 meeting when considering the dupilumab submission (para. 7.10, dupilumab PSD, PBAC November 2020 Meeting). The ESC considered that this was reasonable.

6.72 The cost-minimisation approach used a time horizon of 1 year. This was consistent with the duration of the tezepelumab trials. The PBAC previously accepted a 1-year time horizon for the cost-minimisation approach in the assessment of dupilumab (para. 7.9, dupilumab PSD, November 2020 PBAC Meeting).

6.73 The submission accounted for the loading dose(s) relating to dupilumab. The inclusion of the fixed loading doses in estimating the equi-effective doses was consistent with the previous PBAC consideration of dupilumab (para. 7.9, dupilumab PSD, November 2020 PBAC Meeting).

6.74 Tezepelumab and dupilumab were assumed to incur a one-off injection training cost (MBS item 82215). The PBAC had previously considered it appropriate to include a

one-off SC injection training cost for patients or carers before self-injection (para. 7.10, dupilumab PSD, November 2020 PBAC Meeting).

6.75 Table 17 presents the cost-minimisation approach of tezepelumab versus dupilumab based on the published price of dupilumab.

**Table 17 Cost-minimisation approach of tezepelumab vs. dupilumab (published price)**

| Parameter | | |
|---|---|---|
| **Dupilumab treatment** | | |
| | **Dupilumab 200 mg every 2 weeks (Non-OCS-dependent)** | **Dupilumab 300 mg every 2 weeks (OCS-dependent)** |
| Dose size per administration (mg) | 200 | 300 |
| Drug cost/pack AEMP (S100 HSD Public) [A][a] | $1,609.86 | $1,609.86 |
| Number of units per Pack [B] | 2 | 2 |
| Drug cost (AEMP) per dose [C= A/B] | $804.93 | $804.93 |
| Units required per loading dose [D] | 2.0 | 2.0 |
| Number of maintenance doses per year [E] | 25 [=(52-2)/2] | 25 [=(52-2)/2] |
| Number of units required [F= D+E] | 27.0 | 27.0 |
| **Total annual drug cost [G=C x F]** | **$21,733.11** | **$21,733.11** |
| Subcutaneous injection training (MBS Item 82215) [H] | $86.80<br>$88.90[c] | $86.80<br>$88.90[c] |
| Administration cost per maintenance injection [I][b] | $0.0 | $0.0 |
| Total annual administration cost [J=H + I] | $86.80<br>$88.90[c] | $86.80<br>$88.90[c] |
| **Total annual drug cost per patient [K=G+J]** | **$21,819.91**<br>**$21,822.01[c]** | **$21,819.91**<br>**$21,822.01[c]** |
| **Tezepelumab treatment** | | |
| | **Tezepelumab 210 mg every 4 weeks** | |
| | **Cost-minimised vs. dupilumab 200 mg every 2 weeks** | **Cost-minimised vs. dupilumab 300 mg every 2 weeks** |
| **Total annual cost-minimised treatment cost [L=K]** | **$21,819.91**<br>**$21,822.01[c]** | **$21,819.91**<br>**$21,822.01[c]** |
| Subcutaneous injection training (MBS Item 82215) [H] | $86.80<br>$88.90[c] | $86.80<br>$88.90[c] |
| Administration cost per maintenance injection [I][b] | $0.00 | $0.00 |
| Total annual administration cost [J=H + I] | $86.80<br>$88.90[c] | $86.80<br>$88.90[c] |
| **Total annual drug cost [M=L-J]** | **$21,733.11** | **$21,733.11** |
| No. of doses in Year 1 [N] | 13 | 13 |
| No. of units per dose [O] | 1 | 1 |
| No. of units per pack [P] | 1 | 1 |
| No. of packs required in year 1 [Q=NxO/P] | 13 | 13 |
| **Drug cost per pack AEMP (S100 HSD Public) [R=M/Q]** | **$1,671.78** | **$1,671.78** |
| Mark-up [S] | $40.00 | $40.00 |
| Dispensing fee [T] | $8.67<br>$8.88[c] | $8.67<br>$8.88[c] |
| **Drug cost per pack (DPMQ, Section 100 HSD, private) [U = R + S + T]** | **$1,720.45**<br>**$1,720.66[c]** | **$1,720.45**<br>**$1,720.66[c]** |

Source: Table 3-3, p255; Table 3-4, p255 of the submission. Italicised text indicates updated costs (as of 12 August 2025) of subcutaneous injection training ($88.90) and dispensing fee ($8.88).

AEMP = Approved Ex-manufacturer Price; DPMQ= Dispensed Price for Maximum Quantity; HSD = Highly Specialised Drugs Program; OCS = oral corticosteroids;

[a] PBS AEMP for S100 HSD Public (PBS, August 2025).

[b] The submission assumed self-administration for maintenance doses in all patients.

[c] Text indicates updated costs (as of 12 August 2025) of subcutaneous injection training ($88.90) and dispensing fee ($8.88).

6.76 Based on the cost-minimisation approach versus dupilumab, the proposed DPMQ per pack for tezepelumab was $1,671.78 for a public hospital and $1,720.66 for a private hospital. The ESC noted that dupilumab may not be the lowest cost therapy for either the uncontrolled severe eosinophilic or allergic asthma population.

## *Drug cost/patient/year*

### Non-eosinophilic and non-allergic SUA

6.77 For the non-eosinophilic and non-allergic SUA population the drug cost per patient per year is presented in Table 18.

**Table 18: Intervention costs per patient per year for non-eosinophilic and non-allergic subgroup on high-dose ICS**

| | Tezepelumab | | |
|---|---|---|---|
| | **Trial** | **Model** | **Financial estimates** |
| Proposed dose | 210 mg injection Q4W | 210 mg injection Q4W | 210 mg injection Q4W |
| Mean compliance | 98.2%[a] | 100% | 93% |
| Mean 4-weekly dose [b] | 206.1 mg | 210 mg | 225.6 mg |
| Mean dose/week [c] | 51.5 mg | 52.5 mg | 56.4 mg |
| Mean duration (Weeks) | 47.9 [d] | 85.1 [e] | 48.3 |
| Cost/ patient over the mean duration [f] | $ | $ | $ |
| Cost/ patient trial-based period (50w) [g,h] | $ | $ | $ |
| **Cost/ patient/ year** [i] | **$** | **$** | **$** |

Source: Complied during the evaluation from Table 2-15, pp53-56 of the submission; 'Attachment 3 2 CEA model Teze SUA July 2025.xlm', Tab 'Other AU inputs'; Tab 'Deterministic Results'; Attachment 4.3 Financial impact nonEOS_nonAllergic SUA teze_July 2025 Tab '3b. Impact- proposed (eff)' NAVIGATOR study CSR, p135; SOURCE study CSR p139; NAVIGATOR CSR 'Tezepelumab - d5180c00007' Table 14.3.1.1, p5; SOURCE CSR 'Tezepelumab - d5180c00009' Table 14.3.1.1. Italicised text (calculated cells) added during the evaluation.

DPMQ = Dispensed Price for Maximum Quantity; ICS= inhaled corticosteroids; NR = Not reported; Q4W= every 4 weeks; w= Weeks

[a] Average compliance reported in the 2 trials: (98.2% = 99.0% (NAVIGATOR)+ 97.3% (SOURCE))/2.

[b] Proposed dose (mg) x compliance rate (%)

[c] Mean 4-weekly dose/4.

[d] Average trial-based tezepelumab exposure: (352.3 days (NAVIGATOR)+ 318.7 days (SOURCE))/7/2.

[e] 85.1= 1.63 (years of exposure in the model) x (365.25/7)

[f] Calculated for the mean trial/model duration=Mean dose/week (mg) x cost per mg ($/210) x mean duration (in weeks).

[g] 50 weeks= Mean of planned follow-up duration of 2 trials: (50 = 52 (NAVIGATOR)+ 48 (SOURCE))/2.

[h] (Cost/patient over the trial or model duration /trial/model duration in weeks) x 50.

[i] (Cost/patient over the trial or model duration /trial/model duration in weeks) x (365.25/7).

### Eosinophilic or allergic SUA

6.78 For the eosinophilic or allergic SUA population the drug cost per patient per year for tezepelumab and dupilumab based on published prices is presented in Table 19.

**Table 19 Drug cost per patient for tezepelumab and dupilumab (published AEMP, public hospital)**

| | Tezepelumab | | | Dupilumab | | |
|---|---|---|---|---|---|---|
| | Trial | CMA | Financial estimates | Trial | CMA | Financial estimates |
| Proposed dose | 210 mg Q4W | | | Loading dose 400mg (non-OCS dependent) or 600mg (OCS dependent) then 200 mg (non-OCS dependent) or 300mg (OCS dependent) Q2W | | |
| Mean duration | 48-52 weeks trial duration | 1 year | Not estimated | 24-52 weeks trial duration | 1 year | Not estimated |
| No. of doses/year 1 | 13 | 13 | 13.04 | 27 | 27 | 27.63 |
| Drug cost/ patient/Year | Not estimated | $21,733.11[a] | Not estimated | Not estimated | $21,733.11[b] | Not estimated |

Source: Table compiled during the evaluation from Table 3-3, p255; Table 3-4, p255 of the submission.
AEMP= = Approved Ex-manufacturer Price; CMA= cost minimisation approach; DPMQ = Dispensed Price for Maximum Quantity; OCS= Oral corticosteroids; Q2W= Once every 2 weeks; Q4W= Once every 4 weeks.
[a] $21,733.11 = $1,671.78 x 13 (proposed published AEMP for tezepelumab, public hospital based on cost-minimisation against dupilumab).
[b] $21,733.11 = ($1,609.86/2) x 27 (published AEMP for dupilumab, public hospital).

## *Estimated PBS usage & financial implications*

6.79 This submission was considered by DUSC. Separate estimated PBS usage and financial implications were presented for the non-eosinophilic and non-allergic SUA population and the eosinophilic or allergic SUA population.

### Non-eosinophilic and non-allergic SUA

6.80 An epidemiological approach was used for the non-eosinophilic and non-allergic population. The evaluation considered this was reasonable.

6.81 As tezepelumab was an add-on therapy to SoC, the submission did not substitute other or apply cost offsets for SoC costs into the model. The submission did not apply minor PBS/MBS cost offsets for associated adverse events. The evaluation considered this was appropriate.

6.82 Table 20 presents the key inputs used in the financial estimates.

**Table 20: Key inputs for financial estimates (non-eosinophilic and non-allergic SUA)**

| Data | Value | Source and comment |
|---|---|---|
| **Eligible population** | | |
| Australian adult population (12+ years) | Yr 1: 23,780,244<br>Yr 2: 24,125,467<br>Yr 3: 24,463,128<br>Yr 4: 24,804,118<br>Yr 5: 25,126,404<br>Yr 6: 25,458,711 | ABS population statistics (3222.0 Series B). 23,780,244 in 2025 increasing to 25,458,711 in 2030. DUSC considered this was reasonable. |
| Prevalence of asthma | 11.5% | AIHW 2022, National Health Survey, 11.5% based on adults aged 15+ years. DUSC considered this was reasonable. |
| Difficult to treat/control asthma | 21.7% | Davis 2024. DUSC considered this parameter uncertain and possibly underestimated. DUSC noted the source provided may under-represent certain populations (e.g. older Australians, those with a language other than English and those from Aboriginal and Torres Strait Islander backgrounds) therefore underestimating SUA. The pre-PBAC response argued that the study provided the first population |

| Data | Value | Source and comment |
|---|---|---|
| | | based real world study using standard criteria for difficult to treat asthma and hence remained the most reliable and current source for Australia. |
| High-dose ICS/LABA | 41.1% | Davis 2024. DUSC considered this parameter to be underestimated. DUSC considered there could be a higher proportion on high dose ICS/LABA – particularly considering Davis underrepresents older Australians. DUSC noted the NAVIGATOR study where approximately 75% of patients were on a high dose ICS. The pre-PBAC response (p3) noted that in the PATHWAY study only 48% of patients were on high dose ICS. The pre-PBAC response (p3) also noted that Reddel et al., 2017 reported that Australian general practice data found that among those on ICS/LABA, 30.2% were on high dose ICS and argued that the 41.1% may be an overestimate. |
| Severe treatment refractory asthma | 20.5% | Hekking 2015. DUSC considered this to be reasonable. |
| Proportion of all SUA patients not eligible for biologics based on biomarker status (i.e., non-eosinophilic and nonallergic) | 22.7% | NAVIGATOR and PATHWAY trials, 22.7%.<br>DUSC considered this to be reasonable. |
| **Treatment utilisation** | | |
| Uptake rate | Yr 1: [redacted]%<br>Yr 2: [redacted]%<br>Yr 3: [redacted]%<br>Yr 4: [redacted]%<br>Yr 5: [redacted]%<br>Yr 6: [redacted]% | Estimated by the submission.<br>The evaluation considered this likely underestimated based on dupilumab's utilisation more than tripled from 2021 (first listed on PBS) to 2022, prescriptions in 2022 were 2.2 times more than projected and in 2023 reached the market share predicted for 2027[a]. The evaluators considered this increased dupilumab uptake could have resulted during the COVID-19 pandemic when many reports on asthma patients indicated increased severity due to IL-13 pathway disruption. However, the magnitude of this impact could not be quantified.<br>DUSC considered the uptake rate to be underestimated. |
| Proportion continuing treatment | 75.9% | Based on NAVIGATOR, PATHWAY and SOURCE trial results and assuming only responders continue treatment.<br>Uncertain. The continuing rate was assumed to equal the response rate and was based on all trial patients as opposed to the subgroup of non-eosinophilic and non-allergic patients on high-dose ICS.<br>The response rate was also different to that used in the economic model which used pooled NAVIGATOR and SOURCE data (42.3% with OCS and 48.7% without OCS).<br><br>DUSC considered this parameter to be uncertain and potentially overestimated as the proportion of patients continuing treatment varied at different time points in the trial. |
| Compliance rate | 93.01% | Based on persistence rate in NAVIGATOR. The evaluation considered this input likely underestimated. Compliance rate was 99% in the NAVIGATOR trial and 97.3% in the SOURCE trial (Average=98.2%).<br>DUSC considered this input to be reasonable. |
| Scripts | Initiators: 7.44/year<br>Continuers: 12.09/ year | Based on 93.01% compliance, initiating scripts calculated for 32 weeks and continuing scripts calculated over 52 weeks.<br>Initiators receive 32 weeks of treatment, after which they are assessed |

| Data | Value | Source and comment |
|---|---|---|
| | | for response. Continuers receive treatment if they respond, for 12.09 x 4 weeks= 48.4 weeks (0.93 years).<br>The total scripts for continuers and therefore time on treatment was likely underestimated based on median time on treatment of 1.2 years for dupilumab. [b] |
| **Costs** | | |
| Proposed medicine | Published: $1,690.74<br>Effective: $[redacted] | Requested price: weighted DPMQ (AEMP $[redacted]). |
| Public/Private split | 61.05% public,<br>38.95% private | Based on the distribution of dupilumab market.<br>This was reasonable. |
| MBS costs | $86.80 | MBS item 82215. Training of injection technique<br>The evaluators noted the fee for this item at the time of evaluation was $88.90. |

Source: Table 4-26, pp334-335 of the submission; 'Attachment 4.3 Financial impact nonEOS_nonAllergic SUA teze_July 2025'. ABS= Australian Bureau of Statistics; AEMP = Approved ex-manufacturer price; AIHW= Australian Institute of Health and Welfare; DPMQ = Dispensed Price for Maximum Quantity; DUSC= drug utilisation sub-committee; ICS= Inhaled corticosteroids; LABA= Long Acting Beta Antagonists; MBS= Medicare Benefits Schedule; OCS = oral corticosteroids; PBS= Pharmaceutical Benefits Scheme; RCT = Randomised controlled trial; RPBS = Repatriation Pharmaceutical Benefits Scheme; SUA= severe uncontrolled asthma.

[a] Table 10, p23, p26 of Public Release Document, Dupilumab, February 2024 DUSC meeting.

[b] p20 of Public Release Document, dupilumab, February 2024 DUSC meeting.

6.83 The estimated use and financial implications of listing tezepelumab for non-eosinophilic and non-allergic SUA are presented in Table 21.

**Table 21: Estimated use and financial implications (non-eosinophilic and non-allergic SUA).**

| | Year 1 | Year 2 | Year 3 | Year 4 | Year 5 | Year 6 |
|---|---|---|---|---|---|---|
| **Estimated extent of use** | | | | | | |
| Number of patients treated | [redacted][1] | [redacted][1] | [redacted][1] | [redacted][1] | [redacted][2] | [redacted][2] |
| Number of scripts dispensed [a] | [redacted][2] | [redacted][3] | [redacted][3] | [redacted][4] | [redacted][5] | [redacted][5] |
| **Estimated financial implications of tezepelumab** | | | | | | |
| Cost to PBS/RPBS less copayments [b] | $[redacted][6] | $[redacted][7] | $[redacted][7] | $[redacted][8] | $[redacted][8] | $[redacted][9] |
| **Estimated financial implications for standard of care** | | | | | | |
| Cost to PBS/RPBS less copayments | $0 | $0 | $0 | $0 | $0 | $0 |
| **Net financial implications** | | | | | | |
| Net cost to PBS/RPBS | $[redacted][6] | $[redacted][7] | $[redacted][7] | $[redacted][8] | $[redacted][8] | $[redacted][9] |
| Net cost to MBS/ Services [b] | $[redacted][6] | $[redacted][6] | $[redacted][6] | $[redacted][6] | $[redacted][6] | $[redacted][6] |
| Net cost to PBS/RPBS/MBS [b] | $[redacted][6] | $[redacted][7] | $[redacted][7] | $[redacted][8] | $[redacted][8] | $[redacted][9] |

Source: Developed during the evaluation from Table 4-44, p348 of the submission; Attachment 4.3 Financial impact nonEOS_nonAllergic SUA teze_July 2025', Sheet '7. Net changes - MBS'.

DPMQ = dispensed price for maximum quantity; MBS= Medicare Beneficiary Services; PBS= Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme.

[a] Assuming 12.09 scripts per year as estimated by the submission: 7.44 scripts in initiators and 4.65 scripts for those continuing beyond 32 weeks.

[b] Cost obtained using updated MBS item fee for MBS item 82215 and using patients as a unit of analysis as opposed to patient years (submission base case).

*The redacted values correspond to the following ranges:*

*[1] 500 to < 5,000*

*[2] 5,000 to < 10,000*

*[3] 10,000 to < 20,000*

*[4] 20,000 to < 30,000*

*[5] 30,000 to < 40,000*

*[6] $0 to < $10 million*

*[7] $10 million to < $20 million*

*[8] $20 million to < $30 million*

*[9] $30 million to < $40 million*

6.84 The total cost to the PBS/RPBS of listing tezepelumab was estimated to be $30 million to < $40 million in Year 6, and a total of $100 million to < $200 million in the first 6 years of listing.

6.85 The total cost to the Government was most sensitive to plausible variations in the proportion of difficult-to-control asthma patients on high-dose ICS/LABA, the proportion of patients who were not currently eligible for biologics based on biomarker status and expected uptake rates.

6.86 Tezepelumab is proposed to be prescribed as first-line treatment for non-eosinophilic and non-allergic SUA for patients on high-dose ICS, who currently are not eligible for PBS-listed biologics. Based on high uptake of dupilumab in a market as the 4$^{th}$ biologic for the eosinophilic/allergic subgroup, the uptake of tezepelumab as the first biologic for this population would likely be higher. Consequently, the estimates of total financial implications to the PBS/RPBS may be higher than estimated in the submission.

6.87 DUSC considers the estimates presented in the submission to be potentially highly underestimated for the non-eosinophilic and non-allergic SUA population. The main issues are:

- DUSC considered the first in class uptake rate for the non-eosinophilic and non-allergic SUA population to be underestimated, particularly in the first few years. Based on high uptake of dupilumab in a market as the 4th biologic for the eosinophilic or allergic subgroup, the uptake of tezepelumab as the first biologic for this population would likely be higher.
- DUSC noted the prevalence of difficult to treat/control asthma was likely underestimated and there was potential for leakage due to the low bar to qualify for treatment. The pre-PBAC response argued that the Davis et al. (2024) study remained the most reliable and current source for Australia. The pre-PBAC response also did not agree that the proposed PBS restriction for non-eosinophilic/non-allergic SUA patients - aligned with exiting biologic access criteria – constituted a "low bar". The pre-PBAC response argued that in practice current SUA restrictions are highly stringent with stakeholders having previously sought to reduce their complexity with limited success.[12]

**Eosinophilic or allergic SUA**

6.88 A market share approach was used for the eosinophilic or allergic SUA population. The evaluation considered this was reasonable.

6.89 Table 22 presents the key inputs used for the financial estimates.

**Table 22: Key inputs for financial estimates (eosinophilic or allergic SUA)**

| Data | Value | Source and comment |
|---|---|---|
| **Market growth** | | |
| Annual market growth (patient years of treatment) | Assumed a growth in the market of 1,414 patient years of treatment each year across Year 1 to Year 6.<br>Assumed no additional market growth due to tezepelumab listing | Continued linear market growth assumed over the analysis period based on PBS item statistics from 2020-2024. DUSC considered this assumption was underestimated given the likelihood tezepelumab will grow the market. DUSC commented this was due to the monthly dosing advantage over dupilumab's fortnightly dosing, the different mode of action, and patients' total time on biologic therapy for SUA would likely be extended. |

[12] https://www.pbs.gov.au/industry/listing/elements/pbacmeetings/pbac-stakeholder-meetings/Asthma-Stakeholder-Meeting-Dec-2018-Outcome-Statement.pdf

| Data | Value | Source and comment |
|---|---|---|
| Base year to source historical PBS utilisation data | 2020-2024 | PBS item statistics. The submission used utilisation data from 2020-2024 and applied the annual market growth rates and displacement rates of comparator drugs to estimate the predicted utilisation for the first 6 years of listing (2026-2031). DUSC considered this was reasonable. |
| Market growth rates for comparator drugs | Dupilumab: 21.3% in Yr 1 to 7.7% in Yr 6.<br>Benralizumab: 8.5% in Yr 1 to 7.7% in Yr 6.<br>Mepolizumab: 8.5% in Yr 1 to 7.7% in Yr 6.<br>Omalizumab: 8.5% in Yr 1 to 7.7% in Yr 6. | Assumption by submission. DUSC considered this assumption to be reasonable and noted dupilumab would likely reach 35% based on prior trends. |
| **Uptake/displacement rate** | | |
| Uptake rate of tezepelumab | [redacted]% in Yr 1 to [redacted]% in Yr 6. | Assumed by the submission. DUSC considered the [redacted]% uptake rate in Yr 1 was likely underestimated, however reaching [redacted]% by Yr 5 was reasonable. |
| **Unit equivalence** | | |
| Unit equivalence | Dupilumab: 1:0.89 for initiating scripts, 1:1 for continuing scripts<br>Benralizumab: 1:1.6 for initiating scripts 1:2 for continuing scripts<br>Mepolizumab: 1:1<br>Omalizumab 75 mg: 1:0.26<br>Omalizumab 150 mg: 1:1.02 | The evaluation noted the submission used the dupilumab PSD to derive an average dose of omalizumab (593 mg) that is substituted by tezepelumab. This was greater than the proposed equi-effective dose (398 mg). The evaluation noted that correction of this input in a sensitivity analysis did not significantly impact the net result.<br>DUSC noted the calculations in the financial model were done incorrectly for omalizumab and favoured tezepelumab. DUSC noted that it is not appropriate to use the average number of Medicare services and benefits and that script equivalences should be calculated based on the total amount of scripts required. This method would also result in a 1:1 substitution rate with omalizumab which would be more appropriate. |
| Use in public vs. private hospital | Public: 65.3%<br>Private: 34.7% | This split was used to estimate the service use of tezepelumab. For the comparators, the submission used prices adjusted for packs dispensed using 2024 PBS/RPBS data and published DPMQs for respective item numbers. The evaluation considered this was reasonable. |
| **COSTS** | | |
| **PBS costs** | | |
| Tezepelumab 210 mg | $1,688.68 | Weighted DPMQ based on public/ private service split: $1,688.68 (=$1,671.78 x 65.3% + $1,720.45 x 34.7%).<br>Proposed published price. |

| Data | Value | Source and comment |
|---|---|---|
| Dupilumab<br>200 mg/300 mg | Public DPMQ= $1,609.86<br>Private DPMQ=$1,658.53 | Based on PBS published DPMQs (Date not specified). Adjusted for packs dispensed per service=1.0. The evaluation considered this approach was reasonable. |
| Benralizumab<br>30 mg | Public DPMQ= $3,145.45<br>Private DPMQ=$3,145.45 | Based on PBS published DPMQs (Date not specified). Adjusted for packs dispensed per service=1.0.<br>Private DPMQ=$3,194.33 (As of August 2025). It did not have any impact on the net financial implications. |
| Mepolizumab<br>100 mg | Public DPMQ= $1,556.10<br>Private DPMQ=$1,604.77 | Based on PBS published DPMQs (Date not specified). Adjusted for packs dispensed per service=1.0. Private DPMQ=$1,604.98 (As of August 2025), which is not significantly different from the submission's estimate. |
| Omalizumab<br>75 mg<br>150 mg | 75 mg dose:<br>Public dispensing price= $204.44<br>Private dispensing price =$220.99<br>150 mg dose:<br>Public dispensing price= $796.20<br>Private dispensing price =$836.42 | Based on PBS published DPMQs (Date not specified). Adjusted for packs dispensed per service=1.9 for 75 mg dose and 3.7 for 150 mg dose. Submission did not use DPMQ of omalizumab as of August 2025: Resulting estimates did not significantly impact the net budget. |
| **Medical service costs** | | |
| Subcutaneous injection | $14.20 | MBS item 82200 (July 2025).<br>Applied to all omalizumab scripts. The evaluation considered this was not appropriate as the Product Information of omalizumab recommends that the first 3 doses be administered under the supervision of a healthcare professional. The PBAC previously considered it appropriate for the subcutaneous injection administration cost-offsets and the costs for post-administration monitoring of anaphylaxis be included for the first three doses of omalizumab (para. 7.10, dupilumab PSD, November 2020 PBAC Meeting). DUSC agreed with the evaluation that the injection administration cost should be included for the first three doses of omalizumab only.<br>August 2025 MBS item fee= $14.55. |
| Monitoring of anaphylaxis events | $58.85 | MBS item 82210 (July 2025).<br>Applied to all omalizumab scripts. DUSC agreed with the evaluation that the costs for post-administration monitoring of anaphylaxis should be included for the first three doses of omalizumab only.<br>August 2025 MBS item fee= $60.25. |

Sources: Table 4-5, p317; Table 4-6, p318; Table 4-17, p327 of the submission; 'Attachment 4.1 financial impact EOS_Allergic SUA Tezepelumab July 2025', Sheet '2e. Scripts- market' of the submission.
AEMP = Approved ex-manufacturer price; DPMQ = Dispensed Price for Maximum Quantity; MBS = Medicare Benefits Schedule; PBAC = Pharmaceutical Benefits Advisory Committee; PBS = Pharmaceutical Benefits Scheme; PSD = Public Summary Document.

6.90 Table 23 presents the estimated use and financial implications of listing tezepelumab for patients with eosinophilic or allergic SUA based on published prices.

**Table 23: Estimated use and financial implications (eosinophilic or allergic SUA) – based on published prices**

| | Year 1 | Year 2 | Year 3 | Year 4 | Year 5 | Year 6 |
|---|---|---|---|---|---|---|
| **Estimated extent of use** | | | | | | |
| Number of scripts of tezepelumab dispensed | [redacted]1 | [redacted]2 | [redacted]3 | [redacted]4 | [redacted]5 | [redacted]6 |
| **From replacing [a]:** | | | | | | |
| Dupilumab | [redacted]7 | [redacted]1 | [redacted]2 | [redacted]2 | [redacted]8 | [redacted]8 |
| Mepolizumab | [redacted]7 | [redacted]7 | [redacted]1 | [redacted]1 | [redacted]2 | [redacted]2 |
| Benralizumab | [redacted]7 | [redacted]7 | [redacted]1 | [redacted]1 | [redacted]2 | [redacted]2 |
| Omalizumab | [redacted]7 | [redacted]7 | [redacted]7 | [redacted]1 | [redacted]1 | [redacted]1 |
| **Estimated financial implications of tezepelumab to PBS/RPBS** | | | | | | |
| Cost of tezepelumab to PBS/RPBS (less co-payment) | $[redacted]9 | $[redacted]10 | $[redacted]11 | $[redacted]12 | $[redacted]13 | $[redacted]14 |
| **Estimated financial implications for other medicines to PBS/RPBS** | | | | | | |
| Cost from substitution of other medicines to PBS/RPBS (less co-payment) | -$[redacted] 9 | -$[redacted] 15 | -$[redacted] 16 | -$[redacted] **17** | -$[redacted] 13 | -$[redacted] 13 |
| **Net cost to PBS/RPBS** | $[redacted]18 | $[redacted]18 | $[redacted]18 | $[redacted]18 | $[redacted]18 | $[redacted]18 |
| **Estimated financial implications to MBS** | | | | | | |
| Net cost to MBS [b] | -$[redacted]18 | -$[redacted]18 | -$[redacted]18 | -$[redacted]18 | -$[redacted]18 | -$[redacted]18 |
| **Net financial implications** | | | | | | |
| **Net cost to PBS/RPBS/MBS [b]** | $[redacted]**18** | $[redacted]18 | $[redacted]18 | $[redacted]18 | $[redacted]18 | $[redacted]18 |

Source: Table 4-23, Table 4-24 pp330-331; Attachment 4.1 financial impact EOS_Allergic SUA Tezepelumab July 2025', Sheet '7. Net Changes- MBS' of the submission.

MBS = Medicare Benefits Schedule; PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme.

[a] Projected number of scripts displaced by tezepelumab listing. This was calculated as the number of scripts estimated in the year based on 2024 PBS/RPBS utilisation data, multiplied by the displacement rate of tezepelumab and the annual market growth rate. To ascertain tezepelumab script numbers, this number was further multiplied by dose equivalence rates (not presented in this table).

[b] Updated during the evaluation using MBS item fees as of 15 August 2025

*The redacted values correspond to the following ranges:*

*[1] 5,000 to < 10,000*
*[2] 10,000 to < 20,000*
*[3] 30,000 to < 40,000*
*[4] 40,000 to < 50,000*
*[5] 50,000 to < 60,000*
*[6] 60,000 to < 70,000*
*[7] 500 to < 5,000*
*[8] 20,000 to < 30,000*
*[9] $10 million to < $20 million*
*[10] $30 million to < $40 million*
*[11] $50 million to < $60 million*
*[12] $70 million to < $80 million*
*[13] $90 million to < $100 million*
*[14] $100 million to < $200 million*
*[15] $20 million to < $30 million*
*[16] $40 million to < $50 million*
*[17] $60 million to < $70 million*
*[18] $0 to < $10 million*

6.91 The submission estimated the net financial implication to the PBS/RPBS of listing tezepelumab as $1.0 million in Year 1 of listing, increasing to $0 to < $10 million in

Year 6, with an estimated total cost of $20 million to < $30 million over 6 years based on published prices.

6.92 The evaluation considered it may not be reasonable to assume no additional market growth of SUA with tezepelumab listing in this population. In 2024, the DUSC noted that the market for biologics for SUA grew further than was predicted in the dupilumab submission. The DUSC concluded that the market was larger than predicted and the uptake of dupilumab within the market was higher than predicted (p22, dupilumab, Public Release Document, February 2024 DUSC meeting). The 2024 DUSC report also suggested that the number of supplied prescriptions and the number of treated patients had not plateaued and continued to grow (p26, dupilumab, Public Release Document, February 2024 DUSC meeting).

6.93 The DUSC considered the estimates presented in the submission to be underestimated for the eosinophilic or allergic SUA population. The main issues were:

- DUSC considered the market growth for the eosinophilic or allergic SUA population to be underestimated as patients' total time on biologic therapy for asthma will likely be extended with the addition of a 5th biologic.
- DUSC considered that as a new/unique mode of action in class drug, and with the benefit of monthly dosing over dupilumab's fortnightly dosing tezepelumab will likely grow the market.

6.94 The pre-PBAC response proposed increasing the linear market growth estimates by 153 patients each year, increasing the uptake rate in Year 1 from [redacted]% to [redacted]% and in Year 2 from [redacted]% to [redacted]% and adding <500 grandfathered patients. In addition, the pre-PBAC response proposed updating the unit equivalence values to those proposed by the evaluation and applying the SC injection and monitoring of anaphylaxis events related MBS item numbers (82200 and 82210) fees to the first three doses of omalizumab only. The pre-PBAC response stated that under the new assumptions the net impact doubled in Year 1 but has a reducing rate of increase until year 6. A revised utilisation and cost model workbook was not provided with the pre-PBAC response.

## *Quality Use of Medicines*

6.95 The submission described a comprehensive plan for patient and clinical education to support quality and optimal use of medications for SUA. It included dissemination of educational materials for health care providers and patients, a Patient Support Program (PSP) to include information/brochures to drive quality use of tezepelumab (from prescribing through to administration and ongoing treatment) and a website containing tools and information to support healthcare providers and patients. The submission also indicated that Asthma Australia activities will be supported, which were aimed at educating patients and carers on SUA, including treatment options, and the importance of medication adherence and device technique. In addition, DUSC

noted that post-marketing surveillance activities will be undertaken as part of the Risk Management Plan for tezepelumab.

### *Financial Management – Risk Sharing Arrangements*

6.96 The submission did not propose a risk-sharing arrangement, stating that it was consistent with the arrangements for the current asthma biologics.

*For more detail on PBAC's view, see section 7 PBAC outcome.*

## 7 PBAC Outcome

7.1 The PBAC recommended the Section 100 (Highly Specialised Drugs Program [HSD]) listing of tezepelumab for the treatment of patients aged 12 years and older with severe uncontrolled asthma (SUA) that is non-eosinophilic and non-allergic. The PBAC was satisfied that tezepelumab provides, for some patients, a significant improvement in efficacy over standard of care (SoC). The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of tezepelumab would be acceptable with a price reduction to achieve an incremental cost effectiveness ratio (ICER) of $45,000 to < $55,000 per quality adjusted life year (QALY) gained using the ESC respecified economic model.

7.2 The PBAC recommended the Section 100 (HSD) listing of tezepelumab for the treatment of patients aged 12 years and older with SUA that is eosinophilic or allergic. The PBAC's recommendation for listing was based on, amongst other matters, its assessment that the cost-effectiveness of tezepelumab would be acceptable if it were cost minimised to the least costly biologic for uncontrolled severe eosinophilic and/or allergic asthma populations over a 1-year time frame.

7.3 The PBAC noted the input from health care professionals and organisations supporting the listing of tezepelumab for this indication. The PBAC noted that comments emphasised that there is a clinical need for patients with non-eosinophilic and non-allergic SUA as they are ineligible, and not suitable, for biologics currently subsidised through the PBS. Comments highlighted that monoclonal antibodies generally have a favourable side effect profile, especially when compared to the cumulative harms associated with long-term oral corticosteroids (OCS) use. The PBAC also noted the comments highlighted that tezepelumab provides a steroid-sparing option for individuals who remain dependent on OCS despite high-dose inhaled therapy, while preserving asthma control. Comments also noted the high cost of tezepelumab and considered that the listing of tezepelumab on the PBS would ensure equitable access to treatment.

7.4 The PBAC noted there was a moderate clinical need for alternative biologic treatment for patients with SUA on the PBS, particularly for non-eosinophilic and non-allergic population, given there are no specific agents currently available for these patients.

The PBAC noted that there were a number of alternative biologics available for the eosinophilic or allergic population.

**Non-eosinophilic and non-allergic SUA**

7.5 The PBAC advised that the restrictions for the non-eosinophilic and non-allergic SUA population, as amended by the Secretariat in Section 8, were appropriate. The PBAC considered that treatment should not be used in combination with and within 4 weeks of another PBS-biological medicine prescribed for nasal polyps, uncontrolled severe allergic asthma or uncontrolled severe asthma. The PBAC noted the proposed patient access program was for those with eosinophilic or allergic SUA and advised that a grandfathering restriction would not be required for the non-eosinophilic and non-allergic SUA population.

7.6 The PBAC considered that SoC, as defined by the submission, was the appropriate comparator for the non-eosinophilic and non-allergic SUA population.

7.7 The PBAC noted that to support the clinical claim of superiority of tezepelumab versus SoC in the non-eosinophilic and non-allergic SUA population, the submission presented post-hoc subgroup analyses of patients who were on high-dose inhaled corticosteroids (ICS) from the NAVIGATOR and PATHWAY clinical trials. The PBAC noted that only one of the two subgroup analyses for the annualised asthma exacerbation rate (AAER) was statistically significant, and that the result was marginal with the upper bound of the confidence interval (CI) almost crossing 1 (0.99). Although, the effect direction was consistent between the two studies, the inconsistency in significance increases uncertainty. The PBAC noted additional data presented in the Pre-Sub-Committee Response (PSCR), including a meta-analysis (odds ratio [OR] 0.62, 95% CI 0.42–0.92; p=0.02) and published pooled analyses (see paragraph 6.22), demonstrating statistically significant reductions in AAER with tezepelumab versus placebo. The PBAC agreed with the ESC that while a reduction in AAER was evident across all subgroups the level of reduction was consistently higher for the subgroups with patients who were both higher eosinophil levels (i.e. BEC ≥ 150 cells/µL) and either FeNO or IgE positive.

7.8 The PBAC considered that overall, despite some uncertainty in the evidence, the clinical claim appeared adequately supported by the data. However, the PBAC noted that the clinical benefit observed for tezepelumab versus placebo appeared smaller for this population compared with the benefit observed for the eosinophilic or allergic SUA population.

7.9 The PBAC noted that the submission did not provide a subgroup analysis on safety for this population. However, the PBAC agreed with the ESC that disease phenotype was not likely to affect safety. The PBAC considered that the frequency of adverse events was generally balanced between the tezepelumab and placebo groups in the clinical trials. Overall, the PBAC considered that the claim of non-inferior safety was reasonable for the non-eosinophilic and non-allergic SUA population.

7.10 The PBAC noted that the submission presented a cost-utility analysis of tezepelumab versus SoC. The PBAC noted that the ESC raised concerns regarding the long lifetime time horizon of 40 years compared to the relatively short duration of follow-up in the NAVIGATOR (52 weeks) and the SOURCE trial (48 weeks) and the data informing the economic model not aligning with the proposed PBS population. The PBAC noted additional concerns related to the assumed risk reduction in exacerbation associated with non-OCS tezepelumab group versus SoC and the likelihood of asthma related deaths. The PBAC noted the ESC proposed a respecified base case with a shorter time horizon (from a lifetime to a 20-year time horizon); a smaller exacerbation risk reduction in the non-OCS tezepelumab group relative to SoC (from 50% to 38%); and reduced exacerbation-related mortality rates consistent with the mepolizumab economic model (OCS burst: 0.43%; ED or hospitalisation: 1.13%). The PBAC noted that incorporating these inputs increased the base case ICER from $75,000 to < $95,000 per QALY gained to $115,000 to < $135,000 per QALY gained. The PBAC noted the justification provided in the pre-PBAC Response for the inclusion of a fixed percentage for asthma-related deaths across all event types (1.13%), however considered that while the assumed differential was uncertain, it was more reasonable to assume a difference in mortality across these events rather than a fixed percentage.

7.11 Overall, the PBAC accepted the ESC respecified base case, however considered the ICER was high and remained uncertain. Considering the model uncertainties as outlined, the PBAC advised that the cost-effectiveness of tezepelumab would be acceptable with a price reduction to achieve an ICER of $45,000 to < $55,000 per QALY gained using the ESC respecified economic model.

7.12 The PBAC agreed with the DUSC that the financial estimates presented in the submission were underestimated. The PBAC noted the concerns raised by DUSC that the percentage of patients who are difficult to treat/control (21.7%) and the percentage of patients receiving high-dose ICS/long-acting beta-2 agonist (LABA) were likely underestimated but accepted the pre-PBAC response arguments that these inputs were reasonable. The PBAC noted that the submission assumed from Year 1 to Year 6, treatment uptake would be expected to grow from [redacted]% to [redacted]%, with a [redacted]% year-on-year increase. However, the PBAC noted that tezepelumab is proposed to be a first-line treatment for the non-eosinophilic and non-allergic SUA population who currently are not eligible to receive PBS-listed biologics. For this reason, the PBAC considered the uptake of treatment would be higher than estimated in the submission and advised that it would more likely reflect a sharp increase in first 3 years ([redacted]%, [redacted]%, [redacted]%) and slower thereafter ([redacted]%, [redacted]%, [redacted]%). The PBAC considered that with the amendments to the uptake rates, and with the price reduction required to achieve cost effectiveness it would be reasonable to accept the financial estimates.

7.13 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 tezepelumab:

a) The treatment is not expected to provide a substantial and clinically relevant improvement in efficacy over SoC, as while clinically relevant improvements in AAER were evident, the magnitude of benefit was uncertain and likely to be modest rather than substantial;

b) The treatment is not expected to address a high and urgent unmet clinical need;

c) It was not necessary to make a finding in relation to whether it would be in the public interest for the subsequent pricing application to be progressed under Pricing Pathway A because one or more of the preceding tests had failed.

**Eosinophilic and allergic SUA population**

7.14 The PBAC noted that the proposed listings for eosinophilic or allergic asthma were consistent with the current restrictions for omalizumab, mepolizumab, benralizumab and dupilumab for SUA. The PBAC advised that the proposed restrictions for eosinophilic or allergic asthma population, as amended by the Secretariat, were appropriate. The PBAC advised that the flow-on changes, as suggested by the Secretariat, for benralizumab, dupilumab, mepolizumab and omalizumab, were also appropriate. The PBAC also noted that a grandfathering listing would also be required for patients accessing tezepelumab under a patient access program, for this population only.

7.15 The submission nominated dupilumab as the main comparator, and benralizumab, mepolizumab and omalizumab as secondary comparators. The PBAC considered that this was appropriate.

7.16 The PBAC noted that to support the clinical claim of non-inferiority of tezepelumab compared to dupilumab (primary comparator) and additional comparators (benralizumab, mepolizumab and omalizumab) the submission conducted a series of indirect treatment comparisons (ITCs), based on meta-analysed outcomes from post-hoc subgroups from the tezepelumab trials (NAVIGATOR, PATHWAY and SOURCE) and 14 comparator trials of dupilumab (QUEST, DRI12544, VENTURE), benralizumab (CALIMA, SIROCCO, ZONDA, ANDHI, MIRACLE), mepolizumab (MENSA, MUSCA, SIRIUS, 201536) and omalizumab (EXTRA, INNOVATE) with placebo as the common reference. The PBAC noted that there were transitivity issues between the trials included in the ITCs, which likely introduced bias (paragraphs 6.13−6.14). While noting the uncertainty related to the ITCs presented in the submission, the PBAC agreed with the ESC that the claim of non-inferiority of tezepelumab to dupilumab (primary comparator) and additional comparators (benralizumab, mepolizumab and omalizumab) was adequately supported by the data.

7.17 The PBAC considered that the claim of non-inferior safety compared to dupilumab and additional comparators (benralizumab, mepolizumab and omalizumab) was reasonable.

7.18 The PBAC noted that the submission presented a cost-minimisation analysis of tezepelumab versus dupilumab. The PBAC recalled that omalizumab, mepolizumab and benralizumab for the treatment of severe asthma were cost-minimised to each other and recalled that for the consideration of dupilumab for the treatment of uncontrolled severe eosinophilic or allergic asthma, it had previously considered that the cost-minimisation analysis should be against the least costly biologic for asthma rather than a weighted combination of the nominated comparators (paragraph 7.8, dupilumab public summary document [PSD], November 2020 PBAC Meeting). Consistent with its previous advice, the PBAC considered it was also appropriate that the cost-minimisation analysis for tezepelumab be against the least costly biologic for uncontrolled severe eosinophilic and/or allergic asthma populations.

7.19 In addition, the PBAC considered that tezepelumab and its comparator should be costed over a one year time horizon and that the cost-minimisation approach should account for any comparator loading doses that may be relevant.

7.20 Thus, the PBAC considered the equi-effective doses for eosinophilic SUA were:

- tezepelumab 210 mg by subcutaneous (SC) injection every 4 weeks (13 doses over 1 year);
- dupilumab 400 mg (non-OCS dependent) or 600 mg (OCS dependent) by SC injection followed by 200 mg (non-OCS dependent) or 300 mg (OCS dependent) SC given every 2 weeks (27 doses over 1 year);
- benralizumab 30 mg by SC injection every 4 weeks for the first 3 doses, then every 8 weeks (7.5 doses over 1 year); and
- mepolizumab 100 mg by SC injection every 4 weeks (13 doses over 1 year).

In patients with allergic SUA, the PBAC considered the equi-effective doses were:

- tezepelumab 210 mg by SC injection every 4 weeks (13 doses over 1 year);
- dupilumab 400 mg (non-OCS dependent) or 600 mg (OCS dependent) by SC injection followed by 200 mg (non-OCS dependent) or 300 mg (OCS dependent) given every 2 weeks (27 doses over 1 year); and
- omalizumab 398 mg by SC injection every 4 weeks (dosed at 2 or 4 weeks depending on patient weight and immunoglobulin E levels; 13 doses over 1 year).

7.21 The PBAC recalled that the Product Information for all biologics considered state that after proper training in SC injection technique, patients or the caregiver may self-inject via pre-filled syringe if a physician determines that it is appropriate. The PBAC therefore advised it would be appropriate for the cost-minimisation approach to

include a one-off SC injection training for patients or carers before self-injection (MBS item 82215). The PBAC noted this would be consistent with the cost-minimisation approach for dupilumab (paragraph 7.10, dupilumab PSD, November 2020 PBAC Meeting).

7.22 The PBAC also recalled that in relation to the administration of omalizumab, the Product Information recommended the first three doses be administered under the supervision of a healthcare professional. Consistent with previous advice, for any comparison against omalizumab, the PBAC considered it appropriate for SC injection administration cost-offsets (MBS item 82200) and the costs for post-administration monitoring of anaphylaxis (MBS item 82210) be included for the first three doses of omalizumab (paragraph 7.10, dupilumab PSD, November 2020 PBAC Meeting).

7.23 The PBAC noted the issues related to the financial estimates raised by the DUSC concerning market growth and treatment uptake in this population. The PBAC agreed with the DUSC that these assumptions had been underestimated by the submission. The PBAC considered the approach proposed in the pre-PBAC response which increased the linear market growth estimates by 153 patients each year, increased the uptake rates in Year 1 from [redacted]% to [redacted]% and in Year 2 from [redacted]% to [redacted]% and added < 500 grandfathered patients was appropriate. The PBAC also considered it appropriate for the unit equivalence values along with the SC injection and monitoring of anaphylaxis inputs to be updated as proposed in the pre-PBAC response (see paragraph 6.94). The PBAC considered that with these amendments, and with incorporation of the price resulting from the cost minimisation approach outlined above, it would be reasonable to accept the financial estimates.

7.24 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because tezepelumab is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over dupilumab, benralizumab, mepolizumab or omalizumab, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met.

7.25 The PBAC advised that tezepelumab is not suitable for prescribing by nurse practitioners.

7.26 The PBAC recommended that the Early Supply Rule should not apply.

7.27 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

**Outcome:**
Recommended

# 8 Recommended listing

8.1 Add new listings as follows:

**Non-eosinophilic and non-allergic SUA**

Initial treatment phase:

| **MEDICINAL PRODUCT medicinal product pack** | **PBS item code** | **Max. qty packs** | **Max. qty units** | **№.of Rpts** | **Available brands** |
|---|---|---|---|---|---|
| TEZEPELUMAB | | | | | |
| tezepelumab 210 mg/1.91 mL injection, 1.91 mL pen device | NEW/ Public | 1 | 1 | 7 | Tezspire |
| tezepelumab 210 mg/1.91 mL injection, 1.91 mL pen device | NEW/ Private | 1 | 1 | 7 | Tezspire |
| | | | | | |
| **Restriction Summary [new4] / Treatment of Concept: [new4A]** | | | | | |
| **Concept ID** (for internal Dept. use) | **Category / Program:** ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS) | | | | |
| | **Prescriber type:** ☒Medical Practitioners | | | | |
| | **Restriction type:** ☒Authority Required (FULL assessment) in writing only via OPA/post/HPOS upload)) | | | | |
| | **Authority type:** ☒ Complex Authority Required (CAR) | | | | |
| | **Administrative Advice:** Special Pricing Arrangements apply. | | | | |
| | **Episodicity:** Active | | | | |
| | **Severity:** Uncontrolled Severe | | | | |
| | **Indication:** Uncontrolled severe asthma (non-eosinophilic/non allergic) | | | | |
| | **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) | | | | |
| | **Treatment criteria:** | | | | |
| | Must be treated by a medical practitioner who is either a: (i) respiratory physician, (ii) clinical immunologist, (iii) allergist, (iv) 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 | | | | |
| | **OR** | | | | |
| | Patient must have been diagnosed by a multidisciplinary severe asthma clinic team. | | | | |
| | **AND** | | | | |
| | **Clinical criteria:** | | | | |
| | Patient must not have received PBS-subsidised treatment with a biological medicine for severe asthma; | | | | |
| | **OR** | | | | |
| | Patient must have had a break in treatment of at least 12 months from the most recently approved PBS-subsidised biological medicine for severe asthma. | | | | |
| | **AND** | | | | |
| | **Clinical criteria:** | | | | |

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| | Patient must have a diagnosis of asthma confirmed and documented in the patient's medical records by either a: (i) respiratory physician, (ii) clinical immunologist, (iii) allergist, (iv) general physician experienced in the management of patients with severe asthma, defined by at least one of the following standard clinical features: (a) 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), (b) 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, (c) 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 with the details document in the patients' medical records |
| | **AND** |
| | **Clinical criteria:** |
| | Patient must have a duration of asthma of at least 1 year. |
| | **AND** |
| | **Clinical criteria:** |
| | Patient must have a blood eosinophil count of less than 300 cells per microlitre in the 12 months prior to initiating treatment with this drug; |
| | **OR** |
| | Patient must have blood eosinophil count of less than 150 cells per microlitre while receiving treatment with oral corticosteroids in the 12 months prior to initiating treatment with this drug; |
| | **AND** |
| | Patient must have total serum human immunoglobulin E less than 30 IU/mL, measured in the last 12 months prior to initiating treatment with this drug and no past or current evidence of atopy, documented by either: (i) skin prick testing; (ii) an in vitro measure of specific IgE |
| | **AND** |
| | **Clinical criteria:** |
| | Patient must have failed to achieve adequate control with optimised asthma therapy, despite formal assessment of and adherence to correct inhaler technique, which has been documented. |
| | **AND** |
| | **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 any of: (i) nasal polyps, (ii) uncontrolled severe allergic asthma, (iii) uncontrolled severe asthma, |
| | **Population criteria:** |
| | Patients must be aged 12 years or older. |

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| | **Prescribing Instructions:**<br>Optimised asthma therapy includes adherence to maximal inhaled therapy, including high dose inhaled corticosteroid (ICS) plus long-acting beta-2 agonist (LABA) therapy for at least 12 months, unless contraindicated or not tolerated.<br><br>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:**<br>The following initiation criteria indicate failure to achieve adequate control and must be demonstrated in all patients at the time of the application:<br><br>(a) an Asthma Control Questionnaire (ACQ-5) score of at least 2.0, as assessed in the month prior to initiating this drug, AND<br><br>(b) while receiving optimised asthma therapy in the 12 months prior to initiating this drug, experienced at least 1 admission to hospital for a severe asthma exacerbation, OR 1 severe asthma exacerbation, requiring documented use of systemic corticosteroids (oral corticosteroids initiated or increased for at least 3 days, or parenteral corticosteroids) prescribed/supervised by a physician.<br><br>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.<br><br>This assessment, which will be used to determine eligibility for the first continuing treatment, should be conducted within 4 weeks of the last dose of biological medicine. To avoid an interruption of supply for the first continuing treatment, the assessment should be provided no later than 2 weeks prior to the patient completing their current treatment course, unless the patient is currently on a treatment break.<br><br>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.<br><br>A multidisciplinary severe asthma clinic team comprises of:<br>(i) A respiratory physician; and<br>(ii) A pharmacist, nurse or asthma educator.<br>At the time of the authority application, medical practitioners should request up to 7 repeats to provide for an initial course of tezepelumab sufficient for up to 32 weeks of therapy, at a dose of 210 mg every four weeks, which is consistent with arrangements for the currently listed biologics. |

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| | **Prescribing Instructions:**<br>The following must be provided at the time of application and documented in the patient's medical records:<br>(a) details (treatment, date of commencement, duration of therapy) of prior optimised asthma drug therapy; and<br>(b) If applicable, details of contraindications and/or intolerances of a severity necessitating permanent treatment withdrawal to standard therapy according to the relevant TGA-approved Product Information; and<br>(c) details of severe exacerbation/s experienced in the 12 months prior to initiating this drug while receiving optimised asthma therapy (date and treatment); and<br>(d) Asthma Control Questionnaire (ACQ-5) score; and<br>(e) if applicable, the eosinophil count and date; and<br>(f) if applicable, the IgE result and date. |
| | **Administrative Advice:**<br>For copies of the ACQ and the calculation sheets please contact AstraZeneca Medical Information on 1800 805 342. |
| | ***Administrative Advice:***<br>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.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). |

Continuing treatment phase:

| **MEDICINAL PRODUCT**<br>**medicinal product pack** | **PBS item code** | **Max. qty packs** | **Max. qty units** | **№.of Rpts** | **Available brands** |
|---|---|---|---|---|---|
| TEZEPELUMAB | | | | | |
| tezepelumab 210 mg/1.91 mL injection, 1.91 mL pen device | NEW/ Public | 1 | 1 | 5 | Tezspire |
| tezepelumab 210 mg/1.91 mL injection, 1.91 mL pen device | NEW/ Private | 1 | 1 | 5 | Tezspire |

| | |
|---|---|
| **Concept ID** (for internal Dept. use) | **Category / Program:**<br>☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS) |
| | **Prescriber type:** ☒Medical Practitioners |
| | **Restriction type:**<br>☒Authority Required (FULL assessment) in writing only via OPA/post/HPOS upload)) |
| | **Authority type:** ☒ Complex Authority Required (CAR) |
| | **Administrative Advice:** Special Pricing Arrangements apply. |
| | **Episodicity:** Active |
| | **Severity:** Uncontrolled Severe |
| | **Indication:** Uncontrolled severe asthma (non-eosinophilic/non allergic) |
| | **Treatment Phase:** Continuing treatment |
| | **Treatment criteria:** |
| | Must be treated by a medical practitioner who is either a: (i) respiratory physician, (ii) clinical immunologist, (iii) allergist, (iv) general physician experienced in the management of patients with severe asthma |
| | **Clinical criteria:** |

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| | Patient must have received this drug as their most recent course of PBS-subsidised biological agent treatment for this condition in this treatment cycle |
| | **AND** |
| | **Clinical criteria:** |
| | Patient must have demonstrated or sustained an adequate response to PBS-subsidised treatment with this drug for this condition |
| | **AND** |
| | **Clinical criteria:** |
| | The treatment must not be used in combination with and within 4 weeks of another PBS-subsidised biological medicine prescribed for any of: (i) nasal polyps, (ii) uncontrolled severe allergic asthma, (iii) uncontrolled severe asthma, |
| | **AND** |
| | **Clinical criteria:** |
| | Patient must not receive more than 24 weeks of treatment under this restriction |
| | **Population criteria:** |
| | Patients must be aged 12 years or older. |
| | **Prescribing Instructions:**<br>An adequate response to this biological medicine is defined as:<br>(a) a reduction in the Asthma Control Questionnaire (ACQ-5) score of at least 0.5 from baseline, OR<br>(b) maintenance oral corticosteroid dose reduced by at least 25% from baseline, and no deterioration in ACQ-5 score from baseline or an increase in ACQ-5 score from baseline less than or equal to 0.5. |
| | **Prescribing Instructions:**<br>All applications for second and subsequent continuing treatments with this drug must include a measurement of response to the prior course of therapy. The Asthma Control Questionnaire (5 item version) assessment of the patient's response to the prior course of treatment or the assessment of oral corticosteroid dose, should be made from 20 weeks after the first dose of 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 continuing therapy to be processed.<br><br>The assessment should, where possible, be completed by the same physician who initiated treatment with this drug and should be conducted within 4 weeks of the last dose of biological medicine.<br><br>Where treatment was ceased for clinical reasons despite the patient experiencing improvement, an assessment of the patient's response to treatment made at the time of treatment cessation or retrospectively will be considered to determine whether the patient demonstrated or sustained an adequate response to treatment.<br><br>A patient who fails to respond to treatment with this biological medicine for uncontrolled severe asthma will not be eligible to receive further PBS-subsidised treatment with this biological medicine for severe asthma within the current treatment cycle. |
| | **Prescribing Instructions:**<br>The following information must be provided at the time of application and must be documented in the patient's medical records:<br>(a) Asthma Control Questionnaire (ACQ-5) score; and<br>(b) If applicable, maintenance oral corticosteroid dose. |

## Eosinophilic or allergic SUA

Initial 1, Initial 2 and Grandfathering treatment phases:

| MEDICINAL PRODUCT medicinal product pack | PBS item code | Max. qty packs | Max. qty units | №.of Rpts | Available brands |
|---|---|---|---|---|---|
| TEZEPELUMAB | | | | | |
| tezepelumab 210 mg/1.91 mL injection, 1.91 mL pen device | NEW/ Public | 1 | 1 | 7 | Tezspire |
| tezepelumab 210 mg/1.91 mL injection, 1.91 mL pen device | NEW/ Private | 1 | 1 | 7 | Tezspire |

| | |
|---|---|
| **Restriction Summary [new1] / Treatment of Concept: [new1A]** | |
| **Concept ID** (for internal Dept. use) | **Category / Program:** ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS) |
| | **Prescriber type:** ☒Medical Practitioners |
| | **Restriction type:** ☒Authority Required (FULL assessment) in writing only via OPA/post/HPOS upload)) |
| | **Authority type:** ☒ Complex Authority Required (CAR) |
| | **Administrative Advice:** Special Pricing Arrangements apply. |
| | **Administrative Advice:** Overarching new AA1 long note |
| | **Episodicity:** Active |
| | **Severity:** Uncontrolled Severe |
| | **Indication:** Uncontrolled severe asthma |
| | **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) |
| | **Treatment criteria:** |
| | Must be treated by a medical practitioner who is either a: (i) respiratory physician, (ii) clinical immunologist, (iii) allergist, (iv) 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 |
| | **OR** |
| | Patient must have been diagnosed by a multidisciplinary severe asthma clinic team. |
| | **AND** |
| | **Clinical criteria:** |
| | Patient must not have received PBS-subsidised treatment with a biological medicine for severe asthma; |
| | **OR** |
| | Patient must have had a break in treatment of at least 12 months from the most recently approved PBS-subsidised biological medicine for severe asthma. |
| | **AND** |
| | **Clinical criteria:** |

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| | Patient must have a diagnosis of asthma confirmed and documented in the patient's medical records by either a: (i) respiratory physician, (ii) clinical immunologist, (iii) allergist, (iv) general physician experienced in the management of patients with severe asthma, defined by at least one of the following standard clinical features: (a) 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), (b) 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, (c) 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 with the details document in the patient's medical records. |
| | **AND** |
| | **Clinical criteria:** |
| | Patient must have a duration of asthma of at least 1 year. |
| | **AND** |
| | **Clinical criteria:** |
| | Patient must have blood eosinophil count of at least 300 cells per microlitre in the 12 months prior to initiating treatment with this drug; |
| | **OR** |
| | Patient must have blood eosinophil count of at least 150 cells per microlitre while receiving treatment with oral corticosteroids in the 12 months prior to initiating treatment with this drug; |
| | **OR** |
| | Patient must have total serum human immunoglobulin E of at least 30 IU/mL, measured in the 12 months prior to initiating treatment with this drug that has past or current evidence of atopy, documented by either: (i) skin prick testing; (ii) an in vitro measure of specific IgE. |
| | **AND** |
| | **Clinical criteria:** |
| | Patient must have failed to achieve adequate control with optimised asthma therapy, despite formal assessment of and adherence to correct inhaler technique, which has been documented in the patient's medical records. |
| | **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 any of: (i) nasal polyps, (ii) uncontrolled severe allergic asthma, (iii) uncontrolled severe asthma |
| | **Population criteria:** |
| | Patients must be aged 12 years or older. |

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| | **Prescribing Instructions:**<br>Optimised asthma therapy includes adherence to maximal inhaled therapy, including high dose inhaled corticosteroid (ICS) plus long-acting beta-2 agonist (LABA) therapy for at least 12 months, unless contraindicated or not tolerated.<br><br>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:**<br>The following initiation criteria indicate failure to achieve adequate control and must be demonstrated in all patients at the time of the application:<br><br>(a) an Asthma Control Questionnaire (ACQ-5) score of at least 2.0, as assessed in the month prior to initiating this drug, AND<br><br>(b) while receiving optimised asthma therapy in the 12 months prior to initiating this drug, experienced at least 1 admission to hospital for a severe asthma exacerbation, OR 1 severe asthma exacerbation, requiring documented use of systemic corticosteroids (oral corticosteroids initiated or increased for at least 3 days, or parenteral corticosteroids) prescribed/supervised by a physician.<br><br>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.<br><br>This assessment, which will be used to determine eligibility for the first continuing treatment, should be conducted within 4 weeks of the last dose of biological medicine. To avoid an interruption of supply for the first continuing treatment, the assessment should be provided no later than 2 weeks prior to the patient completing their current treatment course, unless the patient is currently on a treatment break.<br><br>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.<br><br>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 all eligible biological medicines within the same treatment cycle.<br><br>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 recommencement of treatment with a biological medicine under the new treatment cycle.<br>There is no limit to the number of treatment cycles that a patient may undertake in their lifetime.<br><br>A multidisciplinary severe asthma clinic team comprises of:<br>(i) A respiratory physician; and<br>(ii) A pharmacist, nurse or asthma educator. |

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| | At the time of the authority application, medical practitioners should request up to 7 repeats to provide for an initial course of tezepelumab sufficient for up to 32 weeks of therapy, at a dose of 210 mg every four weeks. |
| | **Prescribing Instructions:**<br>The following must be provided at the time of application and documented in the patient's medical records:<br>(a) details (treatment, date of commencement, duration of therapy) of prior optimised asthma drug therapy; and<br>(b) If applicable, details of contraindications and/or intolerances of a severity necessitating permanent treatment withdrawal to standard therapy according to the relevant TGA-approved Product Information; and<br>(c) details of severe exacerbation/s experienced in the 12 months prior to receiving this drug, while receiving optimised asthma therapy (date and treatment); and<br>(d) Asthma Control Questionnaire (ACQ-5) score; and<br>(e) if applicable, the eosinophil count and date; and<br>(f) if applicable, the IgE result and date. |
| | **Administrative Advice:**<br>For copies of the ACQ and the calculation sheets please contact AstraZeneca Medical Information on 1800 805 342. |
| | **Administrative Advice:**<br>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.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). |
| | |
| **Restriction Summary [new2] / Treatment of Concept: [new2A]** | |
| **Concept ID** (for internal Dept. use) | **Category / Program:**<br>☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS) |
| | **Prescriber type:**<br>☒Medical Practitioners |
| | **Restriction type:**<br>☒Authority Required (FULL assessment) in writing only via OPA/post/HPOS upload) |
| | **Authority type:**<br>☒ Complex Authority Required (CAR) |
| | **Episodicity:** Active |
| | **Severity:** Uncontrolled Severe |
| | **Indication:** Uncontrolled severe asthma |
| | **Treatment Phase:** Initial treatment – Initial 2 (Change of treatment) |
| | **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. |

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| | **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 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 biological medicine treatment for severe asthma; |
| | **OR** |
| | Patient must have each of: i) total serum human immunoglobulin E greater than or equal to 30 IU/mL measured no more than 12 months prior to initiating PBS-subsidised treatment with a biological medicine for severe asthma, ii) past or current evidence of atopy, documented by skin prick testing or an in vitro measure of specific IgE in the past 12 months or in the 12 months prior to initiating treatment with a biological medicine 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 any of: (i) nasal polyps, (ii) uncontrolled severe allergic asthma, (iii) uncontrolled severe asthma, |
| | **Treatment criteria:** |
| | Must be treated by a medical practitioner who is either a: (i) respiratory physician, (ii) clinical immunologist, (iii) allergist, (iv) general physician experienced in the management of patients with severe asthma |
| | **Population criteria:** |
| | Patients must be aged 12 years or older. |

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| | **Prescribing Instructions:**<br>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.<br>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.<br>This assessment, which will be used to determine eligibility for the first continuing treatment, should be conducted within 4 weeks of the last dose of biological medicine. Where a response assessment is not undertaken and provided, the patient will be deemed to have failed to respond to treatment with this biological medicine.<br>At the time of the authority application, medical practitioners should request up to 7 repeats to provide for an initial course of tezepelumab sufficient for up to 32 weeks of therapy, at a dose of 210 mg every four weeks.<br>A multidisciplinary severe asthma clinic team comprises of:<br>(i) A respiratory physician; and<br>(ii) A pharmacist, nurse or asthma educator. |
| | **Prescribing Instructions:**<br>The authority application must be made in writing and must include:<br>(1) details of the proposed prescription; and<br>(2) a completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice). |
| | **Prescribing Instructions:**<br>The following must be provided at the time of application and documented in the patient's medical records:<br>(a) 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<br>(b) details (treatment, date of commencement, duration of therapy) of prior biological medicine treatment; and<br>(c) if applicable, the eosinophil count and date; and<br>(d) if applicable, the dose of the maintenance oral corticosteroid (where the response criteria or baseline is based on corticosteroid dose); and<br>(e) if applicable, the IgE result and date; and<br>(f) the reason for switching therapy (e.g. failure of prior therapy, partial response to prior therapy, adverse event to prior therapy). |
| | |
| **Restriction Summary [new3] / Treatment of Concept: [new3A]** | |
| **Concept ID** (for internal Dept. use) | **Category / Program:**<br>☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS) |
| | **Prescriber type:** ☒Medical Practitioners |
| | **Restriction type:**<br>☒Authority Required (FULL assessment) in writing only via OPA/post/HPOS upload)) |
| | **Authority type:** ☒ Complex Authority Required (CAR) |
| | **Administrative Advice:** Special Pricing Arrangements apply. |
| | **Administrative Advice:** Overarching new AA1 long note |

| | | |
|---|---|---|
| | | **Episodicity:** Active |
| | | **Severity:** Uncontrolled Severe |
| | | **Indication:** Uncontrolled severe asthma |
| | | **Treatment Phase:** Transitioning from non-PBS to PBS-subsidised supply – Grandfathering arrangements |
| | | **Treatment criteria:** |
| | | Must be treated by a medical practitioner who is either a: (i) respiratory physician, (ii) clinical immunologist, (iii) allergist, (iv) general physician experienced in the management of patients with severe asthma |
| | | **Clinical criteria:** |
| | | Patient must have received non-PBS-subsidised treatment with this biological medicine for this PBS-indication prior to [listing date] |
| | | **AND** |
| | | **Clinical criteria:** |
| | | Patient must have a diagnosis of asthma confirmed and documented in the patient's medical records by either a: (i) respiratory physician, (ii) clinical immunologist, (iii) allergist, (iv) general physician experienced in the management of patients with severe asthma, defined by at least one of the following standard clinical features: (a) 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), (b) 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, (c) 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 had a diagnosis of asthma from at least two physicians experienced in the management of patients with severe asthma with the details document in the patient's medical records prior to initiation of non-PBS-subsidised treatment with this drug for this condition |
| | | **AND** |
| | | **Clinical criteria:** |
| | | Patient must have had a duration of asthma of at least 1 year prior to initiating non-PBS-subsidised treatment with this drug for this condition. |
| | | **AND** |
| | | **Clinical criteria:** |
| | | Patient must have had blood eosinophil count at least 300 cells per microlitre in the 12 months prior to initiation of non-PBS-subsidised treatment with this drug for this condition.; |
| | | **OR** |
| | | Patient must have had blood eosinophil count at least 150 cells per microlitre while receiving treatment with oral corticosteroids in the 12 months prior to initiation of non-PBS-subsidised treatment with this drug for this condition. |
| | | **OR** |
| | | Patient must have had total serum human immunoglobulin E of at least 30 IU/mL, measured in the 12 months prior to initiation of non-PBS subsidised treatment with this drug for this condition that had past or current evidence of atopy, documented by either: (i) skin prick testing; (ii) an in vitro measure of specific IgE no more than 12 months prior to initiation of non-PBS-subsidised treatment with this drug for this condition |
| | | **AND** |
| | | **Clinical criteria:** |

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| | Patient must have documented a failure to achieve adequate control with optimised asthma therapy, despite formal assessment of and adherence to correct inhaler technique, prior to initiating non-PBS-subsidised treatment with this drug for this condition. |
| | **AND** |
| | **Clinical criteria:** |
| | Patient must have demonstrated or sustained an adequate response to treatment with this drug if the patient has received at least 28 weeks of treatment with this drug for this condition. |
| | **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 any of: (i) nasal polyps, (ii) uncontrolled severe allergic asthma, (iii) uncontrolled severe asthma, |
| | **Population criteria:** |
| | Patients must be aged 12 years or older. |
| | **Administrative Advice:**<br>This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria. |
| | **Prescribing Instructions:**<br>Optimised asthma therapy includes adherence to maximal inhaled therapy, including high dose inhaled corticosteroid (ICS) plus long-acting beta-2 agonist (LABA) therapy for at least 12 months, unless contraindicated or not tolerated.<br><br>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:**<br>The following initiation criteria indicate failure to achieve adequate control and must be demonstrated in all patients at the time of the application:<br><br>(a) an Asthma Control Questionnaire (ACQ-5) score of at least 2.0, as assessed in the month prior to starting treatment with this drug, AND<br><br>(b) while receiving optimised asthma therapy in the12 months prior to starting treatment with this drug, experienced at least 1 admission to hospital for a severe asthma exacerbation, OR 1 severe asthma exacerbation, requiring documented use of systemic corticosteroids (oral corticosteroids initiated or increased for at least 3 days, or parenteral corticosteroids) prescribed/supervised by a physician.<br><br>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.<br><br>This assessment, which will be used to determine eligibility for the first continuing treatment, should be conducted within 4 weeks of the last dose of biological medicine. To avoid an interruption |

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| | of supply for the first continuing treatment, the assessment should be provided no later than 2 weeks prior to the patient completing their current treatment course, unless the patient is currently on a treatment break.<br><br>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.<br><br>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 all eligible biological medicines within the same treatment cycle.<br><br>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 recommencement of treatment with a biological medicine under the new treatment cycle.<br>There is no limit to the number of treatment cycles that a patient may undertake in their lifetime.<br><br>A multidisciplinary severe asthma clinic team comprises of:<br>(i) A respiratory physician; and<br>(ii) A pharmacist, nurse or asthma educator.<br>At the time of the authority application, medical practitioners should request up to 7 repeats to provide for an initial course of tezepelumab sufficient for up to 32 weeks of therapy, at a dose of 210 mg every four weeks. |
| | **Prescribing Instructions:**<br>The following must be provided at the time of application and documented in the patient's medical records:<br>(a) details (treatment, date of commencement, duration of therapy) of prior optimised asthma drug therapy; and<br>(b) If applicable, details of contraindications and/or intolerances of a severity necessitating permanent treatment withdrawal to standard therapy according to the relevant TGA-approved Product Information; and<br>(c) details of severe exacerbation/s experienced in the 12 months prior to receiving this drug, while receiving optimised asthma therapy (date and treatment); and<br>(d) Asthma Control Questionnaire (ACQ-5) score; and<br>(e) if applicable, the eosinophil count and date; and<br>(f) if applicable, the IgE result and date. |
| | **Prescribing Instructions:**<br>A patient may only qualify for PBS-subsidised treatment under this restriction once only. |
| | **Administrative Advice:**<br>For copies of the ACQ and the calculation sheets please contact AstraZeneca Medical Information on 1800 805 342. |
| | **Administrative Advice:**<br>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.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). |
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| | **Administrative Advice:** |

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| | **TREATMENT OF ADULT AND ADOLESCENT PATIENTS WITH UNCONTROLLED SEVERE ASTHMA**<br>The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of the biological medicines for uncontrolled severe asthma. Where the term biological medicine appears in the following notes and restrictions it refers to all PBS benefits with the specific PBS indication of 'uncontrolled severe asthma'.<br><br>A patient is eligible for PBS-subsidised treatment with only 1 biological medicine for uncontrolled severe asthma at any one time.<br><br>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.<br><br>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.<br><br>A patient currently receiving PBS-subsidised treatment as of 1 April 2021 is considered to have started a cycle of treatment.<br><br>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.<br><br>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.<br><br>Once a patient has either failed to achieve or sustain a response to treatment with each of the biological medicines they are eligible for, 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].<br><br>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.<br><br>There is no limit to the number of treatment cycles that a patient may undertake in their lifetime.<br><br>How to prescribe PBS-subsidised biological medicine treatment for uncontrolled severe asthma.<br>(1) Initial treatment:<br>Applications for initial treatment should be made where:<br>(i) a patient has not received prior PBS-subsidised biological medicine treatment and wishes to commence such therapy (Initial 1 restriction); or<br>(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<br>(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]. |

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| | 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.<br><br>(2) Continuing treatment:<br>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.<br><br>(3) Baseline measurements to determine response:<br>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.<br>For patients transitioned from the paediatric to the adolescent/adult restriction, the exacerbation history may also be used to determine response.<br>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.<br><br>(4) Swapping therapy within the same treatment cycle.<br>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.<br>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.<br>Within the same treatment cycle a patient may alternate between therapy with any biological medicine of their choice (1 at a time) providing:<br>(i) they have not received PBS-subsidised treatment with that particular biological medicine previously; or<br>(ii) they have demonstrated an adequate response to that particular biological medicine if they have previously trialled it on the PBS; and<br>(iii) they have not previously failed to respond to treatment with all eligible biological medicines in this treatment cycle.<br><br>(5) Re-commencement of a new treatment cycle after a treatment break in PBS-subsidised therapy:<br>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, must re-qualify through an Initial 1 restriction.<br><br>(6) Monitoring of patients:<br>Omalizumab only:<br>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. |

Continuing treatment phase:

| **MEDICINAL PRODUCT**<br>**medicinal product pack** | **PBS item code** | **Max. qty packs** | **Max. qty units** | **№.of Rpts** | **Available brands** |
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| TEZEPELUMAB | | | | | |

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|---|---|---|---|---|---|
| tezepelumab 210 mg/1.91 mL injection, 1.91 mL pen device | NEW/ Public | 1 | 1 | 5 | Tezspire |
| tezepelumab 210 mg/1.91 mL injection, 1.91 mL pen device | NEW/ Private | 1 | 1 | 5 | Tezspire |

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| **Concept ID** (for internal Dept. use) | **Category / Program:** ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS) |
| | **Prescriber type:** ☒Medical Practitioners |
| | **Restriction type:** ☒Authority Required (FULL assessment) in writing only via OPA/post/HPOS upload)) |
| | **Authority type:** ☒ Complex Authority Required (CAR) |
| | **Administrative Advice:** Special Pricing Arrangements apply. |
| | **Episodicity:** Active |
| | **Severity:** Uncontrolled Severe |
| | **Indication:** Uncontrolled severe asthma |
| | **Treatment Phase:** Continuing treatment |
| | **Treatment criteria:** |
| | Must be treated by a medical practitioner who is either a: (i) respiratory physician, (ii) clinical immunologist, (iii) allergist, (iv) general physician experienced in the management of patients with severe asthma |
| | **Clinical criteria:** |
| | Patient must have received this drug as their most recent course of PBS-subsidised biological agent treatment for this condition in this treatment cycle |
| | **AND** |
| | **Clinical criteria:** |
| | Patient must have demonstrated or sustained an adequate response to PBS-subsidised treatment with this drug for this condition |
| | **AND** |
| | **Clinical criteria:** |
| | The treatment must not be used in combination with and within 4 weeks of another PBS-subsidised biological medicine prescribed for any of: (i) nasal polyps, (ii) uncontrolled severe allergic asthma, (iii) uncontrolled severe asthma, |
| | **AND** |
| | **Clinical criteria:** |
| | Patient must not receive more than 24 weeks of treatment under this restriction |
| | **Population criteria:** |
| | Patients must be aged 12 years or older. |
| | **Prescribing Instructions:**<br>An adequate response to this biological medicine is defined as:<br>(a) a reduction in the Asthma Control Questionnaire (ACQ-5) score of at least 0.5 from baseline, OR<br>(b) maintenance oral corticosteroid dose reduced by at least 25% from baseline, and no deterioration in ACQ-5 score from baseline or an increase in ACQ-5 score from baseline less than or equal to 0.5. |

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| | **Prescribing Instructions:**<br>All applications for second and subsequent continuing treatments with this drug must include a measurement of response to the prior course of therapy. The Asthma Control Questionnaire (5 item version) assessment of the patient's response to the prior course of treatment or the assessment of oral corticosteroid dose, should be made from 20 weeks after the first dose of 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 continuing therapy to be processed.<br><br>The assessment should, where possible, be completed by the same physician who initiated treatment with this drug and should be conducted within 4 weeks of the last dose of biological medicine.<br><br>Where treatment was ceased for clinical reasons despite the patient experiencing improvement, an assessment of the patient's response to treatment made at the time of treatment cessation or retrospectively will be considered to determine whether the patient demonstrated or sustained an adequate response to treatment.<br><br>A patient who fails to respond to treatment with this biological medicine for uncontrolled severe asthma will not be eligible to receive further PBS-subsidised treatment with this biological medicine for severe asthma within the current treatment cycle. |
| | **Prescribing Instructions:**<br>The following information must be provided at the time of application and must be documented in the patient's medical records:<br>(a) Asthma Control Questionnaire (ACQ-5) score; and<br>(b) If applicable, maintenance oral corticosteroid dose. |

8.2 Flow on changes required – change the numeral '4' to 'all eligible' for the following PBS item codes:

| Replace concept ID 32243 | With new concept ID |
|---|---|
| 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 for severe asthma within the same treatment cycle. | 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 *all eligible* biological medicines for severe asthma within the same treatment cycle. |
| PBS Item Codes to be changed to concept ID 32243 | |
| 10109C / omalizumab 150 mg/mL injection, 1 mL syringe<br>10122R / omalizumab 150 mg/mL injection, 1 mL syringe<br>10118M / omalizumab 75 mg/0.5 mL injection, 0.5 mL syringe<br>10110D / omalizumab 75 mg/0.5 mL injection, 0.5 mL syringe<br>14949T / omalizumab 75 mg/0.5 mL injection, 0.5 mL pen device<br>14904K / omalizumab 75 mg/0.5 mL injection, 0.5 mL pen device<br>14884J / omalizumab 150 mg/mL injection, 1 mL pen device<br>14923K / omalizumab 150 mg/mL injection, 1 mL pen device<br>14885K / omalizumab 300 mg/2 mL injection, 2 mL pen device<br>14953B / omalizumab 300 mg/2 mL injection, 2 mL pen device | |

| Replace concept ID 32221 | With new concept ID |
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| 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. | 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 *all eligible* biological medicines for severe asthma within the same treatment cycle. |
| PBS Item Codes to be changed to concept ID 32221 | |
| 11997K / benralizumab 30 mg/mL injection, 1 mL pen device<br>11994G / benralizumab 30 mg/mL injection, 1 mL pen device | |

| Replace concept ID 32182 | With new concept ID |
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| 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. | 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 *all eligible* biological medicines for severe asthma within the same treatment cycle. |
| PBS Item Codes to be changed to concept ID 32182 | |
| 12051G / mepolizumab 100 mg/mL injection, 1 mL pen device<br>12007Y / mepolizumab 100 mg/mL injection, 1 mL pen device | |

| Replace concept ID 32226 | With new concept ID |
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| 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. | 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 *all eligible* biological medicines for severe asthma within the same treatment cycle. |
| PBS Item Codes to be changed to concept ID 32226 | |
| 12309W / dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes<br>12313C / dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes | |

| Replace concept ID 32233 | With new concept ID |
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| 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. | 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 *all eligible* biological medicines for severe asthma within the same treatment cycle. |
| PBS Item Codes to be changed to concept ID 32233 | |

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| 12293B / dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes<br>12310X / dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes |

| Replace concept ID 32182 | With new concept ID |
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| 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. | 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 *all eligible* biological medicines within the same treatment cycle. |
| PBS Item Codes to be changed to concept ID 32182 | |
| 12051G / mepolizumab 100 mg/mL injection, 1 mL pen device<br>12007Y / mepolizumab 100 mg/mL injection, 1 mL pen device | |

| Replace concept ID 32169 | With new concept ID |
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| Within the same treatment cycle a patient may alternate between therapy with any biological medicine of their choice (1 at a time) providing:<br>(i) they have not received PBS-subsidised treatment with that particular biological medicine previously; or<br>(ii) they have demonstrated an adequate response to that particular biological medicine if they have previously trialled it on the PBS; and<br>(iii) they have not previously failed to respond to treatment with all 4 biological medicines in this 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:<br>(i) they have not received PBS-subsidised treatment with that particular biological medicine previously; or<br>(ii) they have demonstrated an adequate response to that particular biological medicine if they have previously trialled it on the PBS; and<br>(iii) they have not previously failed to respond to treatment with all *all eligible* biological medicines in this treatment cycle. |
| 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. | 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 *all eligible* times within a treatment cycle), must re-qualify through an Initial 1 restriction. |
| 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]. | Once a patient has either failed to achieve or sustain a response to treatment *all eligible* 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 |

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| | after a treatment break in PBS-subsidised therapy' below]. |
| PBS Item Codes to be changed to concept ID 32169: | |
| 10109C / omalizumab 150 mg/mL injection, 1 mL syringe<br>10122R / omalizumab 150 mg/mL injection, 1 mL syringe<br>10118M / omalizumab 75 mg/0.5 mL injection, 0.5 mL syringe<br>10110D / omalizumab 75 mg/0.5 mL injection, 0.5 mL syringe<br>11824H / omalizumab 150 mg/mL injection, 1 mL syringe<br>11864K / omalizumab 150 mg/mL injection, 1 mL syringe<br>11835X / omalizumab 75 mg/0.5 mL injection, 0.5 mL syringe<br>11840E / omalizumab 75 mg/0.5 mL injection, 0.5 mL syringe<br>11828M / omalizumab 150mg/mL injection, 1 mL syringe<br>11825J / omalizumab 150 mg/mL injection, 1 mL syringe<br>11846L / omalizumab 75 mg/0.5 mL injection, 0.5 mL syringe<br>11826K / omalizumab 75 mg/0.5 mL injection, 0.5 mL syringe<br>12051G / mepolizumab 100 mg/mL injection, 1 mL pen device<br>12007Y / mepolizumab 100 mg/mL injection, 1 mL pen device<br>12052H / mepolizumab 100 mg/mL injection, 1 mL pen device<br>12064Y / mepolizumab 100 mg/mL injection, 1 mL pen device<br>12043W / mepolizumab 100 mg/mL injection, 1 mL pen device<br>12021Q / mepolizumab 100 mg/mL injection, 1 mL pen device<br>11997K / benralizumab 30 mg/mL injection, 1 mL pen device<br>11994G / benralizumab 30 mg/mL injection, 1 mL pen device<br>11996J / benralizumab 30 mg/mL injection, 1 mL pen device<br>11999M / benralizumab 30 mg/mL injection, 1 mL pen device<br>11995H / benralizumab 30 mg/mL injection, 1 mL pen device<br>12000N / benralizumab 30 mg/mL injection, 1 mL pen device<br>12309W / dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes<br>12313C / dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes<br>12318H / dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes<br>12316F / dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes<br>12293B / dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes<br>12310X / dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes<br>12302L / dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes<br>12294C / dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes<br>14947Q / omalizumab 75 mg/0.5 mL injection, 0.5 mL syringe<br>14919F / omalizumab 75 mg/0.5 mL injection, 0.5 mL syringe<br>14948R / omalizumab 150 mg/mL injection, 1 mL syringe<br>14927P / omalizumab 150 mg/mL injection, 1 mL syringe<br>14949T / omalizumab 75 mg/0.5 mL injection, 0.5 mL pen device<br>14904K / omalizumab 75 mg/0.5 mL injection, 0.5 mL pen device<br>14884J / omalizumab 150 mg/mL injection, 1 mL pen device<br>14923K / omalizumab 150 mg/mL injection, 1 mL pen device | |

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| 14885K / omalizumab 300 mg/2 mL injection, 2 mL pen device |
| 14953B / omalizumab 300 mg/2 mL injection, 2 mL pen device |
| 14950W / omalizumab 75 mg/0.5 mL injection, 0.5 mL pen device |
| 14921H / omalizumab 75 mg/0.5 mL injection, 0.5 mL pen device |
| 14922J / omalizumab 150 mg/mL injection, 1 mL pen device |
| 14928Q / omalizumab 150 mg/mL injection, 1 mL pen device |
| 14906M / omalizumab 300 mg/2 mL injection, 2 mL pen device |
| 14951X / omalizumab 300 mg/2 mL injection, 2 mL pen device |
| 14905L / omalizumab 75 mg/0.5 mL injection, 0.5 mL pen device |
| 14939G / omalizumab 75 mg/0.5 mL injection, 0.5 mL pen device |
| 14929R / omalizumab 150 mg/mL injection, 1 mL pen device |
| 14883H / omalizumab 150 mg/mL injection, 1 mL pen device |
| 14952Y / omalizumab 300 mg/2 mL injection, 2 mL pen device |
| 14912W / omalizumab 300 mg/2 mL injection, 2 mL pen device |

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

# 9 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.

# 10 Sponsor's Comment

The sponsor had no comment.