5.05 DEPEMOKIMAB, Solution for subcutaneous injection 100 mg in 1 mL, Exdensur®, GLAXOSMITHKLINE AUSTRALIA PTY LTD

1 Purpose of submission

1.1 The Category 2 submission requested a Section 100, Highly Specialised Drugs (HSD), Authority Required, listing of depemokimab (DEPE) for the treatment of uncontrolled severe eosinophilic asthma (SEA), in patients aged 12 years or older with a blood eosinophil count greater than or equal to 300 cells per microlitre in the last 12 months, or with a blood eosinophil count of at least 150 cells per microlitre, while receiving treatment with oral corticosteroids (OCS), in the last 12 months.

1.2 The listing was requested on the basis of a cost-minimisation approach (CMA) versus mepolizumab (MEPO).

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

Component	Description
Population	Adults and adolescents aged ≥ 12 years with uncontrolled SEA with a background of high-dose ICS and LABA.
Intervention	DEPE 100 mg by SC injection every 6 months.
Comparator	Main comparator: MEPO 100 mg SC injection every 4 weeks (Q4W). Secondary comparator: BENRA 30 mg by SC injection Q4W for the first 3 doses, and Q8W thereafter. Supplementary comparators: omalizumab, dupilumab and tezepelumab.
Outcomes	Efficacy: Annualised rate of clinically significant asthma exacerbations. Safety: AEs and SAEs.
Clinical claim	In the treatment of patients aged ≥ 12 years with uncontrolled SEA, DEPE is non-inferior to MEPO and BENRA with respect to efficacy and safety.

Source: Table 1-1, p18 of the submission.
AEs = adverse events; BENRA = benralizumab; DEPE = depemokimab; ICS = inhaled-corticosteroids; LABA = long-acting beta-agonist; MEPO = mepolizumab; Q4W = every 4 weeks; Q8W = every 8 weeks; SAEs = serious adverse events; SC = subcutaneous; SEA = severe eosinophilic asthma.

2 Background

Registration status

2.1 **TGA status at time of PBAC advice**: Not registered. The submission was made under the TGA/PBAC Parallel Process. At the time of evaluation for PBAC consideration, the outcome of the first-round TGA clinical evaluation report (CER) was available.[1] The TGA registration of DEPE for this indication was requested as an add-on treatment for uncontrolled SEA in adults and adolescents aged 12 years or older. The Round 1 TGA CER noted that the magnitude of exacerbation reduction is clinically relevant and consistent with other IL-5 inhibitors. The report noted the safety profile appeared

[1] The TGA dossier also included a request for registration for chronic rhinosinusitis with nasal polyps (CRSwNP).

comparable to other IL-5 inhibitors with no new safety signals identified. The report noted that long term efficacy and safety beyond 52 weeks remain unestablished with durability of benefit and optimal discontinuation criteria unclear. The first-round recommendation regarding authorisation stated that the benefit-risk profile for asthma is favourable, driven by robust exacerbation reduction and acceptable safety. However, uncertainties regarding broader clinical benefit and long-term outcomes warrant caution and post-marketing surveillance. The second-round TGA CER was provided with the Pre-Sub-Committee Response (PSCR). The second-round report stated the recommendation for approval of DEPE was unchanged from that outlined in the first-round TGA CER. The TGA Delegates Overview was provided prior to the PBAC meeting. The Delegate proposed to approve DEPE as an add-on maintenance treatment of severe asthma in patients aged 12 years and older with type 2 inflammation characterised by an eosinophilic phenotype who are inadequately controlled on medium- to high-dose inhaled corticosteroids (ICS) plus another asthma controller.

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

3 Requested listing

3.1 An abridged version of the restrictions is presented below with the definitions proposed by the submission and the balance of supply restriction not presented.

MEDICINAL PRODUCT medicinal product pack	Dispensed Price for Max. Qty	Max. qty packs	Max. qty units	№.of Rpts	Available brands
DEPEMOKIMAB					
Depemokimab, 100 mg, subcutaneous injection 100 mg in 1 mL single dose pre-filled pen (auto-injector)	Published $[redacted] public $[redacted] private Effective $[redacted] public $[redacted] private	1	1	1	EXDENSUR GlaxoSmithKline Australia Pty Ltd

Requested restriction (initial 1 – new patients or recommencement of treatment in a new treatment cycle)

Category / Program: Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)
Prescriber type: ☒Medical Practitioners
Restriction type: ☒Authority Required (in writing only via post/HPOS upload)
Severity: Uncontrolled severe
Condition: Eosinophilic asthma
Indication: Uncontrolled severe eosinophilic asthma
Treatment Phase: Initial
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 a diagnosis of asthma confirmed and documented by a respiratory physician, clinical immunologist, allergist or general physician experienced in the management of patients with severe asthma, defined by the following standard clinical features: (i) forced expiratory volume (FEV1) reversibility greater than or equal to 12% and greater than or equal to 200 mL at baseline within 30 minutes after administration of salbutamol (200 to 400 micrograms), or (ii) airway hyperresponsiveness defined as a greater than 20% decline in FEV1 during a direct bronchial provocation test or greater than 15% decline during an indirect bronchial provocation test, or [153] 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 documented in the patient's medical records,
AND
Patient must have a duration of asthma of at least 1 year
AND
Patient must have blood eosinophil count greater than or equal to 300 cells per microlitre in the last 12 months, OR Patient must have blood eosinophil count of at least 150 cells per microlitre while receiving treatment with oral corticosteroids in the last 12 months
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 in the patient's medical records
AND
Patient must not receive more than 12 months of treatment under this restriction
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 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 or older.

Source: Table 1-11, pp 55-56 of the submission.
HPOS = health professional online services; PBS = Pharmaceutical Benefits Scheme.

Requested restriction (initial 2 - change of treatment)

Category / Program: Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)
Prescriber type: ☒Medical Practitioners
Restriction type: ☒Authority Required (in writing only via post/HPOS upload)
Severity: Uncontrolled severe
Condition: Eosinophilic asthma
Indication: Uncontrolled severe eosinophilic asthma
Treatment Phase: Initial
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
Patient must have had a blood eosinophil count of at least 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 of at least 150 cells per microlitre while receiving treatment with oral corticosteroids and that is no older than 12 months immediately prior to commencing PBS-subsidised biological medicine treatment for severe asthma,
AND
Patient must not receive more than 12 months of treatment under this restriction
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 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 or older.

Source: Table 1-12, pp57-58 of the submission.
HPOS = health professional online services; PBS = Pharmaceutical Benefits Scheme.

Requested restriction (continuing treatment)

Category / Program: Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)
Prescriber type: ☒Medical Practitioners
Restriction type: ☒Authority Required (STREAMLINED)
Severity: Uncontrolled severe
Condition: Eosinophilic asthma
Indication: Uncontrolled severe eosinophilic asthma
Treatment Phase: Continuing
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
Patient must have demonstrated or sustained an adequate response to PBS-subsidised treatment with this drug for this condition
AND
The treatment must not be used in combination with and within 4 weeks of another PBS-subsidised biological medicine prescribed for severe asthma
AND
Patient must not receive more than 12 months of treatment under this restriction
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 or older.

Source: Table 1-13, pp58-59 of the submission.
PBS = Pharmaceutical Benefits Scheme.

3.2 The submission requested a Special Pricing Arrangement (SPA) and the proposed prices for DEPE were [redacted]. Refer to paragraph 6.49 for issues noted in the CMA relating to the derivation of the AEMP for DEPE.

3.3 The submission requested the PBS listing of DEPE for patients with uncontrolled SEA. The requested PBS listing was narrower than the proposed TGA indication. The requested restrictions were intended to include the following patient groups: i) new patients or patients recommencing treatment in a new treatment cycle, ii) patients changing treatment from an alternative asthma biologic to DEPE, and iii) patients who have demonstrated an adequate response to initial treatment with DEPE and in whom treatment with DEPE is to be continued for up to 12 months.

3.4 The submission requested a maximum treatment duration of 12 months for both initial and continuing treatment. The submission noted that this was in line with DEPE's dosing regimen and would allow for assessment of treatment response 11 months after the first dose. The evaluation noted that this was considerably longer than the treatment durations of other biologics listed on the PBS for the treatment of uncontrolled severe asthma, i.e., 32 weeks and 24 weeks for initial and continuing treatment. In addition, the clinical evidence did not show that DEPE needs a longer timeframe for assessment of response. In the SWIFT-1/-2 trials, DEPE showed treatment effect in terms of the percentage reduction in the annualised rate of

clinically significant exacerbations during the first 13-weekly interval (SWIFT-1 RR 0.38, 95% CI: 0.24, 0.62 for 1-13 weeks; SWIFT-2 RR 0.43, 95% CI 0.27, 0.71 for 1-13 weeks). The treatment effect was maintained over the trial period, i.e., 52 weeks in the overall trial populations. The ACQ 5 score data for the overall trial populations also showed a response to DEPE treatment from week 2. The PSCR argued that under the submissions proposed initiation phase (1+1), clinicians would still retain the flexibility to review patients at 6 months to evaluate tolerability and clinical progress and to decide whether a second dose is appropriate. The Sub-Committees agreed with the evaluation that there was no clinical evidence to suggest that DEPE needs a longer timeframe for assessment of response. The Sub-Committees considered that assessment of response prior to the second dose of DEPE at 6 months would be more appropriate. Similarly, the Sub-Committees considered that 6 months of therapy at a time was appropriate for continuing treatment and advised that no repeats would be required for either initial or continuing treatment restrictions. The pre-PBAC response reiterated arguments made in the submission and PSCR. In addition, the pre-PBAC response argued that testing of DEPE response prior to the second dose of DEPE at 6 months would be earlier than for all other currently listed biologics for severe asthma which may increase the likelihood of unintended cessation of therapy through an insufficient period to assess response. The PBAC noted ACQ 5 score data for the overall trial populations showed a response to DEPE treatment from week 2. The PBAC agreed with the Sub-Committees that assessment of response prior to the second dose of DEPE at 6 months was appropriate and that 6 months of therapy was appropriate for continuing treatment.

3.5 The proposed PBS restriction for DEPE broadly aligned with the current restriction for the main comparator, MEPO. However, the restriction does not include the criteria that patients must not have received biologic therapy as part of their baseline maintenance regimen or must not have been treated with an anti-IL-5 antibody in the 12 months prior to initiating DEPE treatment. This is neither consistent with the trial inclusion criteria, nor with the Initial treatment – Initial 1 PBS restrictions for MEPO and benralizumab (BENRA). The Sub-Committees noted that to be consistent with the MEPO and BENRA restrictions for this point the DEPE Initial treatment – Initial 1 restriction should include clinical criteria stating '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'.

3.6 The proposed listing included criteria stating that the treatment must not be used in combination with and within 4 weeks of another PBS-subsidised biological medicine prescribed for severe asthma. The PSCR noted the amendment of the clinical criteria by the Secretariat to include reference to the treatment of nasal polyps. The PSCR also noted the request from the Secretariat for clarification on whether a period of longer than 4 weeks would be required for patients switching from DEPE to another biological medicine for uncontrolled asthma or nasal polyps. The PSCR stated that there are no data available on transitioning to another monoclonal antibody after treatment with

DEPE. The PSCR argued that decisions about switching should be guided by the treating health care professional's clinical judgement. The Sub-Committees noted the PSCR argument and considered it reasonable that health care professionals use clinical judgement when making such decisions. However, noting that both MEPO and DEPE have the same epitope target, the Sub-Committees advised that it may not be reasonable for those who have failed to respond to DEPE to be able to switch directly to MEPO and potentially vice versa. The pre-PBAC response stated that sharing an epitope target does not, in itself, preclude the possibility of a clinically meaningful response to an alternative agent in individual patients. The pre-PBAC response noted that lack of response could reflect factors beyond pharmacology or target engagement, including adherence, administration issues or other patient specific circumstances including out of pocket costs. The pre-PBAC response stated it supported the Sub-Committees' broader position that these decisions are best made by treating specialists using clinical judgement, based on the patient's overall needs.

3.7 The submission also requested a streamlined authority listing for continuing treatment stating that this was to reduce the administrative burden for clinicians involved in the care of patients with SEA. The submission noted that the requested change to authority level is not expected to broaden patient eligibility criteria or increase patient uptake, and therefore, would be unlikely to increase the PBS utilisation of DEPE. The evaluation considered a streamlined authority listing may increase the risk of use of DEPE in patients who do not have adequate response to initial treatment with DEPE. The PBAC noted the restrictions for continuing treatment for MEPO, BENRA, dupilumab (DUPI) and tezepelumab (TEZE) require authority applications to be made in writing and considered that this would be appropriate for DEPE.

3.8 A grandfather listing was not proposed by the sponsor for DEPE. [redacted]

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, which can lead to airway obstruction. The disease is characterised by respiratory wheeze, shortness of breath, chest tightness and cough that vary over time in intensity. About 2.8 million people in Australia (11% of the total population) have asthma, based on self-reported data in the 2022 Australian Bureau of Statistics (ABS) National Health Survey (NHS) [2].

4.2 Severe asthma is a subset of difficult-to-treat asthma, that is uncontrolled despite adherence with maximal optimized high-dose ICS and long-acting beta-agonist (LABA) treatment and management of contributory factors, or that worsens when high-dose treatment is decreased. Difficult to treat asthma is asthma that is uncontrolled despite treatment with medium or high-dose ICS, with a second controller (usually a LABA) or

[2] Australia Bureau of Statistics. Asthma, 20222023.

with maintenance OCS, or that requires high-dose treatment to maintain good symptom control and reduce the risk of exacerbations. Severe asthma occurs in approximately 5-10% of people with asthma[3].

4.3 Most people with asthma have underlying type 2 (T2) inflammation which is driven by T2 inflammatory pathways involving cytokines such as interleukin-5 (IL-5), interleukin-4 (IL-4) and interleukin-13 (IL-13). T2 inflammation asthma can be divided into two main phenotypes: allergic and eosinophilic asthma. SEA is characterised by elevated levels of eosinophils in the blood and these cause eosinophilic inflammation and an increased risk of severe asthma flares. It more commonly presents in adulthood and may occur in the absence of clear allergic triggers. Allergic asthma is primarily driven by IgE levels in blood and is triggered by environmental factors. While some overlap with allergic asthma exists, eosinophilic asthma is not primarily mediated by IgE.

4.4 People with uncontrolled severe asthma and evidence of persistent T2 airway inflammation are indicated for treatment with a biologic (monoclonal antibody). The PBAC has seen this target population previously, in its assessment of other biologic asthma therapies, MEPO, BENRA, DUPI, omalizumab (OMA) and TEZE. The population targeted in the submission was well described, and consistent with the PBS populations for MEPO and BENRA which are also indicated for SEA. DUPI is listed on the PBS for both SEA and severe allergic asthma, while OMA is listed only for severe allergic asthma. At the time of the evaluation, TEZE was not yet listed on the PBS but is indicated for severe asthma, regardless of eosinophilic or allergic status.[4] The Sub-Committees noted that DEPE is included in the Global Initiative for Asthma (GINA), Global Strategy for Asthma Management and Prevention 2026 Guidelines.[5] The guidelines note DEPE as one of the add-on anti-interleukin-5/5Rα agent options, alongside MEPO and BENRA, for patients with SEA.

4.5 DEPE is a recombinant, humanised monoclonal antibody that targets the IL-5 pathway and is the first ultra-long acting biologic. The recommended dose for adults and adolescents aged 12 years or older is 100 mg of DEPE, administered by subcutaneous (SC) injection, once every 6 months.

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

5 Comparator

5.1 The submission nominated MEPO as the main comparator as DEPE and MEPO are both anti-IL-5 humanised monoclonal antibodies that target the IL-5 pathway. BENRA was nominated as a secondary comparator as BENRA targets the IL-5 receptor Rα on the

[3] Wang E, Wechsler ME, Tran TN, Heaney LG, Jones RC, Menzies-Gow AN, et al. Characterization of Severe Asthma Worldwide: Data From the International Severe Asthma Registry. Chest. 2020 2020/04/01/;157(4):790-804.

[4] TEZE was listed on the PBS on the 1 July 2026: Summary of Changes - 1 July 2026 | Pharmaceutical Benefits Scheme (PBS)

[5] Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2026. Updated May 2026. Available from: www,ginasthma.org

surface of eosinophils. Both MEPO and BENRA are indicated for patients with eosinophil counts of 300 per microlitre or more (without mOCS), or eosinophil counts of 150 per microlitre or more (with mOCS) in the 12 months prior to treatment with a biologic. The Sub-Committees agreed with the evaluation that the nomination of MEPO as the main comparator and that of BENRA as the secondary comparator was reasonable.

5.2 The submission nominated DUPI, OMA and TEZE as supplementary comparators due to overlapping populations with that proposed for DEPE. Literature on moderate-to-severe asthma suggests that some patients with T2 inflammation asthma (indicated for DUPI) and patients with allergic asthma (indicated for OMA) may also meet the eligibility criteria for eosinophilic asthma, and therefore, for treatment with DEPE[6]. The Sub-Committees agreed with the evaluation that the nomination of DUPI and OMA as supplementary comparators was reasonable. TEZE was recommended by the PBAC in November 2025 and at the time of the evaluation it was yet to be listed.[4] TEZE was noted to be a near-market comparator.

5.3 In the context of the cost-minimisation approach taken by the submission, 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: MEPO, BENRA, DUPI and OMA. Some of these alternative therapies may be less costly than DEPE.

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 described how there remained a significant unmet need for asthma care particularly in rural and remote regions and the potential advantages of a 6 monthly dosing regimen in this context. The clinician noted that treatment burden and medication adherence are key challenges for patients with severe asthma and suggested that less frequent dosing would likely improve adherence. The clinician indicated that shifting stable patients to annual reviews may help reduce treatment burden. Reduced dispensing fees were also noted as an advantage of 6 monthly versus more frequent dosing. Finally, the clinician argued that assessing treatment effectiveness may be more reliable after two doses. The PBAC noted that no evidence was provided to support the claim of

[6] Chen M, Shepard K, 2nd, Yang M, Raut P, Pazwash H, Holweg CTJ, Choo E. Overlap of allergic, eosinophilic and type 2 inflammatory subtypes in moderate-to-severe asthma. *Clin Exp Allergy.* 2021 Apr;51(4):546-55.

increased assessment reliability after two doses.

Consumer inputs

6.2 The PBAC noted and welcomed input from health care professionals (5) and organisations (4) via the Office of Health Technology Assessment Consultation Hub. Health care professional input described existing biological treatments as highly effective with a significant improvement in the control of SEA. DEPE was considered to have equivalent efficacy to the currently available agents for SEA, with the 6-monthly dosing regimen an important advancement for selected patients with the condition (particularly for the estimated 30% of patients with injection anxiety or needle aversion). DEPE was also considered to potentially improve access for patients living in rural or remote areas and to be a useful alternative for those who travel frequently. Input from health care professionals emphasised treatment adherence is a key determinant of real-world effectiveness and indicated that DEPE is likely to improve adherence as well as reducing treatment burden. Two health care professionals raised concerns regarding the possibility of a 'wearing off' effect towards the end of the dosing interval in some patients.

6.3 Three inputs were received from consumer organisations: ausEE Inc; Asthma Australia; and a joint submission from Allergy & Anaphylaxis Australia and the National Allergy Council. Input from all organisations described the impact of persistent symptoms or unpredictable flare-ups on consumers quality of life with the ability to work or attend school, participate in physical activity and maintain social connections affected by the condition. ausEE Inc stated the potential advantages of DEPE as improved symptom control and fewer exacerbations, reduced reliance on OCS and their associated side effects, improved quality of life and a potentially more convenient dosing schedule. Potential disadvantages highlighted by ausEE Inc included access via PBS criteria, possible side effects and practical considerations around how and where the medicine is administered. Asthma Australia also highlighted the importance of biologics for SEA as a strategy to eliminate long term use of OCS and minimise OCS exposure. The input from Asthma Australia noted that the 6 monthly dose regimen results in fewer injections which could potentially result in less frequent injection site reactions. The input also stated that fewer injections could lead to a reduction in visits to primary care and less frequent pharmacy dispensing, leading to significant cost savings for consumers in co-payments. Asthma Australia stated a potential disadvantage may be the unintended consequence of patients perceiving the extended dosing interval as a reason to reduce regular reviews of their asthma. The joint input from Allergy & Anaphylaxis Australia and the National Allergy Council stated that, for patients who are already exhausted by their disease and the burden of frequent medical appointments, the reduced dosing frequency would be a reduction in treatment burden.

6.4 In addition to points regarding the potential for improved adherence and reduced treatment burden, the Thoracic Society of Australia and New Zealand (TSANZ) noted the findings of the Phase 3 NIMBLE study evaluating switching from existing anti-IL-

5/IL-5 receptor biologics (MEPO and BENRA) to DEPE[7]. TSANZ noted that while the study did not formally meet its predefined non-inferiority endpoint, most participants remained clinically stable with low exacerbation rates and maintained symptom control, lung function and quality of life following switching. The input stated that prespecified subgroup analyses suggested comparable exacerbation rates among patients switched from MEPO to DEPE, while a somewhat higher exacerbation rates were observed among patients switched from BENRA to DEPE compared with those who remained on BENRA. TSANZ concluded that overall, these findings support DEPE as a promising additional treatment option, while reinforcing the importance of individualising patient selection and clinical judgement when considering switching between biological therapies.

Clinical trials

6.5 The submission was based on two Phase 3 DEPE trials: SWIFT-1 and SWIFT-2. Both trials were multicentre, randomised, double-blind, placebo-controlled trials, and with a treatment period of 52 weeks. In both trials, patients were aged ≥ 12 years with SEA (blood eosinophil count (BEC) ≥ 300 cells/µL during the previous 12 months or ≥ 150 cells/µL at screening). Patients were randomly assigned in a 2:1 ratio to receive either DEPE 100 mg SC (pooled DEPE arm, N = 502) or placebo (pooled placebo arm, N = 260) at Weeks 0 and 26, plus standard of care (SoC) (i.e. medium- to high-dose inhaled corticosteroid [ICS] plus additional controller). Randomisation was stratified based on baseline ICS dose (medium or high). The primary endpoint of SWIFT-1/-2 was the annualised rate of asthma exacerbation (AAER) during the 52 week period.

6.6 There were no head-to-head randomised trials comparing DEPE to MEPO or BENRA. Therefore, the submission presented indirect treatment comparisons (ITCs) between DEPE vs MEPO and DEPE vs BENRA, informed by two MEPO trials (MENSA and MUSCA), and three BENRA trials (CALIMA, SIROCCO, ANDHI). Three methodologies — the Bucher pairwise ITCs (using placebo as the common reference arm)[8], network meta-analysis (NMA)[9], and multilevel network meta-regression (ML NMR)[10] were used to compare the efficacy of DEPE with its comparators. NMA was used to indirectly compare the safety of DEPE vs its comparators. The claim of non-inferiority in efficacy and safety was made based on the results of these ITCs. All of the

[7] Chupp G, Nagase H, Skowasch D, Devouassoux G, et al., Switching to twice-yearly depemokimab from mepolizumab/benralizumab in severe asthma: A multicenter, randomized, double-blind, Phase 3A Clinical Trial (NIMBLE). *Am J Respir Crit Care Med.* 2026 May;212(5):921-935

[8] Bucher HC et al. The results of direct and indirect treatment comparisons in meta-analysis of randomised controlled trials. *J Clin Epidemiol* 1997; 50(6): 683-691.

[9] Cochrane Handbook for Systematic Reviews of Interventions. Undertaking network meta-analyses. URL: https://www.cochrane.org/authors/handbooks-and-manuals/handbook/current/chapter-11#:~:text=Network%20meta%2Danalysis%20is%20a,across%20a%20network%20of%20studies.

[10] Phillippo DM et al. Multilevel network meta-regression for population-adjusted treatment comparisons. *J R Stat Soc Ser A* 2020; 183(3): 1189-1210.

comparator trials presented in the submission have been previously evaluated by the PBAC.

6.7 Since the SWIFT-1/-2 trials enrolled a patient population that was broader than the proposed PBS population, in which all eligible patients are required to be receiving high dose-ICS when commencing treatment, a post hoc subgroup analysis of the SWIFT-1/-2 population was presented in the submission to reflect the likely PBS target population. The results of the subgroup analysis were used to inform the ITCs between DEPE and its comparators in the submission. The post hoc subgroup included 31% (n=236) of the SWIFT-1/-2 population. Patients in the subgroup met these two criteria: (1) received high-dose ICS plus LABA therapy for ≥ 12 months, and (2) BEC ≥ 300 cells/µL in the last 12 months or BEC ≥ 150 cells/µL at screening with concurrent maintenance OCS.

6.8 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
Depemokimab trials		
SWIFT-1 (NCT04719832) & SWIFT-2 (NCT04718103)	A 52-week, randomized, double-blind, placebo-controlled, parallel-group, multi-centre study of the efficacy and safety of GSK3511294 adjunctive therapy in adult and adolescent participants with severe uncontrolled asthma with an eosinophilic phenotype (Clinical Study Report) SWIFT-1 final database lock: 20 December 2023 SWIFT-2 final database lock: 7 May 2024 Jackson DJ et al. Twice-yearly depemokimab in severe asthma with an eosinophilic phenotype. Protocol 217780 Depemokimab Asthma (referred as *'SWIFT-1/-2 PBS subgroup analysis output'*).	02 September 2024 *NEJM* 2024; 391(24): 2337-2349. April 2022
SWIFT-1/-2 OLE (AGILE; NCT05243680)	AGILE Full results [GSK Data on File] Jackson DJ et al. Twice-yearly depemokimab demonstrates an acceptable safety profile in a 12-month interim analysis of the AGILE phase III open-label extension study.	14 October 2025 *J Allergy Clin Immunol* 2025;155(2): AB429.
Mepolizumab trials		
MENSA (NCT01691521)	A randomised, double-blind, double-dummy, placebo-controlled, parallel-group, multi-centre study of the efficacy and safety of mepolizumab adjunctive therapy in subjects with severe uncontrolled refractory asthma (Clinical Study Report) Ortega HG et al. Mepolizumab treatment in patients with severe eosinophilic asthma	31 March 2015 *NEJM* 2014; 371(13): 1198-1207.
MUSCA (NCT02281318)	A randomised, double-blind, placebo-controlled, parallel-group, multi-centre 24-week study to evaluate the efficacy and safety of mepolizumab adjunctive therapy in subjects with severe eosinophilic asthma on markers of asthma control – the MUSCA study (Clinical Study Report) Chupp GL 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.	13 December 2016 *Lancet Respir Med* 2017; 5(5): 390-400.
Benralizumab trials		
CALIMA (NCT01914757)	FitzGerold JM 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,	*The Lancet* 2016; 388(10056): 2128-2141.

Trial ID	Protocol title/ Publication title	Publication citation
	placebo-controlled Phase 3 trial.	
SIROCCO (NCT01928771)	Bleecker ER 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.	*The Lancet* 2016; 388(10056): 2115-2127.
ANDHI (NCT03170271)	Harrison TW 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	*Lancet Respir Med* 2021; 9(3): 260 - 274.

Source: Table 2-9, pp78-79 of the submission.
OLE = open-label extension
Note: the MENSA, MUSCA, CALIMA, SIROCCO, and ANDHI trials have been previously considered by the PBAC

6.9 The key features of SWIFT-1 and SWIFT-2 are summarised in Table 3.

Table 3: Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)
Depemokimab trials					
SWIFT-1	382	R, MC, DB, PC 52 weeks	Low [f]	Patients aged ≥ 12 years with uncontrolled SEA who were receiving MD or HD ICS plus an additional controller	Primary: Annualised rate of exacerbations [a] during a 52 week period [c] Secondary and other outcomes: • change from baseline in SGRQ score, • change from baseline in ACQ-5 score • pre-BD FEV1 (pre-BD FEV1) • the Asthma Daytime/Nighttime Symptom Diary (ADSD/ANSD) weekly mean score, • the annualised rate of exacerbations requiring hospitalisation and/or ED visit • time to first clinically significant exacerbation • safety (incidences of AE and SAE) [c]
SWIFT-2	380				
Meta-analysis of SWIFT-1/-2 subgroups	236	Included SWIFT-1 and SWIFT-2; subgroup analysis [b]; assessed annualised rate of clinically significant asthma exacerbations			
Mepolizumab trials [e]					
MENSA	385	R, MC, DB, PC 32 weeks	Low [f]	Patients aged ≥ 12 years with uncontrolled SEA who were receiving HD ICS plus an additional controller	• Annualised rate of exacerbations [a] during a 32 week period [c] • Safety (AEs, SAEs) [c]

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)
MUSCA	556	R, MC, DB, PC 24 weeks	Low [f]	Patients aged ≥ 12 years with uncontrolled SEA who were receiving HD ICS plus an additional controller	• Annualised rate of exacerbations [a] during a 24 week period [c] • Safety (AEs, SAEs) [c]
Benralizumab trials [e]					
SIROCCO	534[d]	R, MC, DB, PC 48 weeks	Low [f]	Patients aged ≥ 12 years with uncontrolled SEA who were receiving HD ICS plus an additional controller and with BEC ≥ 300cells/µL	• Annualised rate of exacerbations [a] during a 48 week period [c] • Safety (AEs, SAEs) [c]
CALIMA	487[d]	R, MC, DB, PC 56 weeks	Low [f]	Patients aged ≥ 12 years with uncontrolled SEA who were receiving HD ICS plus additional controller and with BEC ≥ 300cells/µL	• Annualised rate of exacerbations [a] during a 48 week period • Safety (AEs, SAEs)
ANDHI	656	R, MC, DB, PC 24 weeks	Low [f]	Patients aged ≥ 18 years with uncontrolled SEA who were receiving HD ICS plus additional controller	• Annualised rate of exacerbations [a] during a 24 week period • Safety (AEs, SAEs)

Source: Compiled during the evaluation

ACQ = Asthma Control Questionnaire; AE = adverse event; BD = bronchodilator; BEC = blood eosinophil count; DB = double blind; ED = emergency department; FEV1 = forced expiratory volume in 1 second; HD = high dose; ICS = inhaled corticosteroids; ITC = indirect treatment comparison; MC = multicentre; MD = medium dose; PC = placebo-controlled; R = randomised; SAE = serious adverse event; SEA = severe eosinophilic asthma; SGRQ = St. George's Respiratory Questionnaire

[a] Defined as a worsening of asthma leading to the use of systemic glucocorticoids (or at least a doubling in the dose for ≥3 days in patients who were receiving oral glucocorticoids), hospitalization, or an ED visit.

[b] Received high-dose ICS plus LABA therapy for ≥ 12 months, and had BEC ≥ 300 cells/µL in the last 12 months or BEC ≥ 150 cells/µL at screening with concurrent maintenance OCS

[c] Outcomes that were compared in the ITCs in the submission

[d] The population analysed for the primary endpoint in the original trial

[e] The outcomes from the comparator trials are those included in the ITCs

[f] Although the risk of bias was considered low in each individual trial, the risk of bias of the ITCs was considered high due to the transitivity issues between the trial sets.

Note: The clinical claim of the submission was based on the primary outcome and safety outcomes in the SWIFT-1/-2 trials.

6.10 The submission acknowledged that a non-inferiority (NI) margin of 28% (upper confidence interval [CI] of 1.28 rate ratio) for the analysis of annualised rate of clinically significant exacerbations (AAER) had been nominated in previous PBAC submission for BENRA, DUPI, and TEZE. However, the submission argued that there was no consistent approach in the interpretation or application of the NI margin and stated that a claim of non-inferiority was based on the absence of statistically significant difference. The 28% NI margin was noted in previous PBAC Public Summary

Documents (BENRA PSD, March 2018 PBAC meeting; DUPI Public Summary Document [PSD], November 2020 PBAC meeting; TEZE PSD, November 2025 PBAC meeting), along with other important clinical concerns associated with ITCs, e.g. transitivity issues.

6.11 Research indicates that 21.2% of patients with SEA in Australia and New Zealand are on maintenance oral corticosteroid (mOCS) therapy.[11] This is higher than the percentage of baseline mOCS use in the SWIFT-1/-2 population (5.2%) as well as the post hoc defined subgroup (11%). The GINA guidelines recommend mOCS as the treatment of last resort for patients with severe asthma who, despite regular and optimised inhaled therapy, continue to have heavy symptom burden that is difficult to control[12]. The evaluation considered that compared to the SWIFT-1/-2 populations, the Australian patient population with SEA is likely to have a higher baseline disease burden and more OCS associated toxicities and health issues. The evaluation considered that whether the magnitude of benefit from DEPE in the SWIFT trials would be observed in this apparently more severe SEA PBS population is uncertain. The PSCR noted that the source of the 21.2% was the Australasian Severe Asthma Registry (ASAR) and argued that the higher mean daily OCS dose in the registry should be interpreted in the context of the period from which these data were derived. The PSCR stated the estimates reflect ASAR enrolment over 2013-2021, when maintenance OCS use was more common and prior to the full impact of contemporary OCS-stewardship approaches. The Sub-Committees agreed with the PSCR that clinical practice has changed to minimise the use of OCS. As such, the Sub-Committees considered that the gap between the current use of OCS and the use in the DEPE clinical trials may add some uncertainty but it is unlikely to be to the extent suggested by the older ASAR data.

6.12 The eligibility criteria of SWIFT-1/-2 did not include an ACQ-5 score requirement, while the proposed initiation criteria for DEPE restricts eligible patients to those with an ACQ-5 score ≥ 2 (indicating failure to achieve adequate control despite optimised asthma therapy). In the post hoc subgroup, 37.7% had a baseline ACQ-5 score < 2.[13] The post hoc analyses of the primary efficacy endpoint (AAER) by baseline ACQ-5 value (< 1.5 or ≥ 1.5) in the SWIFT-1/-2 full analysis set (FAS) populations demonstrated a reduction in AAER in DEPE treated patients compared to placebo patients irrespective of the baseline ACQ-5 value (< 1.5 or ≥ 1.5).

6.13 In the post hoc subgroup, a higher proportion of patients in the placebo arm experienced ≥ 4 exacerbations leading to oral/systemic use of corticosteroid in the

[11] Politis J et al. Oral corticosteroid stewardship: key insights from the Australasian Severe Asthma Registry. *Intern Med J* 2024; 54(7): 1136-1145.

[12] Global Initiative for Asthma (GINA) (2023). Difficult-to-treat and severe asthma in adolescent and adult patients – Diagnosis and management v4.0

[13] *Note that the results presented are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for SWIFT-1/-2 trials. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

past 12 months (13% in DEPE arm vs 24% in placebo), and an imbalance in the proportion of patients (mainly in the SWIFT-1 subgroup) with mOCS at baseline (9% in the DEPE arm vs 17% in the placebo arm) was also observed.[13] This led to a higher mean daily dose of OCS used in the placebo arm (10 mg/day [range 5-20 mg/day]) compared to the mean daily dose of 6.67 mg (range 5 – 10 mg/day) used in the DEPE arm. Patients included in the placebo arm in the post hoc subgroup were therefore likely to have had a higher baseline symptom burden compared to the DEPE arm. The PSCR noted the concerns raised by the evaluation but argued that key markers of baseline disease burden were broadly comparable between the DEPE and placebo arms. Specifically, the PSCR noted that mean baseline exacerbation history was similar (2.9 in both arms), as were pre-bronchodilator forced expiratory volume in 1 second (FEV1, 1.74 placebo vs 1.78 DEPE) and the ACQ-5 score (2.29 placebo vs 2.37 DEPE).[14] The Sub-Committees noted the differences between the placebo and DEPE arms of the post hoc subgroup highlighted by the evaluation and the similarities identified by the PSCR. The Sub-Committees acknowledged that as in any subgroup analysis there is loss of randomisation and hence the potential for bias. However, alongside the similarities identified, the Sub-Committees also considered the direction of the AAER results for the placebo and DEPE arms of the SWIFT-1 and SWIFT-2 trials when moving from the full analysis set (Table 4) to the post-hoc subgroup analysis (Table 5) was consistent with what was expected (i.e. an increase in AAER in placebo and DEPE arms when moving from the full analysis set to the post hoc subgroup who have more severe asthma characteristics).

6.14 MENSA, MUSCA and SWIFT-1/-2 had similar trial eligibility criteria and a similar definition of the efficacy outcome that was compared in the ITCs. Mean baseline ACQ-5 scores in the trial populations were similar across the trials. Key differences between the MEPO trials and SWIFT-1/-2 include the following:

- MENSA and MUSCA had a higher percentage of patients receiving mOCS at baseline

  The percentage of patients on mOCS at baseline were 30% and 31% in the MENSA and MUSCA populations, respectively. This compared to 11% in the post hoc subgroup in SWIFT-1/-2.[14] This difference suggests that the MENSA and MUSCA patient populations had a higher baseline disease burden compared to the patients in the post hoc subgroup, as mOCS is recommended by the GINA guideline as the treatment of last resort for patients with severe asthma whose symptom burden is difficult-to-control despite optimised inhaled therapy[15]. The evaluation considered these differences in the common reference arms of the

[14] *Note that the results presented are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for SWIFT-1/-2 trials. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

[15] Global Initiative for Asthma (2023). Difficult-to-treat and severe asthma in adolescent and adult patients – Diagnosis and management v4.0.

indirectly compared trials indicate that the transitivity (exchangeability) assumption has not been met. The PSCR stated that baseline OCS use is influenced not only by disease burden but also by evolving clinical practice. The PSCR argued that pivotal trials for MEPO (and BENRA) were conducted between 2012 and 2015, when clinical practice more commonly relied on maintenance OCS in severe asthma. The PSCR argued that contemporary practice has emphasised OCS stewardship with greater efforts to minimise cumulative OCS exposure.

- Difference in the definition of high-dose ICS between trials

  In SWIFT-1/-2, patients receiving ICS at a dose > 500 µg/day at baseline were considered receiving high-dose ICS. In comparison, in the MEPO trials, patients receiving ICS at a dose ≥ 880 µg/day at baseline were considered to be on high-dose ICS. This difference indicates that, patients included for the ITCs in the SWIFT-1/-2 trials may have a lower baseline disease severity, compared to the patients in the MEPO trials.

6.15 Most of the trial eligibility criteria of the BENRA trials were similar to those of SWIFT-1/-2. The definition of the efficacy outcome being compared in the ITCs was also similar across the trials. Key differences between the BENRA trials and SWIFT-1/-2 include the following:

- Difference in requirement of baseline ACQ score for trial inclusion

  While ACQ-5 score was not an inclusion criterion in SWIFT-1/-2, patients included in the BENRA trials were required to have a baseline ACQ-6 score ≥ 1.5. In SIROCCO, the baseline ACQ-6 scores were 2.80 and 2.87 in the BENRA and placebo arms, respectively; in CALIMA, the baseline ACQ-6 scores were 2.75 and 2.69 in the BENRA and placebo arms, respectively, compared to the mean ACQ-5 scores in the post hoc subgroup in SWIFT-1/-2 which were 2.37 and 2.29 in the DEPE and placebo arms, respectively.[16] Given both ACQ-5 and ACQ-6 have a minimal clinically important difference (MCID) of 0.5, patients enrolled in SIROCCO, particularly in the placebo arm, had more difficult-to-control severe asthma, compared to the post hoc subgroup in SWIFT-1/-2.

- A higher use of mOCS at baseline in the SIROCCO and CALIMA populations

  In the post hoc subgroup in SWIFT-1/-2, 11% of the patients had mOCS use at baseline, with a mean dose of 6.67 mg/day used in the DEPE arm and 10 mg/day used in the placebo arm.[16] In comparison, in SIROCCO, 19% of patients in the BENRA arm and 14% in the placebo arm had mOCS use at baseline, with a mean dose of 15.5 mg/day and 13.9 mg/day used in the two arms, respectively. In CALIMA, although similar percentage of patients were on mOCS at baseline,

[16] *Note that the results presented are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for SWIFT-1/-2 trials. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

compared to the post hoc subgroup in SWIFT-1/-2, patients in CALIMA who were on mOCS at baseline were receiving higher daily dose (mean dose 8.3 mg/day and 14.4 mg/day in the BENRA and placebo arms, respectively). These differences indicate that the patient population in the BENRA trials had a higher baseline disease burden compared to the patients in the post hoc subgroup in SWIFT-1/-2. As outlined in paragraph 6.14, the PSCR stated that baseline OCS use is influenced not only by disease burden but also by evolving clinical practice. The PSCR argued that differences in when the BENRA trials were conducted compared to the DEPE trials potentially influenced OCS use.

Comparative effectiveness

6.16 Results of the primary endpoint (AAER) in SWIFT-1/-2 are presented in Table 4. The full analysis set of SWIFT-1/-2 included patients on medium- to high-dose ICS at baseline.

Table 4: Primary efficacy outcome in SWIFT-1 and SWIFT-2 — AAER over 52 weeks (full analysis set[a])

	SWIFT-1		SWIFT-2		Pooled SWIFT-1/-2	
	DEPE N = 250	Placebo N = 132	DEPE N = 252	Placebo N = 128	DEPE N = 502	Placebo N = 260
Number of patients (%)	78 (31%)	61 (46%)	79 (31%)	64 (50%)	157 (31.3%)	125 (48.1%)
Number events	120	150	153	167	273	317
AAER[b,c] (95% CI)	0.46 (0.36, 0.58)	1.11 (0.86,1.43)	0.56 (0.44, 0.70)	1.08 (0.83, 1.41)	0.51 (0.43, 0.60)	1.11 (0.92, 1.33)
Rate ratio (95% CI) p value	**0.42 (0.30, 0.59) p < 0.001**		**0.52 (0.36, 0.73) p < 0.001**		0.46 (0.36, 0.59)	
% reduction (95% CI)	58% (41%, 70%)		48% (27%, 64%)		54% (41%, 64%)	

Source: Table 2-26, p121 of the submission; Table 15, p80 of the SWIFT-1 final CSR; Table 15, p79 of the SWIFT-2 final CSR

AAER = annual asthma exacerbation rate; BD = bronchodilator; CI = confidence interval; CSR = Clinical Study Report; DEPE = depemokimab; ED = emergency department; FEV1 = forced expiratory volume in 1 second; ICS = inhaled corticosteroid; N = total participants in group.

[a] The full analysis set of SWIFT-1/-2 included patients on medium- to high-dose ICS at baseline.

[b] Defined as a worsening of asthma leading to the use of systemic glucocorticoids (or at least a doubling in the dose for ≥ 3 days in patients who were receiving oral glucocorticoids), hospitalisation, or an ED visit

[c] Multiplicity adjustment level 1

Notes**:** Analysis performed using a generalised linear model assuming a negative binomial distribution and covariates of treatment group, baseline ICS dose (medium or high), exacerbation history (2, 3 or ≥4), geographical region and baseline pre-BD % of the predicted FEV_1 with an offset of $\log_e$ (total number of years in the trial). An additional term for study was used in the pooled analysis model. Percentage reduction in annual rate is calculated as (1-rate ratio)*100.

Note: No hierarchy or multiplicity adjustment was performed for the pooled analysis, therefore, p values were not reported.

Note: Results of the pooled analyses of SWIFT-1/-2 were descriptive.

Bold indicates statistically significant results.

6.17 Over the 52 week period, patients in the DEPE arms in both SWIFT-1 and SWIFT-2 (FAS) had a statistically significant reduction in AAER compared to the placebo arms. In SWIFT-1, the relative reduction was 58% (RR 0.42; 95% CI: 0.30, 0.59; p < 0.001). The SWIFT-2, the relative reduction was 48% (RR 0.52; 95% CI: 0.36, 0.73; p < 0.001).

6.18 Regarding the secondary outcomes, no significant between-arm difference in the change from baseline in the SGRQ score was observed in either SWIFT-1 or SWIFT-2. As such, no statistical inference was drawn on subsequent secondary endpoints.

6.19 In the post hoc analysis of AAER by baseline ICS dose (medium, high) for the FAS populations in SWIFT-1 and SWIFT-2, DEPE treated patients demonstrated a greater reduction in the AAER compared to placebo patients regardless of ICS dose. In SWIFT-1, the reduction was 64% (RR 0.36; 95% CI 0.21, 0.62) and 54% (RR 0.46; 95% CI: 0.29, 0.72) for the medium-dose and high-dose subgroups, respectively. In SWIFT-2, the reduction was 57% (RR 0.43; 95% CI 0.24, 0.77) and 43% (RR 0.57; 95% CI: 0.37, 0.88) for the medium-dose and high-dose subgroups, respectively.

6.20 In SWIFT-1 and SWIFT-2, DEPE was shown to be effective in reducing the frequency of clinically significant asthma exacerbation compared to placebo in patients with uncontrolled SEA who received medium- to high-dose ICS. As the proposed PBS population only includes patients with SEA who are receiving high-dose ICS, the submission presented a subgroup analysis based on a post hoc subgroup representing the PBS subgroup.

6.21 A post hoc subgroup analysis of patients receiving high dose ICS and meeting the PBS BEC eligibility criteria in SWIFT-1/-2 was presented to inform the ITCs in the submission. Results are presented in Table 5.

Table 5: Post hoc subgroup[a] analysis of annual asthma exacerbation rate (AAER[b]) in DEPE arms vs placebo arm in SWIFT-1/-2[17]

	SWIFT-1		SWIFT-2	
	DEPE N = 64	Placebo N = 36	DEPE N = 97	Placebo N = 39
AAER[a] (95% CI)	0.62 (0.41, 0.95)	2.00 (1.28, 3.11)	0.88 (0.64, 1.21)	1.34 (0.85, 2.13)
Rate ratio (95% CI)	0.31 (0.17, 0.58)		0.66 (0.38, 1.14)	
% reduction (95% CI)	69% (42%, 83%)		34% (-14%, 62%)	

Source: Table 2-34, p135 of the submission

BEC = blood eosinophil count; CI = confidence interval; DEPE = depemokimab; ICS = inhaled corticosteroid; LABA = long-acting beta antagonist; N = total participants in group; OCS = oral corticosteroid

[a] All patients in this subgroup met the following criteria: (1) received high-dose ICS plus LABA therapy for ≥ 12 months at baseline, and (2) BEC ≥ 300 cells/µL in the last 12 months or BEC ≥ 150 cells/µL at screening with concurrent maintenance OCS

[b] Defined as a worsening of asthma leading to the use of systemic CS (or at least a doubling in the dose for ≥ 3 days in patients who were receiving oral CS), hospitalisation, or an emergency department visit

6.22 Results of the subgroup analysis demonstrate a numerical reduction in AAER compared to the placebo arm. In SWIFT-1, the reduction was 69% (RR 0.31; 95% CI: 0.17, 0.58). In SWIFT-2, the reduction was 34% (RR 0.66; 95% CI: 0.38, 1.14).[17]

6.23 Since this is a post hoc subgroup analysis, randomisation was not preserved potentially resulting in an imbalance in baseline characteristics between the treatment arms. The placebo arms in the post hoc subgroups (particularly in SWIFT-1) may have a higher baseline disease burden (see paragraph 6.13). This will have resulted in heterogeneity in the pooled post hoc patient subgroup. The Sub-Committees noted the differences between placebo and DEPE arms of the post hoc

[17] *Note that the results presented are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for SWIFT-1/-2 trials. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

subgroup highlighted by the evaluation and the similarities identified by the PSCR (see paragraph 6.13).

Indirect treatment comparison of DEPE vs MEPO and DEPE vs BENRA

Bucher Pairwise ITC

6.24 The results of the meta-analyses of the SWIFT-1/-2 post hoc subgroup, the modified intention to treat (mITT) populations from MENSA and MUSCA, and the efficacy populations from CALIMA, SIROCCO and ANDHI, were used to inform the efficacy of DEPE, MEPO, and BENRA, respectively, in this ITC (placebo as the common reference arm).

Table 6: DEPE vs MEPO for the annualised rate of clinically significant exacerbations (Bucher pairwise ITC)

	DEPE trials		MEPO trials	
	Post hoc subgroup in SWIFT-1 (N = 100)[18]	Post hoc subgroup in SWIFT-2 (N = 136)[18]	MENSA (mITT) (N = 385)	MUSCA (mITT) (N = 551)
Rate in intervention arm	0.62	0.88	0.83	0.51
Rate in PBO arm	2.00	1.34	1.74	1.21
RR (95% CI)	0.31 (0.17, 0.58)	0.66 (0.38, 1.14)	0.47 (0.35, 0.64)	0.42 (0.31, 0.56)
RE IV Meta-analysis	0.46 (0.22, 0.96)		0.44 (0.36, 0.55)	
Heterogeneity	Tau² (DL) = 0.20; Chi² = 3.23, df = 1 (p = 0.07); I² = 69%		Tau² (DL) = 0.00; Chi² = 0.27, df = 1 (p = 0.60); I² = 0%	
Pooled DEPE vs pooled MEPO (95% CI)[a]	1.05 (0.49, 2.25)			

Source: Table 2-41, pp144-145 of the submission

CI = confidence interval; DEPE = depemokimab; df = degrees of freedom; DL = DerSimonian-Laird; ITC = indirect treatment comparison; IV = inverse variance; MEPO = mepolizumab; mITT = modified intent-to-treat; PBO = placebo; PBS = Pharmaceutical Benefits Scheme; RCT = randomised controlled trial; RE = random effects

[a] Using PBO as the common reference

Table 7: DEPE vs BENRA for the annualised rate of clinically significant exacerbations (Bucher pairwise ITC)

	DEPE trials		BENRA trials		
	Post hoc subgroup in SWIFT-1 (N = 100)[18]	Post hoc subgroup in SWIFT-2 (N = 136)[18]	CALIMA[a] (N = 487)	SIROCCO[a] (N = 534)	ANDHI[b] (N = 656)
Rate in intervention arm	0.62	0.88	0.66	0.65	0.94
Rate in PBO arm	2.00	1.34	0.93	1.33	1.86
RR (95% CI)	0.31 (0.17, 0.58)	0.66 (0.38, 1.14)	0.72 (0.54, 0.95)	0.49 (0.37, 0.64)	0.51 (0.39, 0.65)
RE IV Meta-analysis	0.46 (0.22, 0.96)		0.56 (0.45, 0.71)		
Heterogeneity	Tau² (DL) = 0.20; Chi² = 3.23, df = 1 (p = 0.07); I² = 69%		Tau² (DL) = 0.02; Chi² = 4.47, df = 2 (P = 0.11); I² = 55%		
Pooled DEPE vs pooled BENRA (95% CI)[c]	0.82 (0.38, 1.78)				

[18] *Note that the results presented are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for SWIFT-1/-2 trials. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

Source: Table 2-42, p145 of the submission
BENRA = benralizumab; CI = confidence interval; DEPE = depemokimab; df = degrees of freedom; DL = DerSimonian-Laird; FAS = full analysis set; ITC = indirect treatment comparison; IV = inverse variance; PBO = placebo; PBS = Pharmaceutical Benefits Scheme; RCT = randomised controlled trial; RE = random effects
[a] Analysed population in the ITC was the population analysed for the primary endpoint in the original trial
[b] FAS population
[c] Using PBO as the common reference

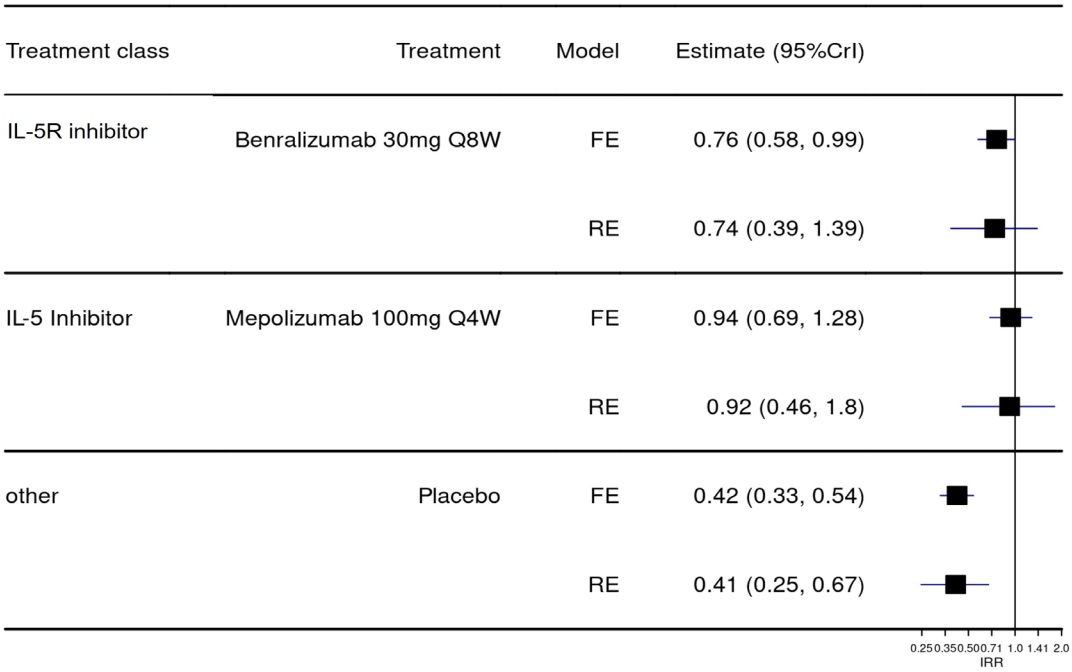
6.25 Despite the point estimates of the rate ratio in the Bucher pairwise ITCs suggesting non-inferiority, the wide – albeit symmetrical – 95% CIs show that inferiority cannot be ruled out, and the upper bound of the 95% CI (2.25) may indicate a clinically relevant worsening of outcome in certain DEPE treated patients. The evaluation considered that the transitivity issues highlighted earlier suggest that the results of the ITCs may not support the claim of non-inferior efficacy of DEPE vs its comparators.

Network meta-analysis

6.26 In the ITCs between DEPE and its comparators using the method of NMA, the submission stated the random effect (RE) fitted model was preferred based on the Deviance Information Criterion (DIC) being 3.9 points lower than the Fixed effects (FE) model and the heterogeneity introduced by the RE model exceeding 30% (I^2 = 50.4%)[19]. The evaluation considered this was reasonable.

[19] The submission stated best fit model selection was based on DIC. A lower DIC value indicates a more favourable trade off. If the RE model has a DIC that is ≥5 points lower than the FE model, it suggests that the RE structure provides a more parsimonious and generalisable explanation of the data. Conversely, if the FE model has a lower DIC or the difference is <5, the added complexity of modelling the between-study heterogeneity parameter may not be justified. When the DIC difference falls within a narrower range (e.g., RE model DIC is 4 to 5 points lower than the FE model), the decision-making is supplemented by calculating I^2. A threshold of ≥ 30% was applied to represent moderate heterogeneity, with the RE model being the preferred approach if the threshold is exceeded.

Figure 1: DEPE vs MEPO and DEPE vs BENRA for the annualised rate of clinically significant exacerbations (NMA)[20]



Source: Figure 2-16, p146 of the submission
CrI = credible interval; DEPE = depemokimab; FE = fixed effects; IL-5 = interleukin-5; IL-5R = interleukin-5 receptor; IRR = indirect rate ratio; NMA = network meta-analysis; Q8W = every 4 weeks for the first 3 doses then every 8 weeks thereafter; Q4W = every 4 weeks; RE = random effects

6.27 The forest plot of the NMAs (using the RE model) demonstrated that, for the estimated RRs of DEPE vs MEPO and DEPE vs BENRA in the annualised rate of clinically significant exacerbations, the upper bounds of the 95% CI are above the NI margin (1.28). Based on these results, the evaluation considered the claim that DEPE is non-inferior to its comparators — MEPO and BENRA — is inconclusive as the analysis does not rule out a clinical worsening in exacerbation rate.

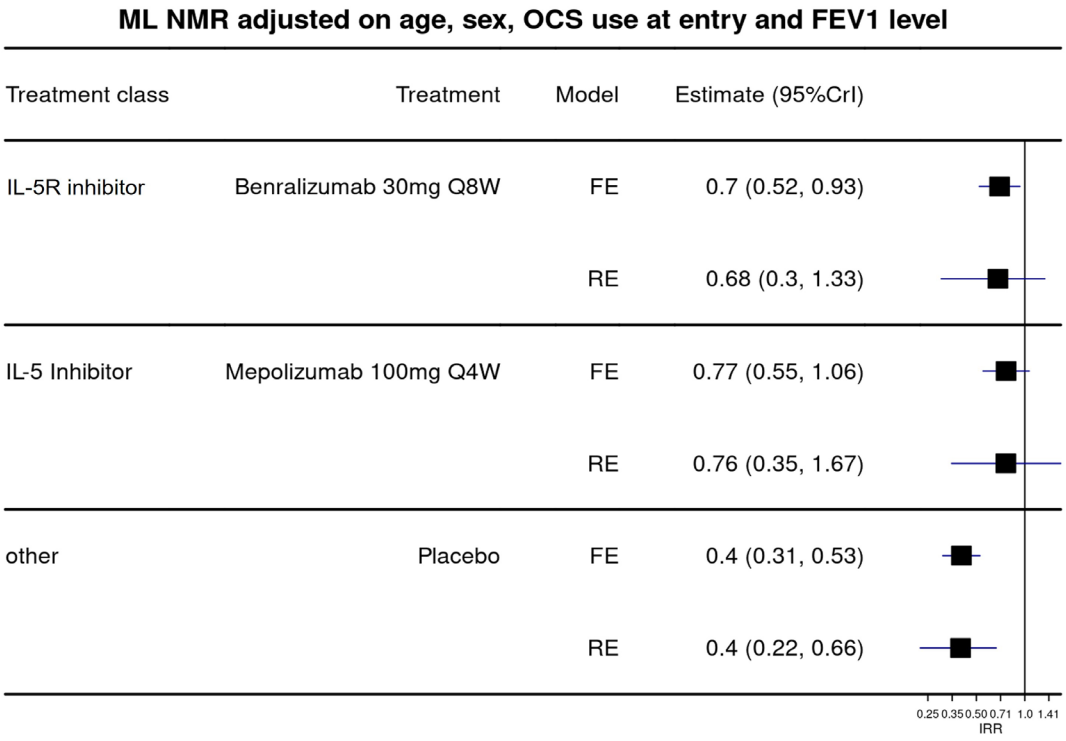
Multilevel network meta-regression

6.28 The ML NMR in the submission was adjusted for age, sex, OCS use, and FEV1 level at baseline. In the analysis, age and FEV1 level at baseline were demonstrated to have no treatment modifying effect. Males were demonstrated to respond better to treatment than female, and baseline mOCS users responded better to therapy compared to non-mOCS users. The literature, however, suggest that lack of or low

[20] *Note that the results presented are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for SWIFT-1/-2 trials. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

dose of mOCS (< 10 mg/day) use is a predictor of response to anti-IL5[21,22]. The submission stated the RE fitted model was the preferred approach based on the DIC being 4.2 points lower than the FE model and the heterogeneity introduced by the RE model exceeding 30% (I^2 = 32.35%).

Figure 2: DEPE vs MEPO and BENRA for the annualised rate of clinically significant exacerbations (ML NMR)[23]



Source: Figure 2-17, p148 of the submission
BENRA = benralizumab; CrI = credible interval; DEPE = depemokimab; FE = fixed effects; FEV1 = forced expiratory volume in 1 second; IL-5 = interleukin-5; IL-5R = interleukin-5 receptor; IRR = indirect rate ratio; MEPO = mepolizumab; ML NMR = multilevel network meta-regression; OCS = oral corticosteroids; Q8W = every 4 weeks for the first 3 doses then every 8 weeks thereafter; Q4W = every 4 weeks; RE = random effects

6.29 The forest plot of the ML NMR (RE model) demonstrates that, for the estimated RRs of DEPE vs MEPO and DEPE vs BENRA in the annualised rate of clinically significant exacerbations, the upper bounds of the 95% CrI are above the NI margin. Based on

[21] Pilette C et al. REALITI-A Study: Real-world oral corticosteroid-sparing effect of mepolizumab in severe asthma. *J Allergy Clin Immunol Pract* 2022; 10(10): 2646-2656.
[22] Rattu A et al. Predictors of response to biologics for severe asthma: A systematic review and meta-analysis. *Allergy* 2026; 81(1): 24-55.
[23] *Note that the results presented are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for SWIFT-1/-2 trials. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

these results, the evaluation considered the claim that DEPE has non-inferior efficacy to its comparators is inconclusive.

6.30 The PSCR stated that the wide confidence intervals across both the unadjusted NMA and the ML-NMR are consistent with a sparse evidence network with limited connectivity, limiting reliable estimation of between-study heterogeneity (NMA τ = 0.21 [0.03, 0.71]; ML-NMR τ = 0.24 [0.04, 0.96]).[24] The PSCR argued that the use of the FE model as the base case where the network is dominated by single-study connections is a pragmatic choice given the difficulty of estimating between study variance. The PSCR noted that the results from the FE model yielded relatively narrower confidence intervals. The Sub-Committees noted that despite favourable and consistent point estimates, the chosen RE fitted model did not meet NI margins for the NMA or the ML NMR. The Sub-Committees did not accept the PSCR argument that the FE model be used to determine non-inferiority and advised that conceptual issues should guide an a priori decision to favour one model or the other. The Sub-Committees noted that alternative meta-analysis methodologies are also available.[25]

Comparative harms

6.31 A summary of the overall safety for a 52 week treatment period of the pooled data from SWIFT-1/-2 is presented in Table 8.

[24] *Note that the results presented are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for SWIFT-1/-2 trials. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

[25] Mathes T, Kuss O. A comparison of methods for meta-analysis of a small number of studies with binary outcomes. *Research Synthesis Methods* 2018; 9(3):366-381

Table 8: Overall safety in patients receiving DEPE vs placebo for 52 weeks in SWIFT-1/-2 (Safety population)

	DEPE N = 501	Placebo N = 261	RD (95% CI)	RR (95% CI)
Any AE, n (%)	362 (72.3)	187 (75.9)	0.01 (-0.06, 0.07)	1.01 (0.92, 1.11)
AEs related to study treatment, n (%)	19 (3.8)	6 (2.3)	0.01 (-0.01, 0.04)	1.65 (0.67, 4.08)
AEs leading to permanent discontinuation of study treatment or withdrawal from study, n (%)	5 (1)	3 (1.2)	0.00 (-0.02, 0.01)	0.87 (0.21, 3.60)
AEs leading to dose interruption/delay, n (%)	1 (<1)	0	0.00 (0.00, 0.01)	NA
Any SAE, n (%)	33 (6.6)	35 (13.4)	-0.07 (-0.11, -0.02)	0.49 (0.31, 0.77)
SAEs related to study treatment, n (%)	0	0	NA	NA
Fatal SAEs, n (%)	0	0	NA	NA
AESI, n (%)				
Allergic (type I hypersensitivity) reactions	0	0	NA	NA
Anaphylaxis	0	0	NA	NA
Other systemic reactions	8 (1.6)	2 (<1)	0.01 (-0.01, 0.02)	2.08 (0.45, 9.74)
Type III hypersensitivity/vasculitis	0	0	NA	NA
Local injection site reactions	7 (1.4)	2 (<1)	0.01 (-0.01, 0.02)	1.82 (0.38, 8.71)

Source: compiled during the evaluation; Table 2-31, p131 of the submission
AE = adverse event; AESI = adverse event of special interest; CI = confidence interval; DEPE = depemokimab; n = number of participants reporting data; N = total participants in group; NA = non-applicable; RD = risk difference; RR = relative risk; SAE = serious adverse event
Note: In SWIFT-1/-2, asthma exacerbations were included as AEs and SAEs.

6.32 Overall, over a 52 week period in SWIFT-1/-2, the proportion of patients with any AE was similar in the two treatment arms. There were no deaths and no SAEs that were considered related to the DEPE treatment.

6.33 In SWIFT-1, the most commonly reported AEs during the 52 week treatment period were COVID-19 (20% with DEPE vs 22% with placebo), nasopharyngitis (12% with DEPE vs 19% with placebo) and upper respiratory tract infection (10% with DEPE vs 11% with placebo). In SWIFT-2, the most commonly reported AEs were nasopharyngitis (13% with DEPE vs. 21% with placebo), COVID-19 (15% in each group), and headache (8% in each group).

6.34 In SWIFT-1, a similar percentage of patients in the two treatment arms had treatment related AEs (8 patients [3%] in DEPE and 5 [4%] in placebo). In the DEPE arm, injection site reaction and headache occurred in 2 patients (< 1%) each. Other treatment related AEs occurred in 1 patient each. In SWIFT-2, 11 patients (4%) and 1 patient (< 1%) in the DEPE and placebo arms, respectively, had treatment related AEs. In the DEPE arm, injection site reaction, headache, and leukopenia (all mild events and later recovered/resolved) occurred in 2 patients (< 1%) each. Other treatment related AEs occurred in 1 patient each.

6.35 In SWIFT-1, 3 patients (1%) in the DEPE arm had an AE leading to treatment discontinuation. These AEs included increased liver enzyme (alanine aminotransferase [ALT]), grief reaction, and myasthenia gravis. All 3 events were non-serious and considered not related to study treatment, and none of the events led to withdrawal from study. In SWIFT-2, 2 patients (< 1%) in the DEPE arm had AE leading to treatment

discontinuation. Among these 2 patients, one met stopping criteria due to AEs of abnormal ALT (serious) and abnormal blood bilirubin (serious) which were considered not related to study treatment. Another patient withdrew from study due to AEs of ovarian cancer with metastases to peritoneum.

6.36 Incidences of SAE were higher in the placebo arm compared to DEPE in SWIFT-1 (6% in DEPE vs 17% in placebo) and similar in the two arms in SWIFT-2 (7% in DEPE and 10% in placebo) during the 52 week treatment period. Asthma was the most commonly reported SAE in both treatment arms in SWIFT-1 (3 patients [1%] in DEPE vs 5 [4%] in placebo) and SWIFT-2 (6 patients [2%] in DEPE vs 6 [5%] in placebo). None of the reported SAEs were considered related to study drug in either trial, and no fatal SAEs reported.

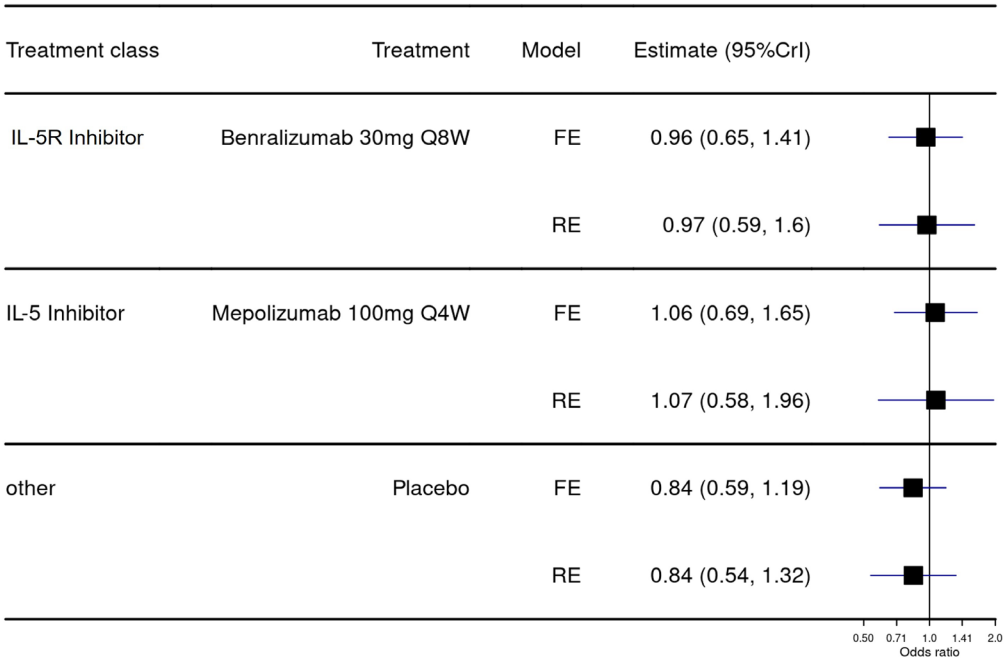
6.37 With regard to adverse events of special interest (AESI), no patients in SWIFT-1/-2 were reported to have an allergic reaction, anaphylaxis, immune complex disease/vasculitis, or QTc prolongation. AEs of other systemic reactions were reported in 2 patients (< 1%) in the DEPE arm (vs 2 patients [2%] in placebo) in SWIFT-1, and 6 patients (2%) in the DEPE arm (vs 0 in placebo) in SWIFT-2. All reported AEs were considered mild or moderate in intensity. Local injection site reactions were reported in 3 patients (1%) in the DEPE arm (vs 1 patient in placebo) in SWIFT-1, and 4 patients (2%) in the DEPE arm (vs 1 in placebo) in SWIFT-2. All reactions were considered to be mild in intensity.

6.38 In SWIFT-1/-2, asthma was included as AE and SAE while it likely represented the condition being treated rather than an AE. As a result, the placebo arm would have a higher rate of AE and SAE if DEPE is considered beneficial. This confounds the relative safety of DEPE to placebo. The Sub-Committees noted that the MEPO and BENRA trials also included asthma as an AE or SAE.

Indirect comparison of DEPE vs MEPO and DEPE vs BENRA

6.39 In the submission, safety (AE and SAE) of DEPE vs MEPO and DEPE vs BENRA was indirectly compared using the method of NMA, and placebo as the common reference arm.

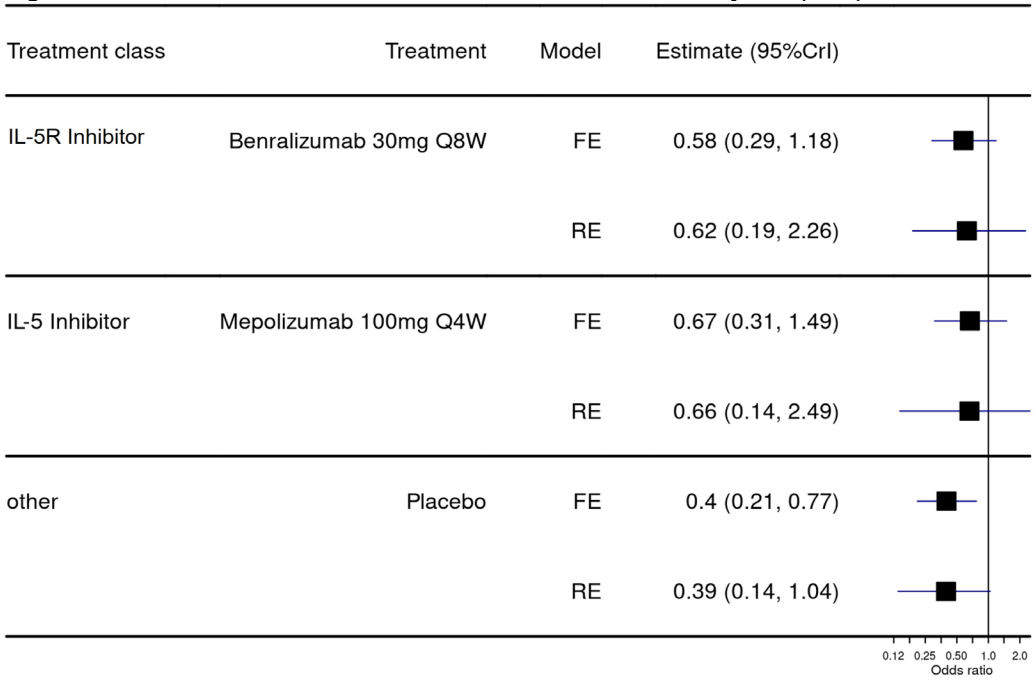
Figure 3: DEPE vs MEPO and DEPE vs BENRA for the incidence of any AE (NMA)[26]



Source: Figure 19, p150 of the submission
AE = adverse event; BENRA = benralizumab; CrI = credible interval; DEPE = depemokimab; FE = fixed effects; IL-5 = interleukin-5; IL-5R = interleukin-5 receptor; MEPOE = mepolizumab; Q8W = every 4 weeks for the first 3 doses then every 8 weeks thereafter; Q4W = every 4 weeks; RE = random effects

[26] *Note that the results presented are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for SWIFT-1/-2 trials. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

Figure 4: DEPE vs MEPO and DEPE vs BENRA for the incidence of any SAE (NMA)[27]



Source: Figure 19, p150 of the submission
BENRA = benralizumab; CrI = credible interval; DEPE = depemokimab; FE = fixed effects; IL-5 = interleukin-5; IL-5R = interleukin-5 receptor; MEPOE = mepolizumab; Q8W = every 4 weeks for the first 3 doses then every 8 weeks thereafter; Q4W = every 4 weeks; RE = random effects; SAE = serious adverse event

Clinical claim

6.40 The submission described DEPE as non-inferior in terms of effectiveness compared to MEPO. The evaluation considered this claim was not adequately supported by the evidence presented. The evaluation considered the main issue was the concerns regarding the transitivity of the trials in the ITCs, mainly, patients in the post hoc subgroups in the DEPE trials had less severe disease than those in the comparator trials. As a result, the evaluation considered the ITCs presented in the submission were inconclusive. The evaluation came to the same conclusion regarding the claim that DEPE was non-inferior in terms of effectiveness compared to BENRA.

6.41 The Sub-Committees acknowledged the concerns raised by the evaluation regarding the transitivity of the trials in the ITCs and the PSCR argument that a ML NMR was undertaken to address cross-trial differences. The Sub-Committees noted the PBAC previously accepted a NI margin of 1.28 for the upper bound of the 95% confidence intervals for the rate ratio of AAER. The Sub-Committees noted that inferiority could not be ruled out with the Bucher pairwise ITC (see paragraph 6.25). In addition, the

[27] *Note that the results presented are derived from ad-hoc/ post-hoc analyses conducted by the applicant specifically for the purposes of informing the PBAC consideration. These analyses were not part of the pre-specified statistical plan for SWIFT-1/-2 trials. Interpretation of the results and their application should therefore be limited to seeking to understand the basis for the PBAC outcome and should not be used for any other purpose.*

Sub-Committees noted that despite favourable and consistent point estimates, the chosen RE fitted model did not meet NI margins for the NMA or the ML NMR (see paragraph 6.30). However, noting that MEPO and DEPE have the same epitope target, the Sub-Committees considered that it was uncertain but biologically plausible and hence likely clinically reasonable to accept a non-inferiority claim for DEPE compared to existing IL-5 therapies. In addition, the Sub-Committees noted that the PBAC had previously accepted BENRA was non-inferior in terms of efficacy to MEPO (paragraph 7.9, benralizumab PSD, March 2018 PBAC Meeting).

6.42 The submission described DEPE as non-inferior in terms of safety compared to MEPO. The submission also described DEPE as non-inferior in terms of safety compared to BENRA as the secondary comparator. The evaluation considered these claims were not adequately supported by the evidence presented in the submission. The evaluation considered the main issue was that the use of AE outcomes which included asthma in the DEPE, MEPO and BENRA trials cannot reliably inform the comparative safety profile of DEPE relative to MEPO or BENRA. The Sub-Committees noted that all trials treated asthma exacerbations in the same way and that the PBAC had previously accepted BENRA was non-inferior in terms of safety to MEPO (paragraph 7.9, benralizumab PSD, March 2018 PBAC Meeting). As such, the Sub-Committees considered a claim of non-inferior safety was likely reasonable for DEPE compared to MEPO or BENRA.

6.43 The PBAC considered that it was uncertain but reasonable to accept the claim of non-inferior comparative effectiveness.

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

Economic analysis

6.45 The submission presented a CMA to support the listing of DEPE for the treatment of uncontrolled SEA.

6.46 The submission considered DEPE 100mg SC 6 monthly (2 doses over one year) to be equi-effective to MEPO 100mg SC injection every 4 weeks (13.04 doses over one year) for patients with uncontrolled SEA. The equi-effective doses of DEPE and MEPO were based on the recommended dosing regimens in respective Product Information (PI) documents and with the interventions in clinical trials. The evaluation noted that the number of doses of MEPO accepted by the PBAC in previous CMAs for other severe asthma treatments was 13 doses (paragraph 7.20, TEZE PSD, November 2025 PBAC meeting; paragraph 7.10, DUPI PSD, November 2020 PBAC meeting; paragraph 7.12, BENRA PSD, March 2018 PBAC meeting). The CMA was updated during the evaluation to round the number of MEPO doses to 13, to be consistent with previous PBAC considerations.

6.47 The time frame of the CMA in the submission was one year. This was reasonable and consistent with previous PBAC considerations where a one year time horizon was accepted for the CMAs of other severe asthma therapies (paragraph 7.9, DUPI PSD,

November 2020 PBAC Meeting; paragraph 7.20, TEZE PSD, November 2025 PBAC meeting).

6.48 The submission included administration cost off-sets in the CMA. Although administration (subcutaneous injection through an auto-injector) can be performed by the patient or caregiver for both medicines (according to their respective PIs), the submission considered that 14% of DEPE or MEPO patients would require a healthcare practitioner to administer maintenance doses based on a clinician survey conducted by the sponsor. The remaining 86% of patients were assumed to incur a once-off injection training cost of $88.90 (MBS item 82215). The inclusion of administration costs for maintenance doses may not be reasonable given PBAC previously accepted that such doses would be self-administered and hence should not incur any costs, other than a once-off injection training cost (Table 17, TEZE PSD, November 2025 PBAC meeting; Table 13, DUPI PSD, November 2020 PBAC meeting). Therefore, the evaluation revised the CMA to exclude administration costs for maintenance doses and to include the once-off injection training cost for all DEPE and MEPO patients (Table 9).

6.49 The submission's CMA considered dispensing fees and patient copayments. The Sub-Committees agreed with the evaluation that the inclusion of patient copayments was not appropriate. It was noted that pricing agreements are made under the *National Health Act 1953* at the ex-manufacturer level. The CMA was revised during the evaluation to remove dispensing fees and patient copayments.

6.50 The CMA was revised during the evaluation on the basis of (1) the cost of the medicine (i.e. removing mark-ups/dispensing fees and patient contributions from the CMA), (2) assuming 13 doses of MEPO per year, (3) removing administration costs for maintenance doses and (4) assuming all patients will require one off injection training. The resulting cost-minimised price of DEPE was reduced from $[redacted] per 100 mg vial in the submission's CMA to $[redacted] per 100 mg vial (see Table 9). The CMA has been presented against the effective price of MEPO as the sponsor of DEPE and MEPO are the same company, and therefore the sponsor is aware of the effective price of MEPO.

Table 9: Revised CMA of DEPE versus MEPO conducted during the evaluation

Row	Description	DEPE	MEPO
A	Dose per administration	100 mg	100 mg
B	Drug cost per administration (effective ex-manufacturer price)	$[redacted]	$[redacted]
C	Number of doses in Year 1	2	13
D	Total annual drug cost (B x C)	$[redacted]	$[redacted]
E	Subcutaneous injection training (MBS item 82215)	$88.90	$88.90
F	Administration cost per maintenance injection	$0.00	$0.00
G	Administration cost (MBS item 82200)	$0.00	$0.00
H	Cost for post-administration monitoring of anaphylaxis event (MBS item 82210)	$0.00	$0.00
I	Toal administration cost (E + F + G + H)	$88.90	$88.90
J	Total cost in Year 1 (D + I)	$[redacted]	$[redacted]
K	Difference in cost per year	$0	Reference

Source: constructed during evaluation
DEPE = depemokimab; MBS = Medicare Benefits Schedule; MEPO = mepolizumab

6.51 While the CMA was conducted against MEPO, this may not be the lowest cost alternative therapy. The PSCR argued that the listing of DEPE would provide benefits for some patients (due to reduced treatment burden, fewer access and administration barriers and lower annual co-payments relative to more frequently dosed biologics) and hence MEPO is a pragmatic choice of comparator. The Sub-Committees noted that OMA does not have an SPA. The pre-PBAC response noted that the current PBS-listed price for OMA is not specific to the severe asthma population. The pre-PBAC response noted that 'the current price of OMA reflects a weighted price across the severe asthma and chronic spontaneous urticaria indications' (paragraph 5.10, OMA (Xolair®) PSD, March 2025 PBAC Meeting).

Drug cost/patient/year

6.52 The drug cost per patient per year for DEPE and MEPO are presented in Table 10 using the submission's proposed ex-manufacturer price (for the CMA) and DPMQ (for financial estimates). As mentioned in paragraph 6.49, the proposed price of DEPE was based on the submission's CMA which considered dispensing fees and patient copayments. The drug cost per patient per year using the revised ex-manufacturer price is $[redacted] for DEPE and MEPO (as presented in Table 9).

Table 10:Drug cost per patient for proposed drug

	DEPE			MEPO		
	Trial (SWIFT 1 & 2)[a]	CMA	Financial estimates	Trial (MENSA & MUSCA)[a]	CMA	Financial estimates
Dosing frequency	100mg every 6 months			100mg every 4 weeks		
Cost per administration	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Cost/patient/month	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]
Cost/patient/year	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]	$[redacted]

Source: Constructed during evaluation
CMA = cost minimisation approach; DEPE = depemokimab; MEPO = mepolizumab

[a] Compliance or relative dose intensities were not reported in the CSR of these trials hence 100% compliance was assumed

Estimated PBS usage & financial implications

6.53 This submission was considered jointly by DUSC and ESC. The submission used a market-share approach to estimate the financial impact of listing DEPE.

6.54 A summary of the data sources and parameter values used in the financial analysis is presented in Table 11.

Table 11: Data sources and parameter values applied in the utilisation and financial estimates

Parameter	Value	Source	Comment
Market: Severe eosinophilic asthma			
Existing Market	114,193 scripts in 2024.	Utilisation for PBS items for MEPO, BENRA, DUPI and OMA.	The evaluation considered the submission likely overestimated the market by the inclusion of all DUPI and OMA scripts which are also used to treat patients with allergic asthma. The Sub-Committees advised adjusting the market estimate by either reducing the existing market by 20% to account for non-eosinophilic asthma or attributing 50% of DUPI prescription volumes to the target market.
% Growth Rate	[redacted]% growth rate assumed throughout the forecasted period.	Assumed market growth from 2022 – 2024.	The evaluation considered the growth rate appeared implausibly high, an alternative approach suggested the growth rate may be 10%. The PSCR provided a revised utilisation and cost model (UCM) which applied a [redacted]% growth rate. The Sub-Committees agreed with the evaluation that a [redacted]% growth rate was appropriate for the existing market, noting that this assumption has been accepted through the PSCR process. However, the Sub-Committees also considered that the bi-annual administration of DEPE may expand the overall market by enabling uptake among patients not previously treated with biologics for severe asthma.
% Treatment Uptake Rate	[redacted]% in Year 1 increasing to [redacted]%.	Clinician survey provided with the submission.	The Sub-Committees considered the assumption that DEPE would achieve a [redacted]% market share to be uncertain. The Sub-Committees considered it was unclear what percentage would switch if their current treatment was effective. In addition, the Sub-Committees noted that TEZE was recommended by the PBAC in November 2025 and considered that, if listed on the PBS, it may also impact on the uptake of DEPE. The Sub-Committees considered that a[redacted]%

Parameter	Value	Source	Comment
			uptake in Year 1 and increasing to [redacted]% by Year 5 and 6 should be explored in a sensitivity analysis.
Script Equivalence	Based on the number of scripts required per year for existing treatments replaced with two DEPE scripts.	Product information for each treatment.	The submission assumed initial scripts for BENRA and DUPI would last for a year, when they only last for 32 and 34 weeks respectively. The Sub-Committees noted the sponsor has addressed this in the revised UCM provided with the PSCR which applied rates of 0.25 for BENRA scripts and 0.14 for DUPI scripts.
MBS Impacts	Reduction in MBS item 82200 based on the lower administration frequency of DEPE. It was assumed that 14% of script for DEPE and the affected medicines would require MBS item 82200 for administration.	As assumed in the CMA.	The Sub-Committees noted that SC therapies are predominantly self-administered and should not incur ongoing MBS administration costs, with only a once-off injection training cost considered appropriate (Table 17, TEZE PSD, November 2025; Table 13, DUPI PSD, November 2020). As this applies across all comparators (MEPO, BENRA, DUPI, OMA and DEPE), these training costs are not incremental. While OMA requires HCP administration and monitoring for the first three doses, the associated MBS costs cannot be attributed given OMA use is not separately modelled. The Sub-Committees considered that inclusion of SC administration cost-offsets (i.e. MBS item 82200) is not consistent with prior advice and should be removed.

Source: Constructed during the evaluation from the "Attachment 4.1_DEPE_Section 4_UCM_MAR-26" attachment provided in the submission.

BENRA = benralizumab; CMA = cost-minimisation approach; MEPO = mepolizumab; DEPE = depemokimab; DUPI = dupilumab; MBS = Medicare Benefits Schedule; OMA = omalizumab; PBS = Pharmaceutical Benefits Scheme; SC = subcutaneous.

6.55 The estimated use and financial impact of listing DEPE are presented in Table 12 based on assumed effective prices for BENRA and DUPI.

Table 12: Estimated use and financial implications – based on assumed effective prices for BENRA and DUPI

Description	2027	2028	2029	2030	2031	2032
Existing market						
MEPO	[redacted][1]	[redacted][2]	[redacted][3]	[redacted][4]	[redacted][4]	[redacted][4]
BENRA initial	[redacted][5]	[redacted][5]	[redacted][6]	[redacted][6]	[redacted][6]	[redacted][7]
BENRA continuing	[redacted][7]	[redacted][8]	[redacted][10]	[redacted][1]	[redacted][9]	[redacted][3]
DUPI initial	[redacted][6]	[redacted][7]	[redacted][7]	[redacted][8]	[redacted][10]	[redacted][1]
DUPI continuing	[redacted][10]	[redacted][1]	[redacted][9]	[redacted][3]	[redacted][4]	[redacted][4]
Uptake rate (assumption)	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
Replaced scripts						
MEPO	[redacted][11]	[redacted][5]	[redacted][6]	[redacted][7]	[redacted][10]	[redacted][2]
BENRA initial	[redacted][12]	[redacted][12]	[redacted][11]	[redacted][11]	[redacted][5]	[redacted][5]
BENRA continuing	[redacted][12]	[redacted][11]	[redacted][5]	[redacted][6]	[redacted][7]	[redacted][8]
DUPI initial	[redacted][12]	[redacted][11]	[redacted][11]	[redacted][5]	[redacted][6]	[redacted][7]
DUPI continuing	[redacted][11]	[redacted][5]	[redacted][6]	[redacted][7]	[redacted][8]	[redacted][1]
Estimated financial implications for DEPE						
Total DEPE scripts[a]	[redacted][12]	[redacted][11]	[redacted][5]	[redacted][6]	[redacted][7]	[redacted][8]
Cost to PBS/RPBS, less copayments[b]	$[redacted] 13	$[redacted] 14	$[redacted] 15	$[redacted] 16	$[redacted] 16	$[redacted] 17
Estimated financial implications for replaced scripts						
Cost savings to the PBS/RPBS, less copayments[b]	$[redacted] 13	$[redacted] 14	$[redacted] 18	$[redacted] 16	$[redacted] 16	$[redacted] 17
Net cost to PBS/RPBS	**-$[redacted] 19**	**-$[redacted] 19**	**-$[redacted] 19**	**-$[redacted] 19**	**-$[redacted] 19**	**-$[redacted] 19**
Net cost to MBS	-$[redacted] 19	-$[redacted] 19	-$[redacted] 19	-$[redacted] 19	-$[redacted] 19	-$[redacted] 19
Net cost to the PBS/RPBS/MBS	-$[redacted] 19	-$[redacted] 19	-$[redacted] 19	-$[redacted] 19	-$[redacted] 19	-$[redacted] 19
Net cost to MBS, revised[c]	-$[redacted] 19	-$[redacted] 19	-$[redacted] 19	-$[redacted] 19	-$[redacted] 19	-$[redacted] 19
Net cost to PBS/RPBS/MBS, revised[c]	**-$[redacted] 19**	**-$[redacted] 19**	**-$[redacted] 19**	**-$[redacted] 19**	**-$[redacted] 19**	**-$[redacted] 19**

Source: Constructed during the evaluation from the "Attachment 4.1_DEPE_Section 4_UCM_MAR-26" attachment provided in the submission.

BENRA = benralizumab; DEPE = depemokimab; DUPI = dupilumab; MBS = Medicare Benefits Scheme; MEPO = mepolizumab; PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme

[a] Script replacement rate of 0.15, 0.25, 0.31, 0.14, 0.15 for MEPO, BENRA initial, BENRA continuing, DUPI initial and DUPI continuing scrips, respectively.

[b] Assuming a cost per DEPE script of $[redacted] and a PBS patient copayment of $14.88 and an RPBS copayment of $4.12.

[c] When calculating the cost reductions to the MBS, the financial workbook considered only half of the replaced scripts in the market, this was revised during the evaluation to ensure all scripts are considered.

The redacted values correspond to the following ranges:

[1] *60,000 to < 70,000*
[2] *80,000 to < 90,000*
[3] *90,000 to < 100,000*
[4] *100,000 to < 200,000*
[5] *10,000 to < 20,000*
[6] *20,000 to < 30,000*
[7] *30,000 to < 40,000*
[8] *40,000 to < 50,000*
[9] *70,000 to < 80,000*
[10] *50,000 to < 60,000*
[11] *5,000 to < 10,000*
[12] *500 to < 5,000*

[13] *$20 million to < $30 million*
[14] *$40 million to < $50 million*
[15] *$70 million to < $80 million*
[16] *$100 million to < $200 million*
[17] *$200 million to < $300 million*
[18] *$80 million to < $90 million*
[19] *net cost saving*

6.56 The total cost saving to the PBS/RPBS of listing DEPE was estimated to be $10 million to < $20 million in Year 6, and a total of $30 million to < $40 million in the first 6 years of listing. This was based on assumed effective prices for BENRA and DUPI scripts. The cost saving was driven by the reduced dosing frequency (the reduction in mark-up and dispensing fees outweighed the average patient co-payment offsets), compared with the current available PBS listed biologic agents.

6.57 A number of concerns were identified regarding the submission's estimation of the size of the existing market:

- The submission included all observed scripts for DUPI and OMA into the proposed market for DEPE (patients with SEA). The evaluation considered this was not reasonable given that OMA is only indicated for allergic asthma and DUPI is indicated for both eosinophilic and allergic asthma under the same PBS item. The literature suggests that 59% of T2 asthma is eosinophilic[5] and noting that BENRA and MEPO already represent 63% of "normalised" scripts in 2024, it is plausible to assume that most eosinophilic asthma patients are already treated with BENRA and MEPO and that patients treated with DUPI and OMA largely express other phenotypes (e.g., IgE/FeNO-driven). Therefore, the evaluation considered that excluding DUPI and OMA from the market estimate may be more reasonable. The PSCR argued that the exclusion of DUPI and OMA scripts entirely from the potential DEPE market was not reasonable as some patients eligible for DUPI and OMA would also remain eligible for DEPE given the overlap between allergic and eosinophilic asthma. The Sub-Committees noted the data suggesting 59% of moderate to severe asthma was eosinophilic was for patients considered to have T2 asthma, which accounted for 28% of the population studied. The Sub-Committees noted that, based on a historical registry study of 1,716 adult patients with severe asthma and available blood eosinophil counts enrolled in the International Severe Asthma Registry, 82.2% of patients were considered to have SEA with the remainder considered to have non-eosinophilic asthma.[28] Noting that DUPI and OMA accounted for 37% of 'normalised' scripts in 2024 and assuming that non-eosinophilic asthma accounts for almost 20% of the market the Sub-Committees agreed with the PSCR that not all of the use of DUPI and OMA would be for non-eosinophilic asthma. Hence, instead of excluding DUPI and OMA from the market estimates, the Sub-Committees advised that it may be reasonable to assume that 50% of the DUPI market may also be eligible for DEPE.

[28] *Heaney L, Perez de Llano L, Al-Ahmad M. Eosinophilic and Noneosinophilic Asthma. CHEST, 2021; 160, 814-830*

- The submission argued that OMA only made up a small proportion of the market (8% in 2024) and there would be difficulties attempting to calculate script replacement rates due to variations in dosing frequency across patients and multiple scripts being required to make up one dose for some patients for OMA. Therefore, it had distributed the OMA scripts to other therapies in the market. The evaluation considered this was not reasonable. The PBS item descriptor for OMA instructs prescribers to request the appropriate number of vials for 32 (initial) or 24 (continuing) weeks of treatment. This suggests that each dose requires only one script. The submission could have also applied the cost of the average dose of OMA (398 mg per four weeks) to each script (by applying a cost per mg approach). This average dose was used when MEPO was cost-minimised against OMA (paragraph 6.16, MEPO PSD, July 2016 PBAC Meeting). This was not able to be easily implemented during the evaluation.
- The submission assumed a market growth rate of [redacted]% derived from the utilisation of the market from 2022 – 2024. The evaluation considered the growth rate appeared implausibly high. An alternative approach, explored during the evaluation, noted that the market growth rate was approximately linear when aggregating the entire market from 2017 – 2024. Extrapolating this growth rate out to 2031 resulted in an average growth rate of approximately [redacted] percent per annum. The Sub-Committees noted that the PSCR provided a revised utilisation and cost model (UCM) which applied a [redacted]% growth rate and considered that this approach was appropriate.

6.58 When calculating the script replacement rate with DEPE (two scripts per year), the submission assumed that initial scripts for the existing market would provide treatment for one year. While this did not impact the replacement rate for MEPO scripts, the initial listings for BENRA and DUPI scripts provide treatment for 32 and 34 weeks, which therefore means it will be replaced by 1.23 and 1.30 DEPE scripts, respectively. The PSCR provided a revised UCM which applied rates of 0.25 for BENRA scripts and 0.14 for DUPI scripts. The Sub-Committees considered that this approach was appropriate.

6.59 The cost of each DEPE script was based the submission's base case cost-minimised price of DEPE (which considered dispensing fees and patient copayments). As mentioned in paragraph 6.49, this was not reasonable with a reduced price reported in the revised CMA against MEPO (see paragraph 6.50). The Sub-Committee noted that MEPO may not be the lowest cost-effective alternative therapy (see paragraph 6.51).

6.60 The Sub-Committees considered the size of the existing market was overestimated by the submission. The Sub-Committees noted that the PSCR provided a revised UCM which reduced the assumed annual growth rate from [redacted]% to [redacted]% and addressed concerns regarding BENRA and DUPI script replacement rates and considered these amendments appropriate. The revised base case proposed in the PSCR is provided in Table 13. The Sub-Committees noted the PSCR revised base case continued to be

based on the submissions base case cost minimised price which was not reasonable. The Sub-Committees noted the impact of amending the price to that reported in the revised CMA versus MEPO is reported in Table 13, and based on applying treatment uptake rates of [redacted]% in Year 1 increasing to [redacted]% by Year 5 and 6. The Sub-Committees considered that amendments in addition to those proposed in the PSCR were required and advised that it would be appropriate to assume that 50% of the DUPI market were eligible for DEPE. As outlined in Table 11 the Sub-Committees considered the SC administration cost-offsets should be removed. The Sub-Committees noted that the estimates were based on assumed effective prices for BENRA and DUPI scripts.

6.61 The Sub-Committees considered that the bi-annual administration of DEPE may expand the overall market by enabling uptake among patients not previously treated with biologics for severe asthma. The Sub-Committees advised that if expansion of the overall market occurred the costs of DEPE would increase without them being offset by cost savings. Acknowledging the potentially important differences between therapeutic areas, the Sub-Committees noted that a 32% increase in the overall number of patients initiating osteoporosis therapy (7,202 patients in 2014 to 9,514 in 2018) was observed with the listing of denosumab which also has bi-annual administration.[29] The Sub-Committees also noted that there would be additional costs associated if patients switched from DEPE within six months.

[29] Drug utilisation sub-committee (DUSC). Denosumab for osteoporosis: utilisation analysis using PBS data. October 2020 denosumab-analysis-PBS-and-MI-dusc-prd-2020-10v2.PDF

Table 13: PSCR revised base case and sensitivity analyses on the net financial impact to the PBS/RPBS

	2027	*2028*	*2029*	*2030*	*2031*	*2032*	*%*
PSCR revised base case[a]	**-$[redacted][1]**	**-$[redacted][1]**	**-$[redacted][1]**	**-$[redacted][1]**	**-$[redacted][1]**	**-$[redacted][1]**	**0%**
Proportion of DUPI scripts attributable to the DEPE market (base case: [redacted]%)							
50%	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	cost saving
Reduce current market by 20%							
Reduce 20%	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	cost saving
Uptake rate (base case: [redacted]% in Year 1 increasing to [redacted]% in Year 6)							
Yr1 [redacted]%, Yr 2 [redacted]%, Yr 3 [redacted]%, Yr4 [redacted]%, Yr 5 [redacted]% yr 6 [redacted]%	-$884,724[1]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	-$[redacted]1[1]	cost saving
DEPE script cost (base case: $[redacted])							
$[redacted][b]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	cost saving
MVSA							
50% DUPI scripts and uptake rate Yr1 [redacted]% to Yr 5 and 6 [redacted]% and $[redacted][b]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	cost saving
50% DUPI scripts and $[redacted][b]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	-$[redacted][1]	cost saving

Source: Constructed during the preparation of the Sub-Committee advice based on Attachment 4.1_DEPE_Section 4_UCM_MAR-26_PSCR.xlsx. BENRA = benralizumab; DEPE = depemokimab; DPMQ = dispensed price for maximum quantity; DUPI = dupilumab; MEPO = mepolizumab; PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme

[a] Applied a [redacted]% annual market growth rate and the replacement rate of 0.25 for BENRA scripts and 0.14 for DUPI scripts.

[b] Weighted price for DEPE DPMQ based on the revised CMA.

The redacted values correspond to the following ranges:

[1] net cost saving

6.62 The pre-PBAC response provided revised financial estimates which made the following amendments to the UCM provided in the PSCR: (i) assumed 50% of the DUPI market was eligible for DEPE; (ii) changed uptake to increase from [redacted]% in Year 1 to [redacted]% in Years 5 and 6; and (iii) removed the subcutaneous administration cost-offsets. In addition, the revised financial estimates introduced a community pharmacy dispensing population split whereby the sponsor assumed that [redacted]% of prescriptions would be dispensed through S90 community pharmacies based on its analysis of IQVIA data.

6.63 The PBAC noted that while a Section 100 HSD has been requested, dispensing in S90 community pharmacies is allowed under a Complex Authority Required (CAR) listing. The PBAC noted an analysis of the dispensing setting for mepolizumab in uncontrolled

severe asthma between 2020 and 2025 was undertaken by the Drug Utilisation Section using line by line patient data from the 100% PBS sample. The analysis reported the percentage of dispensing across public hospital, private hospital and non-hospital settings to be 17%, 31% and 52% respectively.

Quality Use of Medicines

6.64 The submission stated that it was intending to implement medical education activities such as educational meetings with healthcare professionals to identify eligible patients for treatment, patient support programs to facilitate self-administration and disseminating administration training videos. The Sub-Committees considered a greater emphasis on supporting 6-monthly injection reminders should be considered as part of quality use of medicine activities for DEPE.

Financial Management – Risk Sharing Arrangements

6.65 No information was presented.

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 (HSD) listing of depemokimab (DEPE) for the treatment of uncontrolled severe eosinophilic asthma (SEA) in patients aged 12 years or older. The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of DEPE would be acceptable if it were cost-minimised against the least costly biologic for asthma over a 1-year time frame.

7.2 The PBAC noted the input from health care professionals and organisations supporting the listing of depemokimab for this indication. The input described the potential for improvements in medication adherence and treatment burden with DEPE's 6 monthly dosing regimen. The PBAC also noted input from Asthma Australia indicating a potential disadvantage of the extended dosing interval may be the unintended consequence of patients perceiving the extended dosing interval as a reason to reduce regular reviews of their asthma.

7.3 In terms of the proposed restrictions the PBAC considered:

- The indication for treatment was uncontrolled severe asthma in patients aged 12 years or older.
- A Section 100, Highly Specialised Drug Program Authority Required (Written) listing was appropriate for the initial 1, initial 2 and continuing treatment phases (see paragraph 3.7).
- A balance of supply restriction was not required.
- Assessment of response prior to the second dose of DEPE at 6 months was appropriate. Similarly, 6 months of therapy at a time was appropriate for

continuing treatment. As such, no repeats would be required for either initial 2, initial 2 or continuing treatment phases (see paragraph 3.4). Relevant clinical criteria, prescribing instructions and administrative advice be updated to reflect this approach as outlined in paragraph 8.1.

- A grandfathering listing was not required.
- Flow on changes were required to the overarching uncontrolled severe asthma administrative advice as outlined in paragraph 8.2.

7.4 The PBAC considered that the nomination of mepolizumab (MEPO) as the main comparator, benralizumab (BENRA) as the secondary comparator and dupilumab (DUPI), omalizumab (OMA) and tezepelumab (TEZE) as supplementary comparators was appropriate. Notwithstanding differences in the available treatments, the PBAC recalled that it had been of a mind to consider the available biologic treatments for uncontrolled severe asthma as broadly equivalent, and therefore the PBAC considered that any biologic for asthma could be considered appropriate alternative therapies.

7.5 The submission was based on two Phase 3 DEPE trials: SWIFT-1 and SWIFT-2. The PBAC noted that the SWIFT-1/-2 trials enrolled a patient population that was broader than the proposed PBS population (see paragraph 6.7), and hence in addition to the ITT population, a post hoc subgroup analysis was presented to reflect the likely PBS target population. The PBAC acknowledged the loss of randomisation and hence the potential for bias but agreed with the Sub-Committees that this approach was appropriate.

7.6 To support the claim of non-inferiority of DEPE to MEPO the submission conducted a series of indirect treatment comparisons (ITCs). The ITCs between DEPE vs MEPO were informed by two MEPO trials (MENSA and MUSCA). The PBAC noted there were transitivity issues between the trials included in the ITCs and that a multilevel network meta-regression (ML NMR) was undertaken to address cross-trial differences. The PBAC recalled it had previously accepted a non-inferiority (NI) margin of 1.28 for the upper bound of the 95% confidence intervals for the rate ratio of annualised rate of asthma exacerbation (AAER) (see paragraph 6.10). The PBAC noted that inferiority could not be ruled out with the Bucher pairwise ITC, and the chosen random effect (RE) fitted model did not meet the NI margin for the network meta-analysis (NMA) or the ML NMR. The PBAC acknowledged the favourable and consistent point estimates for DEPE for the NMA and the ML NMR and noted that MEPO and DEPE have the same epitope target. Overall, the PBAC agreed with its Sub-Committees it was uncertain but reasonable to accept a non-inferiority claim for DEPE compared to MEPO.

7.7 The PBAC considered the claim of non-inferior safety compared to MEPO was reasonable.

7.8 The PBAC noted the submission presented a cost-minimisation approach of DEPE versus MEPO. The PBAC recalled that OMA, MEPO and BENRA for the treatment of uncontrolled severe asthma were cost-minimised to each other and that for the

consideration of DUPI and TEZE it had previously considered that the cost-minimisation analysis should be against the least costly biologic for asthma (paragraph 7.18, tezepelumab PSD, November 2025 PBAC Meeting). Consistent with its previous advice, the PBAC considered it was also appropriate that the cost-minimisation analysis for DEPE be against the least costly biologic for asthma.

7.9 In addition, the PBAC considered that DEPE 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. Thus, the PBAC considered the equi-effective doses for uncontrolled severe asthma were:

- DEPE 100 mg by subcutaneous (SC) injection 6 monthly (2 doses over one year);
- MEPO 100 mg by SC injection every 4 weeks (13 doses over 1 year);
- BENRA 30 mg by SC injection every 4 weeks for the first 3 doses, then every 8 weeks (7.5 doses over 1 year);
- DUPI 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);
- OMA 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); and
- TEZE 210 mg by SC injection every 4 weeks (13 doses over 1 year).

7.10 The PBAC considered that the cost-minimisation approach for DEPE should occur at the ex-manufacturer level (see paragraph 6.49). In addition, 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 TEZE (paragraph 7.21, TEZE PSD, November 2025 PBAC Meeting). The PBAC considered that the inclusion of administration costs for maintenance doses proposed in the DEPE submission was not reasonable (see paragraph 6.48).

7.11 The PBAC also recalled that in relation to the administration of OMA, 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 OMA (paragraph 7.22, TEZE PSD, November 2025 PBAC Meeting).

7.12 The submission used a market share approach to estimate the financial impact of listing DEPE. The PBAC noted the Pre-Sub-Committee Response (PSCR) provided a revised utilisation and cost model (UCM) which reduced the assumed annual growth

rate from [redacted]% to [redacted]% and addressed concerns regarding BENRA and DUPI script replacement rates. The PBAC noted the Sub-Committees advice that amendments in addition to those provided in the PSCR were required. The PBAC accepted that it would also be appropriate to assume that only 50% of the DUPI market was eligible for DEPE and for SC administration cost-offsets to be removed. The PBAC noted that the pre-PBAC response provided a revised UCM which included each of these revisions. In addition, the PBAC noted the pre-PBAC response revised UCM incorporated the sensitivity analysis proposed by the Sub-Committees whereby an uptake rate of [redacted]% in Year 1 was assumed increasing to [redacted]% by Year 5 and 6. The PBAC noted this was more conservative (i.e. resulted in a smaller estimated savings to the PBS/RPBS) than the submission base case which assumed an uptake rate of [redacted]% in Year 1 increasing to [redacted]% in Year 6. The PBAC considered that the uptake rate was uncertain but accepted that proposed in the pre-PBAC response. The PBAC noted that the pre-PBAC response revised UCM introduced a S90 community pharmacy dispensing population split and considered that the percentage of dispensing across the public, private and non-hospital settings should be based on the analysis undertaken by the Drug Utilisation Section (see paragraphs 6.62 and 6.63). 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.

7.13 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because DEPE is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over MEPO, 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.

7.14 The PBAC recommended that DEPE should not be treated as interchangeable on an individual patient basis with any other drugs.

7.15 The PBAC advised that DEPE is suitable for prescribing by medical practitioners only.

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

7.17 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 item:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
DEPEMOKIMAB					
Depemokimab 100 mg/mL injection, 1 mL pen device	NEW/ Public	1	1	0	Exdensur
Depemokimab 100 mg/mL injection, 1 mL pen device	NEW/ Private	1	1	0	Exdensur

Restriction Summary / Treatment of Concept	
	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: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	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:
	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 a blood eosinophil count of at least 300 cells per microlitre in the 12 months prior to initiating 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 this drug,
	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 24 weeks of treatment under this restriction,
	AND
	Clinical criteria:
	The treatment must not be used in combination with or 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.
	Prescribing Instructions: 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. If the requirement for treatment with optimised asthma therapy cannot be met because of contraindications according to the relevant contraindications or precautions TGA-approved Product Information and/or intolerances of a severity necessitating permanent treatment withdrawal, details of the contraindication and/or intolerance must be provided in the Authority application.
	Prescribing Instructions: The following initiation criteria indicate failure to achieve adequate control and must be demonstrated in all patients at the time of the application: (a) an Asthma Control Questionnaire (ACQ-5) score of at least 2.0, as assessed in the previous month, AND (b) while receiving optimised asthma therapy in the past 12 months, experienced at least 1 admission to hospital for a severe asthma exacerbation, OR 1 severe asthma exacerbation, requiring documented use of systemic corticosteroids (oral corticosteroids initiated or increased for at least 3 days, or parenteral corticosteroids) prescribed/supervised by a physician. 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 20 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. This assessment, which will be used to determine eligibility for the first continuing treatment, should be conducted within 4 weeks of the next due 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. Where a response assessment is not undertaken and provided, the patient will be deemed to have failed to respond to treatment with this drug. 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.

	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. 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. There is no limit to the number of treatment cycles that a patient may undertake in their lifetime. A multidisciplinary severe asthma clinic team comprises of: (i) A respiratory physician; and (ii) A pharmacist, nurse or asthma educator.
	Prescribing Instructions: The authority application must be made in writing and must include: (1) details of the proposed prescription; and (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: The following must be provided at the time of application and documented in the patient's medical records: (a) details (treatment, date of commencement, duration of therapy) of prior optimised asthma drug therapy; and (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 (c) details of severe exacerbation/s experienced in the past 12 months while receiving optimised asthma therapy (date and treatment); and (d) the eosinophil count and date; and (e) Asthma Control Questionnaire (ACQ-5) score.
	Administrative Advice: The Services Australia website (www.servicesaustralia.gov.au) has details of the accepted toxicities, including severity, which will be accepted for the purposes of exempting a patient from the requirement of treatment with optimised asthma therapy.
	Administrative Advice: For copies of the ACQ, please contact GlaxoSmithKline Medical Information on 1800 033 109.
	Administrative Advice: 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 / Treatment of Concept	
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)
	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.
	AND
	Clinical criteria:
	Patient must not have failed, or ceased to respond to, PBS-subsidised treatment with this drug for severe asthma during the current treatment cycle.
	AND
	Clinical criteria:
	Patient must have had a blood eosinophil count greater than or equal to 300 cells per microlitre and that is no older than 12 months immediately prior to commencing PBS-subsidised biological medicine treatment for severe asthma;
	OR
	Patient must have had a blood eosinophil count greater than or equal to 150 cells per microlitre while receiving treatment with oral corticosteroids and that is no older than 12 months immediately prior to commencing PBS-subsidised biological medicine treatment for severe asthma;
	AND
	Clinical criteria:
	Patient must not receive more than 24 weeks of treatment under this restriction
	AND
	Clinical criteria:
	The treatment must not be used in combination with or 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.

	Prescribing Instructions: 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. 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 20 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. This assessment at around 20 weeks, which will be used to determine eligibility for the first continuing treatment, should be conducted within 4 weeks of the next due dose of biological medicine. To avoid 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. Where a response assessment is not undertaken and submitted, the patient will be deemed to have failed to respond to treatment with this biological medicine. A multidisciplinary severe asthma clinic team comprises of: (i) A respiratory physician; and (ii) A pharmacist, nurse or asthma educator.
	Prescribing Instructions: The authority application must be made in writing and must include: (1) details of the proposed prescription; and (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: The following must be provided at the time of application and documented in the patient's medical records: (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 (b) details (treatment, date of commencement, duration of therapy) of prior biological medicine treatment; and (c) eosinophil count and date; and (d) if applicable, the dose of the maintenance oral corticosteroid (where the response criteria or baseline is based on corticosteroid dose); and (f) the reason for switching therapy (e.g. failure of prior therapy, partial response to prior therapy, adverse event to prior therapy).
	Administrative Advice: 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).

	Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001
	Administrative Advice: For copies of the ACQ, please contact GlaxoSmithKline Medical Information on 1800 033 109.
	Administrative Advice: **<u>TREATMENT OF ADULT AND ADOLESCENT PATIENTS WITH UNCONTROLLED SEVERE ASTHMA</u>** 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'. A patient is eligible for PBS-subsidised treatment with only 1 biological medicine for uncontrolled severe asthma at any one time. 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. Under these arrangements, within a treatment cycle, a patient may receive long-term treatment with a biological medicine as long as they sustain a response to therapy. A patient currently receiving PBS-subsidised treatment as of 1 April 2021 is considered to have started a cycle of treatment. Within the same treatment cycle, a patient cannot trial and fail, or cease to respond to, the same PBS-subsidised biological medicine more than once. Therefore, once a patient fails to meet the response criteria for a PBS-subsidised biological medicine, they must change to an alternate biological medicine if they wish to continue PBS-subsidised biological treatment. Once a patient has either failed to achieve or sustain a response to treatment 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]. The length of the break in therapy is measured from the date the most recent treatment with a PBS-subsidised biological medicine is ceased until the date of the first application for recommencement of treatment with a biological medicine under the new treatment cycle.

	There is no limit to the number of treatment cycles that a patient may undertake in their lifetime. How to prescribe PBS-subsidised biological medicine treatment for uncontrolled severe asthma. (1) Initial treatment: Applications for initial treatment should be made where: (i) a patient has not received prior PBS-subsidised biological medicine treatment and wishes to commence such therapy (Initial 1 restriction); or (ii) a patient has received prior PBS-subsidised treatment with a biological medicine and wishes to recommence a new treatment cycle with this biological medicine following a treatment break in PBS-subsidised therapy (Initial 1 restriction); or (iii) a patient has received prior PBS-subsidised biological medicine therapy and wishes to trial an alternate biological medicine within the same treatment cycle (Initial 2 restriction) - [further details are under 'Swapping therapy' below]. Initial applications for depemokimab will be limited to a maximum of 24 weeks of treatment. Initial applications for all other biological medicines will be limited to a maximum of 32 weeks of therapy. 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. (2) Continuing treatment: Following the completion of an initial treatment course with a specific biological medicine, a patient may qualify to receive up to 24 weeks of continuing treatment with that biological medicine providing they have demonstrated an adequate response to treatment. The patient remains eligible to receive continuing biological medicine treatment with the same drug in courses of up to 24 weeks providing they continue to sustain the response. It is recommended that a patient be reviewed the month prior to completing their current course of treatment to ensure uninterrupted biological medicine supply. (3) Baseline measurements to determine response: Baseline measurements of the Asthma Control Questionnaire (ACQ; 5 item version) or oral corticosteroid dose submitted with the Initial authority application for a biological medicine must be used to determine whether an adequate response to treatment has been achieved or sustained. For patients transitioned from the paediatric to the adolescent/adult restriction, the exacerbation history may also be used to determine response. However, prescribers may provide new baseline measurements when a new Initial treatment authority application is submitted and these new baseline measurements may be used to assess response. (4) Swapping therapy within the same treatment cycle. Once initial treatment with the first PBS-subsidised biological medicine is approved, a patient may swap to an alternate biological medicine at any time by qualifying under an Initial 2 restriction. However, they cannot swap to a particular biological medicine if they have failed to respond to prior treatment with that drug within the same treatment cycle. Within the same treatment cycle a patient may alternate between therapy with any biological medicine of their choice (1 at a time) providing: (i) they have not received PBS-subsidised treatment with that particular biological medicine previously; or (ii) they have demonstrated an adequate response to that particular biological medicine if they have previously trialled it on the PBS; and (iii) they have not previously failed to respond to treatment with all eligible biological medicines in this treatment cycle. (5) Re-commencement of a new treatment cycle after a treatment break in PBS-subsidised therapy: A patient who wishes to trial a second or subsequent new treatment cycle, following a break in PBS-subsidised therapy of at least 12 months, must re-qualify through an Initial 1 restriction.

	(6) Monitoring of patients: Omalizumab only: Anaphylaxis and anaphylactoid reactions have been reported following first or subsequent administration of omalizumab (see Product Information). Patients should be monitored post-injection, and medications for the treatment of anaphylactic reactions should be available for immediate use following administration of omalizumab. Patients should be informed that such reactions are possible and prompt medical attention should be sought if allergic reactions occur.

MEDICINAL PRODUCT medicinal product pack	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
DEPEMOKIMAB					
Depemokimab 100 mg/mL injection, 1 mL pen device	NEW/ Public	1	1	0	Exdensur
Depemokimab 100 mg/mL injection, 1 mL pen device	NEW/ Private	1	1	0	Exdensur

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: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Administrative Advice: For copies of the ACQ, please contact GlaxoSmithKline Medical Information on 1800 033 109.
	Administrative Advice: 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).
	Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001
	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 or 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: An adequate response to this biological medicine is defined as: (a) a reduction in the Asthma Control Questionnaire (ACQ-5) score of at least 0.5 from baseline, OR (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: 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. 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 next due dose of biological medicine. 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. 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: The authority application must be made in writing and must include: (1) details of the proposed prescription; and (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:

	The following information must be provided at the time of application and must be documented in the patient's medical records: (a) if applicable, details of maintenance oral corticosteroid dose; and (b) a completed Asthma Control Questionnaire (ACQ-5) score.
	Administrative Advice: **TREATMENT OF ADULT AND ADOLESCENT PATIENTS WITH UNCONTROLLED SEVERE ASTHMA** 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'. A patient is eligible for PBS-subsidised treatment with only 1 biological medicine for uncontrolled severe asthma at any one time. 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. Under these arrangements, within a treatment cycle, a patient may receive long-term treatment with a biological medicine as long as they sustain a response to therapy. A patient currently receiving PBS-subsidised treatment as of 1 April 2021 is considered to have started a cycle of treatment. Within the same treatment cycle, a patient cannot trial and fail, or cease to respond to, the same PBS-subsidised biological medicine more than once. Therefore, once a patient fails to meet the response criteria for a PBS-subsidised biological medicine, they must change to an alternate biological medicine if they wish to continue PBS-subsidised biological treatment. Once a patient has either failed to achieve or sustain a response to treatment 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]. The length of the break in therapy is measured from the date the most recent treatment with a PBS-subsidised biological medicine is ceased until the date of the first application for recommencement of treatment with a biological medicine under the new treatment cycle. There is no limit to the number of treatment cycles that a patient may undertake in their lifetime. How to prescribe PBS-subsidised biological medicine treatment for uncontrolled severe asthma. (1) Initial treatment: Applications for initial treatment should be made where: (i) a patient has not received prior PBS-subsidised biological medicine treatment and wishes to commence such therapy (Initial 1 restriction); or (ii) a patient has received prior PBS-subsidised treatment with a biological medicine and wishes to recommence a new treatment cycle with this biological medicine following a treatment break in PBS-subsidised therapy (Initial 1 restriction); or (iii) a patient has received prior PBS-subsidised biological medicine therapy and wishes to trial an alternate biological medicine within the same treatment cycle (Initial 2 restriction) - [further details are under 'Swapping therapy' below].

	Initial applications for depemokimab will be limited to a maximum of 24 weeks of treatment. Initial applications for all other biological medicines will be limited to a maximum of 32 weeks of therapy. 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. (2) Continuing treatment: Following the completion of an initial treatment course with a specific biological medicine, a patient may qualify to receive up to 24 weeks of continuing treatment with that biological medicine providing they have demonstrated an adequate response to treatment. The patient remains eligible to receive continuing biological medicine treatment with the same drug in courses of up to 24 weeks providing they continue to sustain the response. It is recommended that a patient be reviewed the month prior to completing their current course of treatment to ensure uninterrupted biological medicine supply. (3) Baseline measurements to determine response: Baseline measurements of the Asthma Control Questionnaire (ACQ; 5 item version) or oral corticosteroid dose submitted with the Initial authority application for a biological medicine must be used to determine whether an adequate response to treatment has been achieved or sustained. For patients transitioned from the paediatric to the adolescent/adult restriction, the exacerbation history may also be used to determine response. However, prescribers may provide new baseline measurements when a new Initial treatment authority application is submitted and these new baseline measurements may be used to assess response. (4) Swapping therapy within the same treatment cycle. Once initial treatment with the first PBS-subsidised biological medicine is approved, a patient may swap to an alternate biological medicine at any time by qualifying under an Initial 2 restriction. However, they cannot swap to a particular biological medicine if they have failed to respond to prior treatment with that drug within the same treatment cycle. Within the same treatment cycle a patient may alternate between therapy with any biological medicine of their choice (1 at a time) providing: (i) they have not received PBS-subsidised treatment with that particular biological medicine previously; or (ii) they have demonstrated an adequate response to that particular biological medicine if they have previously trialled it on the PBS; and (iii) they have not previously failed to respond to treatment with all eligible biological medicines in this treatment cycle. (5) Re-commencement of a new treatment cycle after a treatment break in PBS-subsidised therapy: A patient who wishes to trial a second or subsequent new treatment cycle, following a break in PBS-subsidised therapy of at least 12 months, must re-qualify through an Initial 1 restriction. (6) Monitoring of patients: Omalizumab only: Anaphylaxis and anaphylactoid reactions have been reported following first or subsequent administration of omalizumab (see Product Information). Patients should be monitored post-injection, and medications for the treatment of anaphylactic reactions should be available for immediate use following administration of omalizumab. Patients should be informed that such reactions are possible and prompt medical attention should be sought if allergic reactions occur.

8.2 Flow on changes required to overarching USA administrative advice:

Amend existing concept ID 35559	**With new concept ID**
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. 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.	*Initial applications for depemokimab will be limited to a maximum of 24 weeks of treatment. Initial applications for all other biological medicines will be limited to a maximum of 32 weeks of therapy.* 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.
PBS Item Codes to be changed to new concept ID	
10109C / omalizumab 150 mg/mL injection, 1 mL syringe 10122R / omalizumab 150 mg/mL injection, 1 mL syringe 10118M / omalizumab 75 mg/0.5 mL injection, 0.5 mL syringe 10110D / omalizumab 75 mg/0.5 mL injection, 0.5 mL syringe 11824H / omalizumab 150 mg/mL injection, 1 mL syringe 11864K / omalizumab 150 mg/mL injection, 1 mL syringe 11835X / omalizumab 75 mg/0.5 mL injection, 0.5 mL syringe 11840E / omalizumab 75 mg/0.5 mL injection, 0.5 mL syringe 11828M / omalizumab 150mg/mL injection, 1 mL syringe 11825J / omalizumab 150 mg/mL injection, 1 mL syringe 11846L / omalizumab 75 mg/0.5 mL injection, 0.5 mL syringe 11826K / omalizumab 75 mg/0.5 mL injection, 0.5 mL syringe 12051G / mepolizumab 100 mg/mL injection, 1 mL pen device 12007Y / mepolizumab 100 mg/mL injection, 1 mL pen device 12052H / mepolizumab 100 mg/mL injection, 1 mL pen device 12064Y / mepolizumab 100 mg/mL injection, 1 mL pen device 12043W / mepolizumab 100 mg/mL injection, 1 mL pen device 12021Q / mepolizumab 100 mg/mL injection, 1 mL pen device 11997K / benralizumab 30 mg/mL injection, 1 mL pen device 11994G / benralizumab 30 mg/mL injection, 1 mL pen device 11996J / benralizumab 30 mg/mL injection, 1 mL pen device 11999M / benralizumab 30 mg/mL injection, 1 mL pen device 11995H / benralizumab 30 mg/mL injection, 1 mL pen device 12000N / benralizumab 30 mg/mL injection, 1 mL pen device 12309W / dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes 12313C / dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes 12318H / dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes 12316F / dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes 12293B / dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes 12310X / dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes 12302L / dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes 12294C / dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes 14947Q / omalizumab 75 mg/0.5 mL injection, 0.5 mL syringe 14919F / omalizumab 75 mg/0.5 mL injection, 0.5 mL syringe 14948R / omalizumab 150 mg/mL injection, 1 mL syringe 14927P / omalizumab 150 mg/mL injection, 1 mL syringe 14949T / omalizumab 75 mg/0.5 mL injection, 0.5 mL pen device 14904K / omalizumab 75 mg/0.5 mL injection, 0.5 mL pen device 14884J / omalizumab 150 mg/mL injection, 1 mL pen device 14923K / omalizumab 150 mg/mL injection, 1 mL pen device 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
15363N / Tezepelumab 210 mg/1.91 mL injection, 1.91 mL pen device
15364P / Tezepelumab 210 mg/1.91 mL injection, 1.91 mL pen device
15403Q / Tezepelumab 210 mg/1.91 mL injection, 1.91 mL pen device
15413F / Tezepelumab 210 mg/1.91 mL injection, 1.91 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

GSK welcomes the PBAC's recommendation of depemokimab (Exdensur®) for the treatment of uncontrolled severe eosinophilic asthma in patients aged 12 years or older. GSK recognises the substantial input from clinicians, patients and their associated organisations, which has informed this recommendation. GSK looks forward to working with the Department of Health to make Exdensur available on the PBS in a timely manner.