6.04 DUPILUMAB, Injection 300 mg in 2 mL single dose pre-filled syringe, Injection 300 mg in 2 mL single dose pre-filled pen, Dupixent®, Sanofi-Aventis Australia Pty Ltd

1 Purpose of submission

1.1 The Category 1 submission requested a General Schedule, Authority Required listing for dupilumab as an add-on maintenance treatment for adults with uncontrolled chronic obstructive pulmonary disease (COPD) and type 2 inflammation (defined by the submission as blood eosinophil count (BEC) ≥ 300 cells/µL). The proposed use of dupilumab is in combination with stable triple inhaled therapy, including an inhaled corticosteroid (ICS), a long-acting beta-2 agonist (LABA), and a long-acting muscarinic agonist (LAMA).

1.2 Listing was requested on the basis of a cost-effectiveness analysis versus triple inhaled therapy (LABA + LAMA + ICS) alone. The components of the overall clinical claim addressed by the submission are summarised in Table 1.

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

Component	Description
Population	Patients with uncontrolled COPD[a] with type 2 inflammation (defined by the submission as blood eosinophil count ≥ 300 cells/µL) despite treatment with triple therapy.
Intervention	Dupilumab 300 mg administered subcutaneously Q2W as an add-on to triple therapy (LAMA + LABA + ICS)
Comparator	Triple inhaled therapy alone (LAMA + LABA + ICS)
Outcomes	Primary: Annualised rate of moderate to severe acute exacerbations of COPD (AECOPD) Key secondary: • Time to first moderate/severe AECOPD • Change in pre-bronchodilator FEV_1 from baseline to Week 12 and Week 52 • Change in St George Respiratory Questionnaire (SGRQ) total score from baseline to Week 52 • Proportion of patients with improvement ≥ 4 points of SGRQ total score at Week 52 • Change in E-RS: COPD total score from baseline to Week 52 • Safety
Clinical claim	Dupilumab 300 mg Q2W + triple therapy consisting of ICS + LABA + LAMA is superior in terms of efficacy and non-inferior in terms of safety compared to triple therapy (LAMA+LABA+ICS) alone, for the treatment of uncontrolled COPD with type 2 inflammation.

Source: Table 1.1 p2 of the submission.
AECOPD = acute exacerbations of COPD; COPD = chronic obstructive pulmonary disease; E-RS: COPD = Evaluating Respiratory Symptoms (E-RS) in COPD; FEV_1 = forced expiratory volume in one second; ICS = inhaled corticosteroid; LABA = long-acting beta-2 agonist; LAMA = long-acting muscarinic antagonist; Q2W = every 2 weeks; SGRQ = St George Respiratory Questionnaire.
[a] Uncontrolled COPD defined in terms of patients with moderate to severe air flow obstruction (post-bronchodilator FEV_1 <80%) and who have experienced ≥ 2 moderate (an exacerbation that requires systemic corticosteroids and/or antibiotics to treat, with one of the two requiring systemic corticosteroids) or ≥ 1 severe exacerbation (an exacerbation requiring hospitalisation).

2 Background

Registration status

2.1 Dupilumab was approved by the TGA on 26 February 2025 for the following indication: "Dupilumab is indicated in adults as add-on maintenance treatment for uncontrolled COPD characterised by raised blood eosinophils on a stable combination of ICS, a LABA, and a LAMA, or on a combination of a LABA and a LAMA if ICS is not appropriate." The TGA indication does not specify a cut-off for blood eosinophil level.

2.2 Dupilumab is also indicated for other type 2 inflammatory diseases including:

- moderate to severe atopic dermatitis in patients aged 12 years and older who are candidates for chronic systemic therapy;
- severe atopic dermatitis in patients aged 6 months to 11 years old who are candidates for chronic systemic therapy;
- moderate-to-severe prurigo nodularis in adult patients who are candidates for chronic systemic therapy;
- as add-on maintenance treatment for inadequately controlled chronic rhinosinusitis with nasal polyposis in adult patients; and
- as an add-on maintenance treatment in patients aged 6 years and older with moderate to severe asthma with type 2 inflammation (elevated eosinophils or elevated fractional exhaled nitric oxide (FeNO)) that is inadequately controlled despite therapy with other medicinal products for maintenance treatment.

Previous PBAC consideration

2.3 The PBAC has not previously considered dupilumab for the treatment of uncontrolled COPD. Dupilumab is currently PBS listed for chronic severe atopic dermatitis in patients aged 12 years and older, and uncontrolled severe asthma in patients aged 6 years and older.

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

3 Requested listing

MEDICINAL PRODUCT medicinal product pack	Dispensed Price for Max. Qty	Max. qty packs	Max. qty units	№.of Rpts	Available brands
DUPILUMAB					
Dupilumab 300 mg/2 mL injection, 1 x 2 mL syringe Dupilumab 300 mg/2 mL injection, 1 x 2 mL pen	$1,755.99 (published) $[redacted] (effective)	1	2	13	Dupixent

Source: Table 1.4-1 p26 of the submission
Qty = quantity; rpts = repeats.

Restriction Summary: Authority Required (telephone)
Indication: Uncontrolled chronic obstructive pulmonary disease
Treatment Phase: Initial
Clinical criteria:
Patient must have a diagnosis of chronic obstructive pulmonary disease documented in the patient's medical records and confirmed by a respiratory physician or general physician experienced in the treatment of chronic obstructive pulmonary disease, defined by: • post-bronchodilator FEV_1/FVC ratio < 0.70 and • post-bronchodilator FEV_1% predicted < 80%
AND
Patient must have a blood eosinophil count of at least 300 cells per microlitre in the last 12 months
AND
Patients must have significant symptoms despite at least 3 months of stable bronchodilator therapy on a combination of long-acting muscarinic antagonist (LAMA), a long-acting beta-2 agonist (LABA) and an inhaled corticosteroid (ICS)
AND

Patient must have experienced, in the previous 12 months:
• at least one severe COPD exacerbation which required hospitalisation AND/OR
• two or more moderate exacerbations, of which at least;
  ○ one required treatment with systemic corticosteroids and
  ○ one required treatment with systemic corticosteroids or antibiotics

AND
The treatment must be in combination with a LAMA, LABA and ICS
AND
The treatment must be the sole PBS-subsidised biological medicine for this indication
Treatment criteria:
Patient must be treated by a medical practitioner who is a respiratory physician or a general physician experienced in the management of patients with chronic obstructive pulmonary disease
Prescribing Instructions: The following must be provided in the PBS authority application and documented in the patient's medical records: (a) details of therapy with a combination of LAMA, LABA and ICS (treatment, date of commencement, duration of therapy); and (b) in the last 12 months, please document (where applicable): (i) no. of moderate exacerbations requiring treatment with systemic corticosteroids (ii) no. of moderate exacerbations requiring treatment with antibiotics (ii) no. of severe exacerbation/s which required hospitalisation experienced while on stable treatment with LAMA, LABA and ICS (c) the eosinophil count and date in the last 12 months. The details of the number of moderate and/or exacerbations are to inform the basis of determining if an adequate response to treatment has been achieved under the continuing treatment restriction. In addition to stating them in this authority application, document them in the patient's medical records.

Source: Table 1.4-4 pp29-30 of the submission.
COPD = chronic obstructive pulmonary disease; FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; ICS = inhaled corticosteroid; LABA = long-acting beta-2 agonist; LAMA = long-acting muscarinic antagonist; PBS = Pharmaceutical Benefits Scheme; qty = quantity; rpts = repeats.

Restriction Summary: Authority Required (telephone)
Indication: Uncontrolled chronic obstructive pulmonary disease
Treatment Phase: Continuing
Clinical criteria:
Patient must have received PBS-subsidised treatment with this biological medicine for the treatment of uncontrolled chronic obstructive pulmonary disease
AND
Patient must have achieved an adequate response after 52 weeks of treatment
AND
Patient must not receive more than 56 weeks of treatment under this restriction
AND
Patient must have maintained an adequate response to their most recent course of PBS-subsidised treatment
AND
The treatment must be in combination with a LAMA, LABA and ICS
AND
The treatment must be the sole PBS-subsidised biological medicine for this PBS indication
AND
Treatment criteria:
Patient must be treated by a medical practitioner who is a respiratory physician or a general physician experienced in the management of patients with chronic obstructive pulmonary disease
Prescribing Instructions: For the purposes of this restriction, an adequate response to treatment is defined as a maintenance (i.e. no increase) or a reduction in the number of moderate and/or severe exacerbation/s measured at 52 weeks compared to the previous 12 months. All applications for continuing treatment with this biological medicine must include a measurement of response prior to the course of therapy. The following must be provided in the PBS authority application and be documented in the patient's medical records: (a) documented evidence that patient has achieved a maintenance (i.e. no increase) or a reduction in the no. of moderate or severe exacerbation/s measured at 52 weeks of treatment compared to baseline. (b) While patient was dupilumab treatment in the last 12 months, please document (where applicable): (i) no. of moderate exacerbations requiring treatment with systemic corticosteroids (ii) no. of moderate exacerbations requiring treatment with antibiotics (ii) no. of severe exacerbation/s which required hospitalisation The details of the number of moderate and/or exacerbations are to inform the basis of determining if an adequate response to treatment has been achieved under subsequent continuing restriction. In addition to stating them in this authority application, document them in the patient's medical records.

Source: Table 1.4-6 pp32-33 of the submission.

COPD = chronic obstructive pulmonary disease; FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; ICS = inhaled corticosteroid; LABA = long-acting beta-2 agonist; LAMA = long-acting muscarinic antagonist; PBS = Pharmaceutical Benefits Scheme; qty = quantity; rpts = repeats.

3.1 The submission requested a special pricing arrangement (SPA). The requested published ex-manufacturer price (EMP) is $1,609.86 per 300 mg pack of 2 and the requested effective EMP is $[redacted] per 300 mg pack of 2.

3.2 The submission requested a Section 85 - General Schedule listing. This is consistent with the current PBS-listed dupilumab for the treatment of chronic severe atopic dermatitis. However, its listing for the treatment of uncontrolled severe asthma is under Section 100 Highly Specialised Drugs (HSD) Program. In addition, the submission

requested an Authority Required (telephone/online PBS Authorities system) listing for initial and continuing treatment. This is consistent with the PBS-listed dupilumab for the treatment of chronic severe atopic dermatitis. However, the initial and continuing treatment phases for uncontrolled severe asthma are listed as Authority Required (Written) listings. The PBAC considered that a Section 100, HSD Program Authority Required (Written) listing was appropriate for both the Initial and Grandfathering treatment phases. The PBAC considered that a Section 100, HSD Program Authority Required (Telephone/Online) listing was appropriate for the continuing treatment phase.

3.3 The proposed initial restriction requires patients to have had a BEC ≥ 300 cells/µL in the previous 12 months. High blood eosinophil counts can be caused by a number of factors including allergic reactions, infections and certain medicines. In the BOREAS and NOTUS trials, all patients were required to report a BEC ≥ 300 cells/µL at screening. At baseline,60.6% of patients (pooled across trials) had an eosinophil count above the threshold. The time between the screening period to randomisation (i.e., baseline) was 4 ± 1 weeks. The Advisory Committee on Medicines (ACM) noted that over time, the patients most likely to have exacerbations will have BEC > 300 cells/µL and that the commencement of treatment when the eosinophil count is below 300 cells/µL was untested and could provide little benefit to balance the risks of injection (dupilumab, ACM minutes, December 2024 ACM meeting). A post hoc analysis of BOREAS (Christenson et al. 2025) found that the efficacy of dupilumab in the reduction of exacerbations was consistent in all patients (baseline BEC < 300 or ≥ 300 cells/µL), but that the treatment effect was bigger in those who demonstrated an BEC ≥ 300 cells/µL (noting that the trial was not powered to detect these differences). A time frame of up to 12 months between a high eosinophil count and treatment initiation may lead to many patients initiating treatment with a BEC < 300 cells/µL, this may result in a lower observed treatment effect in clinical practice compared to that seen in the clinical trials. The evaluation considered that a shorter time frame, more aligned with the clinical trials, may be considered more clinically appropriate. The ACM considered that eosinophil count should be assessed within 3 months prior to initiation of dupilumab (ACM minutes, December 2024 ACM meeting). The Sub-Committees considered that a 12 month time frame may be considered reasonable and allow for timely access to treatment. The Sub-Committees noted that a 12 month time frame would be consistent with current PBS restrictions for biologic medicines for the treatment of asthma. The PBAC agreed with the Sub-Committees that a 12 month time frame would be reasonable.

3.4 The proposed clinical criteria specifies that patients must have had at least one severe and/or two or more moderate exacerbations in the previous 12 months and separately requires patients to have 'significant symptoms' despite having used triple therapy (LABA + LAMA + ICS) for at least 3 months. This is not in line with the inclusion criteria for the BOREAS and NOTUS trials which specified that at least one exacerbation must have occurred while the patient was taking LABA + LAMA + ICS (or LAMA + LABA if ICS is contradicted). Therefore, some patients would be eligible for

dupilumab even though their exacerbations occurred prior to commencing LABA + LAMA + ICS treatment. The Pre-Sub-Committee Response (PSCR) indicated the sponsor was amenable to the Secretariat's proposed inclusion of a prescribing instruction clarifying that 'at least one of the moderate or severe exacerbations should have occurred while the patient was taking all of (i) LAMA, (ii) LABA, (iii) ICS'.

3.5 In the BOREAS and NOTUS trials patients were required to have been on background triple therapy for 3 months prior to randomisation with a stable dose of medication for at least 1 month prior to the first visit. Double therapy with LABA + LAMA was allowed if ICS was contraindicated. A total of 2.1% of patients in BOREAS and 1.1% of patients in NOTUS were using LABA + LAMA (no ICS) at baseline. The proposed PBS restriction is narrower than the use in the clinical trials and the approved TGA indication as it requires patients to be taking a LABA, LAMA and an ICS. The PBAC considered that intolerance or safety concerns associated with ICS were infrequent and mostly seen in patients with supratherapeutic doses of ICS. The PBAC considered that since the triple inhaler therapy should be 'optimised' without further specification of ICS dose, it was appropriate for the restriction to require patients to be taking a LABA, LAMA and an ICS. The PBAC considered that this would help reduce the risk of dupilumab being used earlier in the treatment algorithm than intended.

3.6 Patients with severe COPD (percent predicted forced expiratory volume in 1 second (ppFEV1) ≤ 30%) were excluded from the BOREAS and NOTUS trials. The proposed PBS listing does not require the use of FEV1 to grade COPD severity prior to commencing treatment (the proposed PBS listing only requires spirometry to record a diagnosis of COPD). When considering fluticasone furoate with umeclidinium and vilanterol for COPD, the PBAC advised that the (proposed) FEV1 requirement in the initial restriction be replaced with specification of exacerbation severity and a 12 month time period for the exacerbation history, to ensure consistency with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines. It was noted that FEV1 lacks precision to be used clinically as a predictor of exacerbations or mortality in patients with COPD and noted that history of previous exacerbations is regarded as the best predictor of future COPD episodes (para 7.3, fluticasone furoate with umeclidinium and vilanterol Public Summary Document [PSD], March 2019 PBAC meeting). Excluding the FEV1 threshold is consistent with the current PBS listings for LABA + LAMA, ICS + LABA, or LABA + LAMA + ICS fixed dose combination (FDC) products for COPD. The evaluation also considered that the proportion of the eligible PBS population with ppFEV1 < 30% is likely to be small.

3.7 The submission proposed that patients must have achieved (and maintained) an adequate response after 52 weeks of treatment to continue dupilumab. An adequate response to treatment was defined as a 'maintenance (i.e., no increase) or a reduction in the number of moderate and/or severe exacerbation/s measured at 52 weeks compared to the previous 12 months'. The primary outcome in the pivotal trials was the annualised rate of acute exacerbations of COPD (AECOPD) in the dupilumab versus placebo arms, the results did not directly assess whether these events reflected a decreased rate for individual patients. The submission did not address whether

maintaining prior exacerbation rates (as per the proposed continuing PBS criterion) is an acceptable outcome or whether it was statistically significantly improved with the addition of dupilumab. The PSCR argued that COPD is a progressive disease characterised by a decline in lung function and the number of exacerbations a patient has had in the prior year is the strongest predictor of a patient's future exacerbation frequency. On this basis, the PSCR argued that stabilisation of disease is a good outcome for patients with Type 2 inflammation who continue to exacerbate despite treatment with triple inhaled therapy.

3.8 On the basis of the clinical data from BOREAS and NOTUS, the submission did not include an interim response criterion at Week 24 based on pre-bronchodilator (pre-BD) FEV_1 improvement ≥ 0.1 L) and/or the St George Respiratory Questionnaire (SGRQ) (≥ 0 point) as some patients who met the Week 52 maintenance or reduction of exacerbation response criterion, would fail to meet the Week 24 interim response criteria. The submission did not consider whether an interim response criterion based on maintenance or reduction of exacerbation at an earlier timepoint might be appropriate. The PSCR noted that given exacerbation rates are seasonal (generally higher during the cooler months and lower in warmer months) a 12 month period is required to capture all seasons and avoid under- or over-estimating a drug's effect due to seasonal peaks or troughs in exacerbation rates. The Sub-Committees considered that an interim clause or treatment phase requiring patients to have achieved an adequate response after at least 24 weeks of dupilumab treatment may be appropriate. Noting the PSCR argument that stabilisation of disease is a good outcome for patients with this condition, the Sub-Committees considered that an adequate response may include patients having no change or a reduction in the number of total exacerbations (moderate + severe) and no change or a reduction in the severity of the exacerbations. The pre-PBAC response maintained that a 12 month period was appropriate for the assessment of a treatment response. The pre-PBAC response presented an ad-hoc analysis of the pooled BOREAS and NOTUS data where the annualised number of exacerbations at Week 24 and Week 52 was compared to baseline. Non-response was defined as an increase in the number of exacerbations. Of the 830 patients from the BOREAS and NOTUS trials included in the analysis, 30 patients (3.6%) who were a non-responder at Week 24 were also a non-responder at Week 52 and 14 patients (1.7%) who were a non-responder at Week 24 were classified as a responder at Week 52. The PBAC considered that, given the small number of patients who were non-responders at Week 24 and then subsequently classified as responders at Week 52, the application of an interim clause requiring patients to have achieved an adequate response after at least 24 weeks of treatment was appropriate. The PBAC noted that in its recommended listing patients who had not achieved a response to treatment would be able to re-trial treatment after a 12-month break.

3.9 The submission stated that approximately 500 to < 5,000patients were likely to access treatment prior to the possible PBS listing of dupilumab. The submission requested a grandfathering restriction for a total of 12 months, requiring patients to have met the baseline eligibility criteria for initiating treatment with dupilumab.

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

4 Population and disease

4.1 COPD is a heterogeneous lung condition characterised by chronic respiratory symptoms (dyspnoea, cough, sputum production and/or exacerbation) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction.[1] It can interrupt daily activities, sleep patterns and the ability to exercise. COPD exacerbations have a major impact on mortality, quality of life (QoL) and mental health.

4.2 There are multiple different cell-types in the airways and lung parenchyma that contribute to inflammation in COPD. COPD was originally believed to be driven solely by type 1 immune responses, which includes neutrophil infiltration. However, 20–40% of patients with COPD exhibit type 2 inflammation which involves eosinophil filtration. In type 2 inflammation epithelial cells lining the airways are activated by toxins which results in the secretion of interleukin (IL)-4, IL-5 and IL-13. IL-4 and IL-13 promote the activation and trafficking of type 2 inflammatory cells, including eosinophils, to the lungs. While concordance between blood and airway type 2 biomarkers is variable, elevated eosinophil counts in COPD patients is associated with increased levels of lung eosinophils and higher levels of type 2 inflammation in the airways.

4.3 Dupilumab is a biologic medication classified as a monoclonal antibody. It works by blocking IL-4 and IL-13 signalling. The submission proposed that dupilumab be considered for patients with uncontrolled COPD (≥ 2 moderate or 1 severe exacerbation) and type 2 inflammation (BEC ≥ 300 cells/µL) as add-on treatment to LABA + LAMA + ICS. This is in line with the GOLD 2026 Report[2]. The proposed place in therapy for dupilumab was reasonable.

4.4 Dupilumab is administered via subcutaneous injection, either self-injected by the patient or administered by the patient's caregiver after guidance has been provided by a healthcare provider on proper subcutaneous injection technique. Not all patients will be able to self-administer, or have a Carer, and will therefore require administration by a healthcare professional.

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

5 Comparator

5.1 The submission estimated approximately [redacted]% of patients with COPD who use triple inhaled therapy (LABA + LAMA + ICS) continue to experience exacerbations and uncontrolled symptoms. There are currently no PBS subsidised pharmacological

[1] Global Initiative for Chronic Obstructive Lung Disease (GOLD), Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease, 2026 Report.
[2] Global Initiative for Chronic Obstructive Lung Disease (GOLD), Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease, 2026 Report.

maintenance treatments available for these patients. The Sub-Committees agreed with the evaluation that the choice of triple inhaled therapy alone as the comparator in the submission was appropriate.

5.2 The submission did not nominate a near market comparator. The evaluators noted that an application for the PBS listing of mepolizumab for the same patient population is scheduled for consideration at the March 2026 PBAC Meeting, and considered this may be a near market comparator. At the time of the evaluation, 2 indirect treatment comparisons (ITCs) of dupilumab versus mepolizumab were available (see paragraph 6.26).

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 noted that in COPD, exacerbations accelerate the decline in lung function. By reducing the frequency of exacerbations, dupilumab is expected to slow that decline and over time and hence the difference in clinical effect should get larger, particularly given the elevated mortality risk associated with exacerbations. The clinician noted that for this reason, limiting the time horizon to 10 years in the economic model may limit the benefits, that are likely to occur, from being captured. The clinician acknowledged the co-existence of asthma and COPD in some patients but expected the overlap to be small. The clinician also considered that a response to treatment should be assessed after 12 months, suggesting that shorter treatment intervals may not provide a reliable indication of a response due to seasonal variation in exacerbations.

6.2 The sponsor noted the primary concerns raised by the Sub-Committees related to the economic model and outlined an international HTA body's perspective on these issues.

Consumer inputs

6.3 The PBAC noted and welcomed input from individuals (7), health care professionals (2) and organisations (3) via the Office of Health Technology Assessment Consultation Hub. Comments from individuals who would like access to dupilumab described the significant impact that COPD had on their quality of life, noting that their ability to work and socialise had been severely affected, leading to increased isolation and a decline in their mental health. Health care professionals noted an unmet clinical need for this population, describing COPD as debilitating and significantly impacting quality of life. Health care professionals noted the lack of effective treatment options for patients who continue to exacerbate despite triple inhaled therapy resulting in the use of oral corticosteroids which can be associated with debilitating or intolerable side effects. Comments from health care professionals also described the benefits of dupilumab in terms of improving outcomes and quality of life for patients with COPD

with a reduction in exacerbations and hospital admissions and improvement to overall lung function.

6.4 Comments from Lung Foundation Australia, the Pharmaceutical Society of Australia and the Centres of Excellence in Treatable Traits and Severe Asthma expressed support for the proposed PBS listing of dupilumab. In addition to the comments noted above, input from Lung Foundation Australia noted that biologic medications have the potential to reduce reliance on oral corticosteroids, which are associated with significant morbidity and downstream health care costs. The Pharmaceutical Society of Australia noted that mepolizumab was being considered at the March 2026 PBAC meeting and highlighted that standardisation of terminology or wording in the PBS listing criteria would be helpful to ensure consistency for prescribers.

Clinical trials

6.5 The submission was based on 2 randomised, double-blind, placebo-controlled, 52-week trials (plus a 12-week safety post-intervention period) comparing dupilumab + triple inhaled therapy to placebo + triple inhaled therapy in patients with uncontrolled COPD and type 2 inflammation, BOREAS (n=939) and NOTUS (n=935). NOTUS ended early because of the positive results from an interim analysis. NOTUS enrolled all intended participants, with 77% of the 935 patients randomised completing the 52-week study intervention period.

6.6 Uncontrolled COPD was defined in the trials as a history of ≥ 2 moderate or ≥ 1 severe exacerbation within the year prior to inclusion (with at least one of these exacerbations occurring while using triple inhaled therapy), and Medical Research Council (MRC) dyspnoea scale ≥ 2. A moderate exacerbation was defined as an event that required treatment with systemic corticosteroids and/or antibiotics. The inclusion criteria for both trials stated that 1 of the 2 moderate exacerbations had to require the use of systemic corticosteroids. Severe exacerbations were defined as an event requiring hospitalisation or observation > 24 hours in emergency department/urgent care facility.

6.7 Type 2 inflammation was defined as a BEC ≥ 300 cells/µL. BOREAS and NOTUS trials required evidence of type 2 inflammation at screening. At baseline 61.0% of patients in BOREAS and 60.2% of patients in NOTUS reported a BEC ≥ 300 cells/µL. The proportion of patients who did not have a BEC ≥ 300 cells/µL at baseline was balanced between the two arms of each trial.

6.8 The World Health Organisation declared COVID-19 a worldwide pandemic on 11 March 2020 and an end to the pandemic phase on 5 May 2023. BOREAS began recruitment in May 2019, and the last patient end-of-treatment visit was completed on 8 February 2023. NOTUS began recruitment in July 2020 with the interim analysis cut-off in September 2023. All patients in BOREAS and NOTUS would have had at least a portion of their 52-week study period during the pandemic. The submission stated that COVID-19 pandemic affected the conduct of the trials, and it is likely that enhanced public health initiatives resulted in fewer exacerbations overall. A

systematic review and meta-analysis suggest that there was a 50% reduction in hospital admissions for COPD exacerbations during the COVID-19 pandemic period compared to pre-pandemic times.[3] The evaluation considered it was unclear the extent to which the conduct of the trials during the pandemic may have affected the observed relative benefits of treatment with dupilumab compared to placebo. The PSCR stated that most patients from the BOREAS and NOTUS trials (97.6%) did not have COVID-19 related disruptions in their trial procedure and considered it unlikely the pandemic had a different impact on dupilumab vs placebo. The Sub-Committees noted that while it may be unlikely the pandemic had a different impact on dupilumab vs placebo, it remained an uncertainty.

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

[3] Alqahtani, J.S. *et al.* (2021) 'Reduction in hospitalised COPD exacerbations during COVID-19: A systematic review and meta-analysis', *PLOS ONE*, 16(8). doi:10.1371/journal.pone.0255659.

Table 2: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
Study EFC15804 BOREAS	A randomised, double-blind, placebo-controlled, parallel-group, 52-week pivotal study to assess the efficacy, safety, and tolerability of dupilumab in patients with moderate-to severe chronic obstructive pulmonary disease (COPD) with type 2 inflammation (BOREAS).	Clinical Study Protocol amendment 8 (BOREAS). Approved 29 September 2020. Clinical Study Report. Data cut-off 7 March 2023.
	Bhatt 2023. Dupilumab for COPD with Type 2 Inflammation Indicated by Eosinophil Counts.	N Engl J Med; 389:205-214. doi: 10.1056/NEJMoa2303951
	Bhatt 2025a. Dupilumab reduces exacerbations and improves lung function in patients with chronic obstructive pulmonary disease and emphysema: Phase 3 randomized trial (BOREAS).	Respir Med; 236(107846). doi: 10.1016/j.rmed.2024.107846
	Christenson 2025. Type 2 inflammation biomarkers and their association with response to dupilumab in COPD (BOREAS): an analysis of a randomised, placebo-controlled, phase 3 trial.	Lancet Respir Med; 13(8): 687-697. doi: 10.1016/S2213-2600(25)00044-X.
	Vogelmeier 2025. Dupilumab reduces acute exacerbations and improves lung function in patients with COPD with type 2 inflammation irrespective of body mass index, airflow obstruction, dyspnea, and exercise capacity index scores.	Respir Med; 241(108015). doi: 10.1016/j.rmed.2025.108015
NCT03930732	Pivotal Study to Assess the Efficacy, Safety and Tolerability of Dupilumab in Patients with Moderate-to-severe COPD With Type 2 Inflammation (BOREAS).	
Study EFC15805 NOTUS	A randomised, double-blind, placebo-controlled, parallel-group, 52-week pivotal study to assess the efficacy, safety, and tolerability of dupilumab in patients with moderate-to severe chronic obstructive pulmonary disease (COPD) with type 2 inflammation (NOTUS).	Clinical Study Protocol amendment 3 (NOTUS). Approved 6 December 2019.Clinical Study Report. Data cut-off 14 December 2023.
	Bhatt 2024. Dupilumab for COPD with Blood Eosinophil Evidence of Type 2 Inflammation.	N Engl J Med; 390:2274-2283. doi: 10.1056/NEJMoa2401304
NCT04456673	Pivotal Study to Assess the Efficacy, Safety and Tolerability of Dupilumab in Patients with Moderate to Severe COPD With Type 2 Inflammation (NOTUS).	
Study EFC15804 and Study EFC15805 pooled results	Sanofi and Regneron. 2.5 Clinical Overview (Chronic Obstructive Pulmonary Disease).	Clinical Overview. 19 December 2023.
	Sanofi and Regeneron. 2.7.3 Summary of Clinical Efficacy (Chronic Obstructive Pulmonary Disease).	Summary of Clinical Efficacy. 18 December 2023.
	Sanofi and Regeneron. 2.7.4 Summary of Clinical Safety (Chronic Obstructive Pulmonary Disease). 19 December 2023.	Summary of Clinical Safety. 19 December 2023.
	Bhatt 2025b. Effect of Dupilumab on Health-Related Quality of Life and Respiratory Symptoms in Patients with COPD and Type 2 Inflammation.	Chest; 168(1):56-66. doi: 10.1016/j.chest.2025.01.029
	Bhatt 2025c. Dupilumab for chronic obstructive pulmonary disease with type 2 inflammation: a pooled analysis of two phase 3, randomised, double-blind, placebo-controlled trials.	Lancet Respir Med;13(3):234-243. doi: 10.1016/S2213-2600(24)00409-0

Source: Table 2.2-1 pp37-38 of the submission.

6.10 The key features of the randomised controlled trials (RCTs) are summarised in Table 3.

Table 3: Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population	Outcomes	Use in modelled evaluation
Dupilumab 300mg Q2W vs placebo						
BOREAS	ITT Dupilumab, n=468 Placebo, n=471	R, DB 52 weeks	Low	Adults using triple inhaled therapy for at least 3 months (or LABA + LAMA if ICS was contraindicated), with uncontrolled COPD with type 2 inflammation (BEC ≥ 300 cells/µL at screening).	Primary: Annualised rate of moderate to severe AECOPD Secondary: - time to first moderate or severe AECOPD - change from baseline in pre-BD FEV_1 at Week 12 - change from baseline in the SGRQ total score at Week 52 - proportion of patients with SGRQ total score improvement ≥ 4 points at Week 52 - change from baseline in the ER-S COPD total score at Week 52	Trial AECOPD used for the dupilumab arm.
NOTUS	ITT Dupilumab, n=470 Placebo, n=465	R, DB 52 weeks[b]				
	ITT52[a] Dupilumab, n=362 Placebo, n=359					

Source: Table 2.5-1 p71; Table 2.5-2 pp71-72 of the submission.

AECOPD = acute exacerbation(s) of COPD; COPD = chronic obstructive pulmonary disease; DB = double blind; BEC = blood eosinophil count; E-RS: COPD = Evaluating Respiratory Symptoms in COPD; FEV_1 = forced expiratory volume in one second; ICS = inhaled corticosteroid; ITT = intention to treat; LABA = long-acting beta-2 agonist; LAMA = long-acting muscarinic antagonist; MMRM = mixed-effect model with repeated measures; MRC = Medical Research Council; pre-BD = pre-bronchodilator; Q2W = every 2 weeks; R = randomised; SGRQ = St George Respiratory Questionnaire.

[a] The Opportunity to reach Week 52 population included patients who completed the 52-week study intervention period or would have completed had they not discontinued.

[b] Not all patients reached Week 52 as the trial was terminated early.

6.11 Overall, the risk of bias in the studies was considered low across the domains of selection bias, performance bias, detection bias, attrition bias and reporting bias, as they were randomised, double-blinded studies with independent committees that evaluated the safety and efficacy data, and adjudicated safety events. As the NOTUS trial ended early, not all patients completed the 52-week study period. Due to the high proportion of patients who did complete the 52-week study intervention period (721, 77%), the power of the study to detect a significant change in the primary outcome was not changed.

6.12 The submission did not nominate a minimal clinically important difference (MCID) for the primary outcome. There is no validated MCID for exacerbations in COPD. The PBAC has previously considered an MCID of 9% to 54% for annual rates of all grades of exacerbations, but considered that the baseline rate, exacerbation severity and study duration were required for interpretation of the MCID (para 6.10, fluticasone furoate with umeclidinium and vilanterol PSD, March 2019 PBAC meeting). The submission did not nominate an MCID for the key secondary endpoint of change from baseline in pre-BD FEV_1. While the PBAC has previously considered MCIDs for trough FEV_1 or $ppFEV_1$, it has not previously considered an MCID for pre-BD FEV_1.

6.13 The submission nominated an MCID of a change of 4 unit difference compared to placebo in the SGRQ total score at week 52 based on Jones (2005). The PBAC has previously considered this MCID (para 6.23, beclometasone with formoterol and glycopyrronium PSD, Nov 2020 PBAC meeting). An MCID of 4 has been widely used in clinical practice. However, recent evidence suggests the MCID should be higher (approximately 7 unit change).[4]

6.14 In the BOREAS trial, the intention to treat (ITT) population was the basis of analysis for the primary and secondary endpoints. At the time of the data cut-off (8 February 2023) all patients had completed their 52-week visit.

6.15 In the NOTUS trial, two populations were used in the analysis. The data cut-off was 29 September 2023. At this date,

- ITT population: included all randomised patients who completed follow-up for the key secondary endpoint of change from baseline in FEV_1 at Week 12. At the time when the last patient had completed their Week 12 visit, 70.9% of all patients had completed the 52-week study intervention period, 9.0% had discontinued and 20.0% were still ongoing. This population was the basis of analysis for the primary efficacy endpoint and key secondary endpoints of time to first moderate/severe AECOPD, and change in pre-BD FEV_1 at Week 12.
- ITT with opportunity to reach Week 52 population: included patients who completed the 52-week intervention period or would have had the opportunity to complete 52 weeks (based on their time since their study enrolment) had they not discontinued. This was the basis of analysis for the patient reported secondary endpoints.

Overall, the assessment of the results following the interim analysis of the NOTUS trial was considered appropriate by the evaluation and unlikely to have introduced bias due to the early stopping of the trial. The submission also presented the pooled ITT efficacy and safety analysis. The submission justified this approach as the studies have very similar designs.

6.16 Baseline characteristics were generally balanced between the two arms in each trial. However, while the mean number of moderate or severe COPD exacerbations experienced within the year prior to visit 1 were consistent at baseline (2.3 events in BOREAS vs 2.1 in NOTUS), differences were evident in the proportion of patients who had experienced ≥ 3 exacerbations over that period. The total proportion of patients who had experienced 3 exacerbations within the year prior to visit 1 was higher in BOREAS versus NOTUS (15.7% versus 11.4%). This proportion was lower in the dupilumab arm versus placebo arm in BOREAS (12.1% versus 19.1%) but not in NOTUS (12.1% versus 10.8%). The proportion of patients in the placebo arm of BOREAS who reported 3 exacerbations was higher than that reported in the placebo arm of NOTUS.

[4] Alma, H. et al. (2018) 'Clinically relevant differences in COPD health status: Systematic review and triangulation', European Respiratory Journal, 52(3), p. 1800412. doi:10.1183/13993003.00412-2018.

The total proportion of patients who had ≥ 4 exacerbations was also higher in BOREAS versus NOTUS (7.7% versus 4.8%). The evaluation noted that patients in BOREAS may have had more severe COPD as measured by exacerbation history and considered that it was not clear whether the approach to pooling taken by the submission was appropriate. The PSCR acknowledged there is a small difference in the baseline exacerbation profile across the studies but noted that exacerbation history is not the only factor which determines COPD severity. The PSCR argued that lung function impairment, as measured by the level of airflow obstruction (FEV_1) was also important and noted that it was consistent across both BOREAS and NOTUS. The PSCR also noted that the pooled results from BOREAS and NOTUS were part of a pre-specified protocol to increase the statistical power. The Sub-Committees agreed with the PSCR that the pooled analyses were likely to be the most robust and appropriate data that was available for determining the clinical and cost-effectiveness of dupilumab.

Comparative effectiveness

Primary endpoint: moderate to severe AECOPD

6.17 Overall, dupilumab led to a statistically significant reduction in the annualised rate of moderate or severe AECOPD compared to placebo (Table 4). The Sub-Committees noted the results show a greater reduction in NOTUS compared to BOREAS (risk difference: 0.44 vs. 0.32, respectively), with a pooled risk difference of 0.36.

6.18 The cumulative total number of exacerbations was lower in the dupilumab arm compared to the placebo arm in both trials, however, at the time of data cut-off, the majority of patients in the dupilumab and placebo arms (61.1% versus 55.0% in BOREAS and 66.8% versus 60.9% in NOTUS), had not experienced a moderate or severe exacerbation.

Table 4: Annualised rate of moderate/severe exacerbations (ITT)

	BOREAS (data cut-off 8 Feb 2023)		NOTUS (data cut-off 29 Sept 2023)		POOLED ITT	
	Dupilumab N=468	Placebo N=471	Dupilumab N=470	Placebo N=465	Dupilumab N=938	Placebo N=936
Number of patients with ≥ 1 moderate or severe exacerbation event, n (%)						
No	286 (61.1)	259 (55.0)	314 (66.8)	283 (60.9)	600 (64.0)	542 (57.9)
Yes	182 (38.9)	212 (45.0)	156 (33.2)	182 (39.1)	338 (36.0)	394 (42.1)
Number of moderate or severe exacerbation events						
0	286 (61.1)	259 (55.0)	314 (66.8)	283 (60.9)	600 (64.0)	542 (57.9)
1	113 (24.1)	106 (22.5)	93 (19.8)	98 (21.1)	206 (22.0)	204 (21.8)
2	47 (10.0)	55 (11.7)	36 (7.7)	41 (8.8)	83 (8.8)	96 (10.3)
3	9 (1.9)	25 (5.3)	15 (3.2)	18 (3.9)	24 (2.6)	43 (4.6)
≥ 4	13 (2.8)	26 (5.5)	12 (2.6)	25 (5.4)	25 (2.7)	51 (5.4)
Total number of moderate or severe exacerbation events	296	422	263	352	559	774
Total patient-years followed	458.2	454.8	422.5	417.3	880.7	872.1
Unadjusted annualised moderate or severe exacerbation event rate per year	0.65	0.93	0.62	0.84	0.63	0.89
Adjusted annualised moderate or severe exacerbation event rate per year[a]						
Estimate (95% CI)	0.78 (0.65, 0.93)	1.10 (0.91, 1.30)	0.86 (0.70, 1.06)	1.30 (1.05, 1.60)	0.79 (0.69, 0.92)	1.16 (1.01, 1.33)
Relative risk vs. placebo (95% CI), p-value	**0.705 (0.58, 0.86) p=0.0005**		**0.664 (0.54, 0.82) p=0.0002**		**0.687 (0.60, 0.79) p<0.0001**	
Risk difference vs. placebo (95% CI)[b]	-0.32 (-0.508, -0.140)		-0.44 (-0.682, -0.188)		-0.36 (-0.508, -0.217)	

Source: Table 2.5-3 p73 of the submission.

AECOPD = acute exacerbation(s) of chronic obstructive pulmonary disease; CI = confidence interval; ICS = inhaled corticosteroid; ITT = intention to treat; n = number of patients with event; N = total patients in group.

Bold indicates a significant result.

[a] Derived using negative binomial model with the total number of the events occurring during the 52-week treatment period as the response variable, and treatment group, study (if pooled), region (pooled country), ICS dose, smoking status at screening, baseline disease severity, and number of moderate or severe COPD exacerbation events within one year prior to the study as covariates, and log-transformed treatment duration as an offset variable.

[b] Derived using delta method.

6.19 The majority of exacerbation events were moderate in nature (see Table 5). The Sub-Committees noted that the submission stated that the COVID-19 pandemic affected the conduct of the trials, and it is likely that enhanced public health initiatives resulted in fewer exacerbations overall (paragraph 6.8). The Sub-Committees considered that it was unclear whether the pandemic had also led to the small number of severe events observed in the trials.

Table 5: Summary of occurrence of moderate or severe COPD exacerbations during the 52-week intervention period (ITT)

	BOREAS (data cut-off 8 Feb 2023)		NOTUS (data cut-off 29 Sept 2023)		Pooled ITT	
	Dupilumab (N=468)	Placebo (N=471)	Dupilumab (N=470)	Placebo (N=465)	Dupilumab (N=936)	Placebo (N=938)
Total number of moderate or severe events	296	422	263	352	559	774
Number of severe events (% of all events)	28 (9.5)	37 (8.8)	26 (9.9)	39 (11.1)	54 (9.7)	76 (9.8)
Number of moderate events (% of all events)	268 (90.6)	385 (91.2)	237 (90.1)	313 (88.9)	505 (90.3)	698 (90.2)
- Only requiring use of SCS (% of moderate events)	84 (31.3)	130 (33.8)	70 (29.5)	107 (34.2)	154 (30.5)	237 (34.0)
- Only requiring use of systemic antibiotics (% of moderate events)	52 (19.4)	68 (17.7)	40 (16.9)	56 (17.9)	92 (18.2)	124 (17.8)
- Requiring use of both SCS and systemic antibiotics (% of moderate events)	132 (49.3)	187 (48.6)	127 (53.6)	150 (47.9)	259 (51.3)	337 (48.3)

Source: Table 24 p72 BOREAS CSR; Table 23 p73 NOTUS CSR; Table 16 2.7.3 p78 Summary of Clinical Efficacy (COPD).
COPD = chronic obstructive pulmonary disease; ITT = intention to treat; n = number of patients with event; N = total patients in group; SCS = systemic corticosteroids.
Percentages are calculated using the number of events as the denominator.

6.20 Dupilumab treatment delayed the time to first moderate or severe COPD exacerbation event compared to placebo in BOREAS (hazard ratio [HR]: 0.803, 95% confidence interval [CI]: 0.658 to 0.980; p=0.0309) and NOTUS (HR: 0.714, 95% CI: 0.574 to 0.887; p=0.0024).

Change from baseline in pre-BD FEV_1 at Week 12

6.21 Dupilumab led to a statistically significant improvement in pre-BD FEV_1 at Week 12 (least squares [LS] mean difference: 0.083 litres [L], p<0.0001, Pooled; Table 6). Subgroup analyses demonstrated a greater treatment benefit for dupilumab versus placebo in patients with higher levels of eosinophils (≥ 500 cells/µL during screening), noting that the trial was not powered to assess this. While these results were statistically significant, it was not clear whether the improvements in pre-BD FEV_1 indicated a clinically meaningful improvement in overall lung function or COPD management. At Week 52, the reduction in pre-BD FEV_1 was maintained (LS mean difference: 0.073 L, p<0.0001, Pooled).

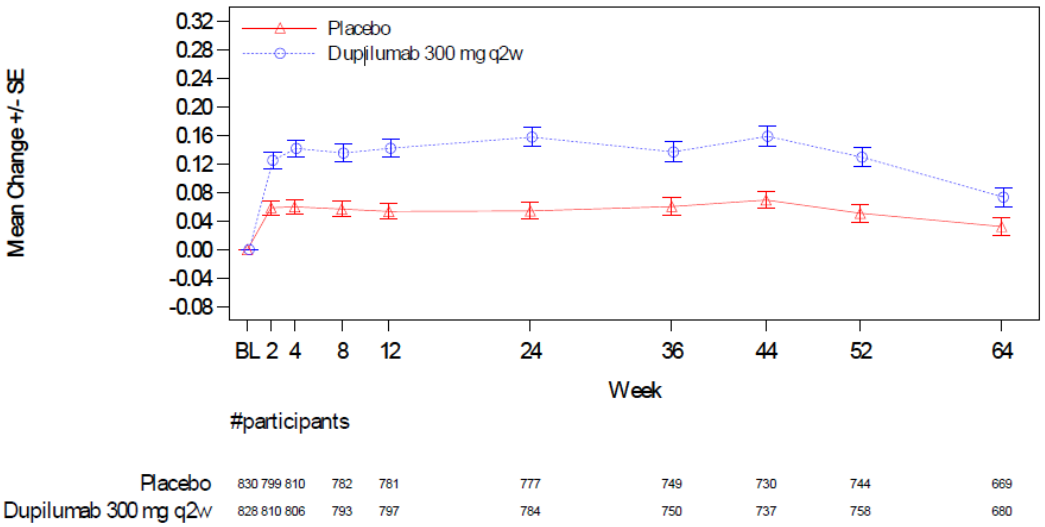
Table 6: Change from baseline in pre-bronchodilator FEV_1 (L) at Week 12 - ITT population

	BOREAS (data cut-off 8 Feb 2023)		NOTUS (data cut-off 29 Sept 2023)		ITT POOLED	
	Dupilumab N=468	Placebo N=471	Dupilumab N=470	Placebo N=465	Dupilumab N=938	Placebo N=936
Baseline pre-BD FEV_1 (L), mean (SD)	1.28 (0.45)	1.32 (0.46)	1.35 (0.49)	1.38 (0.50)	1.32 (0.47)	1.35 (0.48)
Change from baseline at Week 12						
n	449	439	449	444	898	883
Mean (SD)	0.15 (0.37)	0.06 (0.30)	0.14 (0.35)	0.05 (0.31)	0.14 (0.36)	0.05 (0.31)
LS mean (SE)[a]	0.160 (0.02)	0.077 (0.02)	0.139 (0.02)	0.057 (0.02)	0.147 (0.01)	0.064 (0.01)
LS mean difference (95% CI), p-value[a]	**0.083 (0.04, 0.13) p<0.0001**		**0.082 (0.04, 0.12) p=0.0001**		**0.083 (0.05 to 0.11) p<0.0001**	

Source: Table 2.5-5 p78 of the submission.
CI = confidence interval; ITT = intention to treat; L = litres; LS = least squares; MMRM: Mixed-effect Model with Repeated Measures; n = number of patients with event; N = total patients in group; pre-BD FEV_1 = pre-bronchodilator forced expiratory volume in 1 second; SD = standard deviation; SE = standard error.
Bold indicates a significant result.
[a] Derived from MMRM model.

6.22 The Sub-Committees noted that an improvement in pre-BD FEV_1 can be observed from Week 2 and considered that this was maintained until around week 44 with a decline evident thereafter (Figure 1).

Figure 1: Mean change from baseline in pre-BD FEV_1 (L) up to Week 64 - Pooled ITT population with an opportunity to reach Week 52



Source: Figure 40 p155, 2.7.3 Summary of clinical efficacy pooled.
BL = baseline; ITT = intention to treat; L = litre; pre-BD FEV_1 = pre bronchodilator forced expiratory volume in 1 second; q2w = every 2 weeks; SE = standard error.

QoL outcome changes

6.23 Improvements in health related QoL, as measured by the change from baseline in the SGRQ total score, were reported for both dupilumab and placebo (see Table 7). The mean improvement (a numerical reduction in SGRQ) was greater for patients in the dupilumab arm compared to the placebo arms in the BOREAS, NOTUS and pooled

results. The LS mean treatment difference between the dupilumab and placebo was significant but did not meet the submission's nominated MCID of ≥ 4 points for the SGRQ.

6.24 Of the patients who achieved a clinically meaningful change from baseline in SGRQ total score (≥ 4 point reduction), the odds ratio (OR) for the between treatment effect was significant in BOREAS (OR=1.439, p=0.0089) but not NOTUS (OR=1.164, p=0.3329), suggesting that the likelihood of meeting the MCID in NOTUS was independent of the treatment arm.

Table 7: Change from baseline in SGRQ total score at Week 52

	BOREAS (ITT) Data cut-off 8 Feb 2023		**NOTUS (ITT population with opportunity to reach Week 52) Data cut-off 29 Sept 2023**		**POOLED (ITT population with opportunity to reach Week 52)**	
	Dupilumab N=468	Placebo N=471	Dupilumab N=362	Placebo N=359	Dupilumab N=830	Placebo N=830
Baseline SGRQ mean total score (SD)	48.42 (17.04)	48.41 (17.80)	52.66 (17.03)	51.01 (16.14)	50.26 (17.16)	49.53 (17.15)
Change from baseline at Week 52						
n	415	400	317	310	732	710
Mean (SD)	-9.44 (18.30)	-6.16 (17.59)	-9.87 (18.04)	-5.86 (15.76)	-9.63 (18.18)	-6.03 (16.80)
LS mean (SE)[a]	-9.732 (0.810)	-6.369 (0.816)	-9.816 (0.920)	-6.444 (0.922)	-9.945 (0.636)	-6.579 (0.640)
LS mean difference, 95% CI p-value[a]	**-3.363 (-5.459 to -1.266) p=0.0017**		**-3.371 (-5.811 to -0.931) p=0.0068**		**-3.366 (-4.953 to -1.778) p<0.0001**	

Source: Table 2.5-8 p83 of the submission.
CI = confidence interval; ITT = intention to treat; LS = least squares; MMRM = Mixed-effect Model with Repeated Measures; n = number of patients with event; N = total patients in group; pre-BD FEV_1 = pre-bronchodilator forced expiratory volume in 1 second; SD = standard deviation; SE = standard error; SGRQ = St. George's Respiratory Questionnaire.
Bold indicates a significant result.
[a] Derived from MMRM model.

6.25 The mean Evaluating Respiratory Symptoms (E-RS): COPD Total Score improved (reduction in total score) for both treatment arms in BOREAS and NOTUS, indicating an improvement in the severity of self-reported COPD-related respiratory symptoms. The LS mean difference between the dupilumab and placebo arms was significant for BOREAS (-1.137; 95% CI -1.823, -0.450; p=0.0012) but not NOTUS (-0.618; 95% CI -1.430, 0.193; p=0.1351).

<u>Indirect treatment comparison: dupilumab versus mepolizumab</u>

6.26 The Sub-Committees noted that mepolizumab was not identified as a near market comparator in the submission. The Sub-Committees noted that the evaluators identified 2 published ITCs of dupilumab compared to mepolizumab.

- Bhatt et al. (2025) conducted a placebo-adjusted Butcher ITC using aggregate clinical trial data from BOREAS and NOTUS (dupilumab) trials, and METREX, METREO and MATINEE (mepolizumab) trials. They found that dupilumab provided a numerically favourable reduction (rate ratio 0.82; 95% CI 0.66, 1.01) in the rate of moderate-to-severe exacerbations compared with mepolizumab (not

statistically significant, METREO results not included in the primary ITC analysis). The placebo-adjusted Bucher ITC evaluating the change in pre-bronchodilator FEV_1 at week 52, the proportion of patients with SGRQ total score ≥ 4 points, and the proportion of patients with E-RS: COPD total score improvement ≥ 2 points significantly favoured dupilumab versus mepolizumab. The trials differed in their eosinophil count inclusion criteria. BOREAS and NOTUS required BEC ≥ 300 cells/µL in the year prior. METREO allowed counts ≥ 150 cells/µL at screening but ≥ 300 cells/µL in the prior year. MATINEE required BEC ≥ 300 cells/µL at screening and historical counts ≥ 150 cells/µL and METREX enrolled patients with and without elevated eosinophil counts. These variations may have influenced the trial outcomes.[5] The authors stated that a comparison of safety between dupilumab and mepolizumab was not included in the Butcher ITC because no meaningful differences in adverse events or severe adverse events were observed in the studies. The PBAC recalled that in its consideration of dupilumab for uncontrolled severe eosinophilic or allergic asthma the Committee had considered a claim of non-inferior comparative safety versus the nominated comparators (which included mepolizumab) was reasonable (paragraph 7.7, dupilumab PSD, November 2020 PBAC Meeting).

- Suter et al. (2025) conducted an indirect comparison by comparing published crude data for rate ratios or mean differences and their corresponding 95% CIs for dupilumab (BOREAS and NOTUS) and mepolizumab (MATINEE). They concluded that both treatments were effective in reducing exacerbations. When comparing crude 95% CI for the primary outcome, no difference between dupilumab and mepolizumab was apparent, although there was a numerically shorter time interval required to prevent an exacerbation in patients receiving dupilumab (2.3 years in NOTUS and 3.1 years in BOREAS, compared to 4.8 years in MATINEE).[6]

Comparative harms

6.27 A summary of the treatment emergent adverse events (TEAEs) reported in the trials is provided in Table 8.

[5] Bhatt, S.P., Freemantle, N., Soliman, M., Heble, J., Yann Cabon, Herrera, E.M., Yang, J. and Xu, Y. (2025). Dupilumab Versus Mepolizumab for COPD: Evaluating Efficacy Outcomes Using Placebo-Adjusted Indirect Treatment Comparison. Pulmonary Therapy. https://doi.org/10.1007/s41030-025-00322-1.

[6] Suter, P., Greig, R., Chan, R. and Lipworth, B. (2025). Efficacy of dupilumab and mepolizumab in eosinophilic COPD: insights from phase 3 trials. Respiratory Medicine, 248, p.108343. https://doi.org/10.1016/j.rmed.2025.108343.

Table 8: Overview of TEAEs – Safety population

	BOREAS Data cut-off 8 Feb 2023		NOTUS Data cut-off 29 Sept 2023		Pooled Safety			
	Dupilumab N=469	Placebo N=470	Dupilumab N=469	Placebo N=464	Dupilumab N=938	Placebo N=934	RR[a] (95% CI)	RD (95% CI)[a]
Patients with any TEAE	363 (77.4)	357 (76.0)	313 (66.7)	306 (65.9)	676 (72.1)	663 (71.0)	1.02 (0.96, 1.07)	0.01 (-0.03, 0.05)
Patients with any severe TEAE	48 (10.2)	55 (11.7)	60 (12.8)	62 (13.4)	108 (11.5)	117 (12.5)	0.92 (0.72, 1.17)	-0.01 (-0.04, 0.02)
Patients with any treatment emergent SAE	64 (13.6)	73 (15.5)	61 (13.0)	74 (15.9)	125 (13.3)	147 (15.7)	0.85 (0.68, 1.06)	-0.02 (-0.06, 0.01)
Patients with any TEAE leading to discontinuation[b]	14 (3.0)	16 (3.4)	18 (3.8)	12 (2.6)	32 (3.4)	28 (3.0)	1.14 (0.69, 1.87)	0.00 (-0.01, 0.02)
Patients with any treatment emergent AESI	40 (8.5)	43 (9.1)	39 (8.3)	33 (7.1)	79 (8.4)	76 (8.1)	1.04 (0.77, 1.40)	0.00 (0.77, 1.40)
Patients with any TEAE related to IMP	35 (7.5)	18 (3.8)	15 (3.2)	18 (3.9)	50 (5.3)	36 (3.9)	1.38 (0.91, 2.10)	0.02 (0.00, 0.03)
Death on study[c]	8 (1.7)	8 (1.7)	13 (2.8)	8 (1.7)	21 (2.2)	16 (1.7)	1.31 (0.69, 2.49)	0.01 (-0.01, 0.02)
Death during the TEAE period[d]	4 (0.9)	7 (1.5)	11 (2.3)	7 (1.5)	15 (1.6)	14 (1.5)	1.07 (0.52, 2.20)	0.00 (-0.01, 0.01)
Death during the post treatment period[e]	4 (0.9)	1 (0.2)	2 (0.4)	1 (0.2)	6 (0.6)	2 (0.2)	2.99 (0.60, 14.76)	0.00 (0.00, 0.01)

Source: Table 43 p123, Table 45 p127 BOREAS CSR; Table 42 p121 NOTUS CSR, Table 44 p126 NOTUS CSR; Table 2.5-11 pp97-98 of the submission.

AESI: adverse event of special interest; CI = confidence interval; CSR = clinical study report; IMP = investigational medicinal product; n = number of patients with event; N = total patients in group; RD = risk difference; RR = relative risk; SAE = serious adverse event; TEAE = treatment emergent adverse event.

[a] All measures of relative effect were estimated for the purposes of the evaluation using data noted above; these results should be considered as indicative only as the underlying studies were not powered to detect differences in safety outcomes.

[b] Permanent study intervention discontinuation

[c] Includes all deaths that occurred after the start of treatment up to end of study (defined as last protocol planned visit or the resolution/stabilisation of all treatment emergent SAE and adverse event of pre-specified monitoring).

[d] Includes all deaths that occurred after the start of treatment up to last IMP date + 98 days.

[e] Includes all deaths that occurred after the last IMP date + 98 days.

6.28 TEAEs that led to permanent study intervention discontinuation were higher in the dupilumab arm versus the placebo arm in NOTUS (3.8% versus 2.6%) and the pooled safety data (3.4% versus 3.0%), but not in BOREAS. The Sub-Committees noted that TEAEs related to the investigational medicinal product were higher in the dupilumab

arm in BOREAS (7.5% versus 3.8%) and the pooled safety data (5.3% versus 3.9%). The submission attributed this to injection site reactions, which were reported in 14 patients (3.0%) in the dupilumab arm versus 2 patients (0.4%) in placebo arm in BOREAS and 9 patients (1.9%) in dupilumab arm versus 2 patients (0.4%) in placebo arm NOTUS.

6.29 The submission reported that treatment-emergent serious adverse events (SAEs) were assessed by the Investigator as related to the investigational medicinal product (IMP) in 2 patients, both of whom were in the dupilumab arm. The most frequently reported treatment-emergent SAE by preferred-term was COPD (dupilumab: 5.3%; placebo: 6.6%, Pooled), pneumonia (dupilumab: 1.7%; placebo: 1.3%, Pooled), COVID-19 pneumonia (dupilumab: 0.9%; placebo: 0.7%, Pooled), and COVID-19 (dupilumab: 0.6%; placebo: 0.9%, Pooled).

6.30 The total number of deaths reported was numerically higher for dupilumab versus placebo in NOTUS (12 patients, 2.6% versus 7 patients, 1.5%) and the pooled safety data (21, 2.2% versus 16, 1.7%). None of the deaths reported in the trials were considered to be related to the IMP.

Benefits/harms

6.31 A summary of the comparative benefits and harms for dupilumab versus placebo is presented in Table 9.

Table 9: Summary of comparative benefits and harms for dupilumab versus placebo

Trial	Dupilumab n/N	Placebo n/N	RR (95% CI)	Event rate/patient year		RD[b] (95% CI)
				Dupilumab	Placebo	
Benefits						
Adjusted annualised rate of moderate to severe AECOPD[a]						
Pooled	338/938	394/936	0.687 (0.60 to 0.79)	0.794	1.156	-0.362 (-0.51, -0.22)

Change from baseline in SGRQ total score at Week 52							
	Dupilumab			**Placebo**			
	N	**LS mean Δ baseline SGRQ total score**	**SE**	**N**	**LS mean Δ baseline SGRQ total score**	**SE**	**Mean difference: dupilumab vs. placebo (95% CI)**
Pooled	830	-9.95	0.64	830	-6.58	0.64	-3.366 (-4.95 to -1.78)

Change from baseline in pre-BD FEV_1 at Week 12							
	Dupilumab			**Placebo**			
	N	**LS mean Δ baseline pre-BD FEV_1**	**SE**	**N**	**LS mean Δ baseline pre-BD FEV_1**	**SE**	**Mean difference: dupilumab vs. placebo (95% CI)**
Pooled	898	0.147	(0.01)	883	0.064	(0.01)	0.083 (0.05 to 0.11)

Harms						
	Dupilumab n/N	**Placebo n/N**	**RR[c] (95% CI)**	**Event rate/100 patients**		**RD[c] (95% CI)**
				Dupilumab	**Placebo**	
TEAE						
Pooled	676/938	633/934	1.02 (0.96, 1.07)	72	71	0.01 (-0.03, 0.05)
Severe TEAE						
Pooled	108/938	117/934	0.92 (0.72, 1.17)	12	13	-0.01 (-0.04, 0.02)
Treatment emergent SAE						
Pooled	125/938	147/934	0.85 (0.68, 1.06)	13	16	-0.02 (-0.06, 0.01)
Deaths						
Pooled	21/938	16/934	1.14 (0.69, 1.87)	2	2	0.01 (-0.01, 0.02)

Source: Table 2.5-3 p73, Table 2.5-8 p83 of the submission; Table 43 p123 BOREAS CSR; Table 42p121 NOTUS CSR.
AECOPD = acute exacerbation(s) of chronic obstructive pulmonary disease; CI = confidence interval; COPD = chronic obstructive pulmonary disease; ICS = inhaled corticosteroid; ITT = intention to treat; LS = least squares; n = number of patients with event; N = total patients in group; NR = not reported; PBO = placebo; pre-BD FEV_1 = pre-bronchodilator forced expiratory volume in 1 second; RD = risk difference; RR = risk ratio; SGRQ = St George Respiratory Questionnaire; TEAE = treatment emergent adverse event.
[a] Derived using negative binomial model with the total number of the events occurring during the 52-week treatment period as the response variable, and treatment group, study (if pooled), region (pooled country), ICS dose, smoking status at screening, baseline disease severity, and number of moderate or severe COPD exacerbation events within one year prior to the study as covariates, and log-transformed treatment duration as an offset variable.
[b] Derived using delta method.
[c] Estimated for the purposes of the evaluation using data noted above.

6.32 On the basis of the evidence presented by the submission:

- For each 100 patients treated with dupilumab + triple inhaled therapy, compared with triple inhaled therapy alone, approximately 36 fewer moderate or severe COPD exacerbations will occur per year. The submission did not indicate what difference in moderate to severe AECOPD was considered to be clinically meaningful.

- For each patient treated with dupilumab + triple inhaled therapy for 52 weeks compared with triple inhaled therapy alone, there will be a reduction of approximately 3.4 points in the SGRQ score. A reduction of 4 points is considered clinically meaningful.
- For each patient treated with dupilumab + triple inhaled therapy for 12 weeks compared with triple inhaled therapy alone, an increase of approximately 83 mL in pre-BD FEV1 will be reported. The volume change (in mL) that is considered clinically meaningful was not defined.
- For each 100 patients treated with dupilumab + triple therapy in the BOREAS trial, compared with triple inhaled therapy alone, approximately an additional 4 patients experienced treatment related adverse events, and most commonly these were injection-site reactions.

Clinical claim

6.33 The submission described dupilumab + triple inhaled therapy as superior in terms of effectiveness compared to triple inhaled therapy alone, in patients with uncontrolled COPD with type 2 inflammation. The Sub-Committees agreed with the evaluation that this claim was adequately supported by the evidence presented by the submission with respect to the primary outcome. While the efficacy of dupilumab was demonstrated through the primary outcome, it is not clear to what extent COVID-19 impacted the absolute occurrence of moderate/severe AECOPD events in the treatment arms, and whether this treatment effect is likely to be observed in clinical practice.

6.34 Dupilumab demonstrated a statistically significant improvement in pre-BD FEV_1 compared to placebo, and in health-related quality of life (HRQoL) compared to placebo, as measured by the change in SGRQ total score. Maintaining these improvements was dependent on continuing treatment with dupilumab. The submission did not discuss whether the change in pre-BD FEV_1 was clinically meaningful. The change in SGRQ did not meet the pre-specified MCID.

6.35 The submission claimed that dupilumab + triple inhaled therapy was non-inferior in terms of safety, compared to triple inhaled therapy alone, in patients with uncontrolled COPD with type 2 inflammation. The Sub-Committees agreed with the evaluation that this claim was adequately supported. However, the Sub-Committees noted that TEAEs related to the investigational medicinal product were higher in the dupilumab arm in BOREAS (7.5% versus 3.8%) and the pooled safety data (5.3% versus 3.9%) with the submission attributing this difference to a higher number of injection site reactions in patients receiving dupilumab. A longer duration of follow-up is needed to adequately capture the long-term safety of dupilumab in COPD patients.

6.36 The PBAC considered that the claim of superior comparative effectiveness was reasonable.

6.37 The PBAC considered that the claim of non-inferior comparative safety was likely reasonable. However, the PBAC noted that injection site reactions were more

common in dupilumab patients compared with the placebo arms of the BOREAS and NOTUS trials.

Economic analysis

6.38 The submission presented a stepped cost-effectiveness and cost-utility analysis comparing dupilumab + triple inhaled therapy with triple inhaled therapy alone in patients with uncontrolled COPD with type 2 inflammation. The economic evaluation used data from the BOREAS and NOTUS trials (pooled) and the published literature to extrapolate the clinical outcomes beyond the study duration (52 weeks) to estimate the costs and benefits of treatment over time (35 years). The approach to the economic evaluation is summarised in Table 10.

Table 10: Summary of model structure, key inputs and rationale

Component	Summary
Treatments	Dupilumab + triple inhaled therapy vs triple inhaled therapy
Time horizon	35 years (lifetime) in the model base case versus 1 year in pivotal clinical trials
Outcomes	Number of moderate exacerbations, number of severe exacerbations, LYs, QALYs
Methods used to generate results	Year 1: decision tree based on health state distribution at the end of the BOREAS and NOTUS trials Year 2 and beyond: a cohort Markov structure
Health states	COPD severity (mild, moderate, severe, and very severe COPD) with each split into 7 sub-states for exacerbations (none, 1, 2 or 3+ severe exacerbations, 1, 2 or 3+ moderate exacerbations) and a self-absorbing death state (a total of 29 health states in total).
Cycle length	1 year
Transition probabilities	Year 1 decision tree: health state distribution from BOREAS/NOTUS trials Year 2+: annual probability of progressing through health states, which varied by COPD severity and whether there were exacerbations in the prior year, based on FEV_1 decline from TORCH study; exacerbation occurrence each year, which depends on COPD severity and history of exacerbations in the prior year, sourced from Whittaker et al. (2022) and Wallace et al. (2019). Response to treatment: 94.2% based on pooled data from BOREAS and NOTUS trials. Duration of dupilumab treatment effect post discontinuation: 2 years Rate of treatment discontinuation: 15.0% based on sponsor Advisory Board. Death rates based on general population death rates and COPD SMR (by health state) based on Whittaker 2023: Mild COPD: 1 Moderate COPD: 1.45 (95% CI: 1.4–1.5) Severe COPD: 2.33 (95% CI: 2.3–2.4) Very severe COPD: 4.1 (95% CI: 4.0–4.3) A separate case fatality rate (15.6%) was also applied to severe exacerbations based on Hoogendorn 2011).
Extrapolation method	Extrapolation of treatment effect beyond the trial period was based on transition probabilities from the published literature.
Health related quality of life	Health state specific utility values were derived from NOTUS using EQ-5D and valued using Australian tariffs. Mild COPD: 0.907 Moderate COPD: 0.883 Severe COPD: 0.830 Very severe COPD: 0.794 Utility decrements were applied to exacerbation occurrence: Moderate exacerbation: 0.010 Severe exacerbation: 0.042
Costs	Cost of dupilumab, cost of triple inhaled therapy. The cost of exacerbations and the COPD health states were determined from micro-costing based on the frequency of health care resource use reported by patients in the METIS survey. Unit costs have been sourced in accordance with the recommendations of the PBAC Manual of Resource Items and their Associated Costs.

Source: Table 3.1-1, p120; Table 3.5-1, p155; Table 3.5-3, p156 of the submission.
COPD = chronic obstructive pulmonary disease; FEV_1 = forced expiratory volume in 1 second; LY = life years; PBAC = Pharmaceutical Benefits Advisory Committee; QALYs = quality adjusted life years; SMR = standardised mortality ratio

6.39 The submission adopted a hybrid model with a decision tree component representing the first year (trial period) followed by a cohort Markov model structure to extrapolate the trial benefits over the time horizon. Each treatment arm consisted of 4 COPD

severity health states (GOLD stages) split into 7 exacerbation substates. The decision tree component was split into an amelioration phase (first 2 weeks) and maintenance phase (next 50 weeks) based on the improvement of FEV_1 levels observed in the trials. At the end of the decision tree (52 weeks) patients entered the Markov model in the corresponding health state, with patients in the dupilumab arm split by treatment response (responders and non-responders). The responders continued to receive dupilumab + triple inhaled therapy, while the non-responders discontinued dupilumab and continued with triple inhaled therapy. The structure of the economic model followed disease progression, stratified to capture the associated costs and outcomes for each disease stage, and was consistent with published models. The Sub-Committees considered the model structure appropriate, however given that COPD decline in the model is wholly dependent on the expected exacerbation frequency across the two arms, the model is heavily reliant on these inputs/datasets, which were associated with some uncertainty (described herein).

6.40 A lifetime time horizon (35 years, from a starting age of 65) was applied. The evaluation considered that while it is reasonable in the context of a chronic condition to extrapolate effects to a longer time horizon (beyond the 52 weeks of the trials), given the clinical condition (high risk for severe exacerbation despite being on triple therapy) and age of the population in the model, a 35-year time horizon may not be realistic. Median survival of COPD patients after a severe exacerbation is approximately 4.7 years and the risk of mortality has been found to increase with moderate and severe exacerbations[7]. The PBAC previously accepted a 10-year time horizon for the economic model evaluating triple therapy for the treatment of patients with moderate to severe COPD with frequent exacerbations (para 7.9, fluticasone furoate with umeclidinium and vilanterol PSD, March 2019 PBAC meeting). Patients in that setting had less severe disease than those in the proposed listing; therefore, a time horizon of 35 years is unlikely to be appropriate for the current submission. Reducing the time horizon to 10 years increased the incremental cost-effectiveness ratio (ICER) to $55,000 to < $75,000/quality adjusted life year (QALY) gained from the base case ICER of $35,000 to < $45,000/QALY. The impact of the time horizon on the ICER is presented in Figure 2. The PSCR argued that the lifetime time horizon should remain given that the model incorporates an increased risk of mortality due to age and exacerbations in this population and therefore captures the clinical and economic impacts of COPD and the effect of dupilumab treatment. However, the Sub-Committees considered a 10-year time horizon was more appropriate for this patient group and considered the underlying data could not support longer-term projections. The Pre-PBAC Response argued that the time horizon for dupilumab should not be benchmarked against the time horizon applied to an economic model for triple

[7] Santa et al., (2022), Severe exacerbations and mortality in COPD patients: A retrospective analysis of the database of the Hungarian National Health Insurance Fund, *Pulmonology* 29 (2023), pp 284-291, https://doi.org/10.1016/j.pulmoe.2022.11.001.

therapy (fluticasone furoate with umeclidinium and vilanterol). The Pre-PBAC Response argued that triple therapy primarily provides symptomatic relief through bronchodilation and localised anti-inflammatory effects, whereas dupilumab's mechanism of action addresses the immunological drivers of COPD and has disease-modifying effects which compound over the patient's lifetime. The Pre-PBAC Response argued that a meaningful proportion of patients are expected to live beyond 10 years, and a cutoff at 10 years would undervalue dupilumab's cost-effectiveness.

Figure 2: ICER and time horizon

Source: Constructed during the evaluation.
ICER = incremental cost effectiveness ratio, QALY = quality adjusted life years.

6.41 The submission applied a stopping rule at the end of cycle 1 only. The stopping rule was based on pooled response to treatment data from BOREAS and NOTUS trials with non-responders stopping treatment with dupilumab and receiving triple inhaled therapy only from cycle 2. In addition, the submission applied an annual treatment discontinuation rate of 9.3% for dupilumab in cycle 1 based on the pooled trial data. A total of 85.4% of people remained on dupilumab at the end of cycle 1 and continue to cycle 2. From cycle 2 onwards, the submission applied a constant discontinuation rate of 15% per cycle. Due to the lack of direct evidence on the long-term rate of discontinuation of dupilumab in COPD patients, the submission justified its estimates based on the discontinuation rate of dupilumab observed in the PBS 10% sample for asthma (5–25%) and input from a Global Advisory Board (20%) conducted by the sponsor in July 2024 with five respiratory clinicians and two health economists. The evaluation noted the assumed discontinuation rate of dupilumab from cycle 2 onward was within the range observed for dupilumab for asthma. However, it is uncertain if this is applicable to COPD. The impact of changes in the discontinuation rate for dupilumab on the ICER is moderate.

6.42 The submission stated that the exacerbation rates observed in the clinical trials were under-reported as the BOREAS and NOTUS trials were conducted during the COVID-19 pandemic. Therefore, to inform the model, exacerbation rates in the comparator arm (triple inhaled therapy alone) were from the year prior to randomisation (Table 11) and exacerbation rates for dupilumab were derived by applying the within trial relative risk to those pre-trial rates (Table 12). The Sub-Committees noted that while it may be unlikely the pandemic had a different impact on dupilumab vs placebo, it remained an uncertainty and noted that applying the within trial exacerbation rates for the comparator arm increased the ICER to $45,000 to < $55,000/QALY gained.

Table 11: Exacerbation Rates (events per year) of triple inhaled therapy Derived from Year Prior to Randomisation

GOLD Stage	Triple inhaled therapy – All Patients	
	Moderate Exacerbation	Severe Exacerbation
Mild	1.80	0.20
Moderate	1.90	0.30
Severe	2.00	0.30
Very Severe	2.00	0.40

Source: Table 3.4-3, p139 of the submission.
GOLD = Global Initiative for Chronic Obstructive Lung Disease.

Table 12: Relative risk for exacerbation by GOLD severity of dupilumab + triple inhaled therapy vs. triple inhaled therapy (ITT population)

GOLD severity	All Patients		Responders	
	Moderate Exacerbation (95% CI)	Severe Exacerbation (95% CI)	Moderate Exacerbation (95% CI)	Severe Exacerbation (95% CI)
Mild	1.50 (0.5, 4.9)	1 (assumption)	1.19 (0.4, 3.6)	1 (assumption)
Moderate	0.67 (0.5, 0.9)	0.67 (0.3, 1.5)	0.59 (0.5, 0.8)	0.17 (0.1, 0.5)
Severe	0.87 (0.7, 1.1)	0.64 (0.3, 1.4)	0.67 (0.5, 0.9)	0.18 (0.1, 0.5)
Very Severe	0.64 (0.3, 1.2)	1.00 (0.3, 3.7)	0.55 (0.3, 1.1)	0.18 (assume equal to RR for severe COPD)

Source: Table 3.4-4, p140 of the submission.
COPD = chronic obstructive pulmonary disease; GOLD = Global Initiative for Chronic Obstructive Lung Disease; ITT = intention-to-treat., RR = Relative Risk

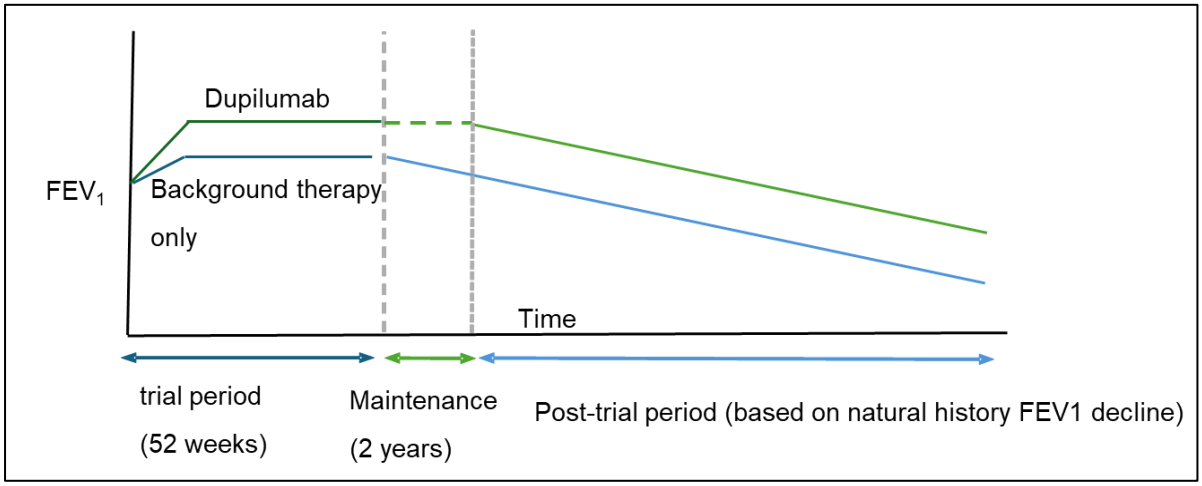
6.43 Transitions between COPD health states in the Markov model were informed by annual probabilities (associated with COPD severity and exacerbation history) reported by Fenwick et al. 2021, which were based on FEV_1 decline over time using data from the 3-year TORCH study. Further the submission applied a multiplier of 1.52 to the Fenwick et al. 2021 estimates based on COPD subgroup data from the CanCOLD study to include the impact of type 2 inflammation (elevated blood eosinophils) on lung function decline. FEV_1 decline estimates from Fenwick et al. 2021 were based on the TORCH study, in which people had dual therapy. The extent to which those rates are applicable to patients on triple therapy is unclear (arguably, triple therapy may be considered more effective than dual therapy, but its use may also signify more severe disease). The Sub-Committees considered that in the absence of long-term trial data, the application of these estimates, while uncertain, was likely reasonable.

6.44 People in the dupilumab arms of BOREAS and NOTUS stopped treatment at the end of the 52-week trial period. Hence, long-term trial data was not available to observe

the long-term changes in the treatment effect (FEV_1 levels and exacerbation rates). In the absence of this, the submission used long-term data from people with moderate or severe asthma receiving dupilumab in the TRAVERSE study. This showed improvements in pre-bronchodilator FEV_1 were maintained from the 52-week trial period and during the 96-week follow up when treatment was extended up to 148 weeks. Based on the TRAVERSE study, the submission assumed that for individuals in the dupilumab arm, the treatment effect was maintained for 2 years, but there was no maintenance of treatment effect in the comparator arm (Figure 3). This effectively increased the incremental treatment effect (with respect to FEV_1). Two years after the trial period the same transition probabilities between COPD health states were applied for both the dupilumab and the comparator arms. Because of the higher FEV_1 for people in the dupilumab arm at 3 years, a treatment effect is maintained throughout the lifetime of the model with no assumption of convergence. Therefore, on average, people in the dupilumab arm continue to stay in less severe COPD severity health states compared with people in the background therapy arm favouring dupilumab.

6.45 The submission justified its approach to extrapolating the treatment effect stating that the mechanism of action of dupilumab is expected to be the same in asthma as in COPD, supporting the use of the TRAVERSE data to inform the treatment effect maintenance period. However, the evaluation considered that people with COPD would be older with more comorbidities, therefore, the treatment effect may be expected to decline more quickly. In the absence of long-term trial data, the assumed sustained treatment effect of dupilumab for 2 years after the trial period remains uncertain. Removing the maintained treatment effect increased the ICER to $45,000 to < $55,000/QALY. The Sub-Committees noted the justifications provided in the submission and PSCR were based on observations from long-term studies in different disease areas (e.g. asthma and atopic dermatitis) and agreed with the evaluation that the maintained treatment effect evident in these studies may not be replicated in COPD. The Sub-Committees noted that COPD is a progressive disease characterised by a decline in lung function and as such considered that the assumption that the trial treatment effect would then be maintained for 2 years should be removed. The Sub-Committees considered that the decline in pre-BD FEV_1 from around week 44 in Figure 1 further supported this advice. The Pre-PBAC Response argued that dupilumab addresses a core driver of Type 2 driven inflammatory disease progression in COPD, providing a biological rationale for maintained treatment effect.

Figure 3: Representation of treatment effect for FEV1 applied in the economic model



Source: Figure 3.4-2, p 143 of the submission.
FEV1 = forced expiratory volume in 1 second.

6.46 The submission applied a case fatality rate (CFR) of 15.6% per severe exacerbation from Hoogendorn et al. 2011 in addition to the standardised mortality rates (SMRs) for COPD estimated from Whittaker et al. 2024. Including a separate CFR for severe exacerbations in addition to SMRs (which have already accounted for deaths due to severe exacerbations) double counts the mortality impact of severe exacerbations, biasing the survival estimates in favour of the dupilumab arm. Removing the CFR for severe exacerbations from the base case increased the ICER to $75,000 to < $95,000/QALY. The PSCR highlighted that exacerbations were associated with an increased risk of death and that Hoogendorn et al. 2011 reported both the acute and long-term mortality impacts of hospitalised exacerbations. The PSCR stated that the CFR applied to the model excludes background mortality due to other causes over this period, thus allowing for the inclusion of SMRs, which separately capture background mortality. The Sub-Committees agreed with the PSCR that there is an association between exacerbations and a higher rate of death, however, considered that the SMRs and CFR do not represent independent risks and the increased risk of death due to exacerbations would, to certain degree, also be captured in the SMRs. The Sub-Committees considered that the inclusion of a CFR of 15.6% was likely too optimistic, but also considered removing it may be too conservative. The Sub-Committees considered a reduction in the CFR input may be appropriate to account for the likely double counting of the mortality impact of severe exacerbations. The Pre-PBAC Response disagreed with the Sub-Committee's approach to reduce the CFR and maintained that a CFR of 15.6% was appropriate. The Pre-PBAC Response argued that the CFR applied to the economic model only captures the excess risk of exacerbations and can therefore be coupled with a background SMR, which was derived from a general COPD population with lower exacerbation and mortality risk than the proposed population. The Pre-PBAC Response also noted that when SMR = 1 the ICER is reduced ($35,000 to < $45,000/QALY gained).

6.47 The cost of exacerbations and the COPD health states were determined from a micro-costing analysis based on the frequency of health care resource use reported by clinicians in the METIS survey (sponsor commissioned). The annual costs for moderate and severe COPD health states were estimated to be $482 and $1,096, respectively. The METIS survey did not ask about resource use for treatment of patients in the mild or very severe COPD health states. The cost of very severe COPD was assumed to be twice the cost of severe COPD, while the cost of mild COPD was assumed to be half that of a moderate COPD. The submission did not provide any justifications for these assumptions. On balance, a higher proportion of events in the comparator arm were very severe, and a higher proportion of events in the dupilumab arm were mild, thus potentially biasing the analysis in favour of dupilumab (if those costs are over and underestimated respectively). The cost of a moderate exacerbation was $752, and the cost of a severe exacerbation was $10,552 (hospital costs of $8,312.66 and non-hospital costs of $2,239.50).

6.48 The model incorporated utility values according to COPD health state and disutilities associated with exacerbations. Health state specific utility values were derived from NOTUS collected using EQ-5D-5L at baseline, week 24 and week 52. The submission noted the BOREAS trial collected the EQ-5D-5L at baseline only and hence this was not included in the analysis. EQ-5D-5L utilities were valued using Australian tariffs (Norman 2023). The submission did not use the treatment group specific utilities, instead the economic model applied the mean values for all patients by health state. The Sub-Committees agreed with the evaluation that while the approach applied in the submission was reasonable, the values applied do not appear realistic; values for mild and moderate COPD are consistent/higher than values for the general population. The submission stated exacerbation events have a profound impact on the HRQoL of patients with COPD and applied disutility to each exacerbation event. The base case applied the values obtained in a time-trade-off study by Rutten Van Molken et al. 2009 conducted in the general population. The Sub-Committees agreed with the evaluation that the application of an additional utility benefit for dupilumab over and above the COPD health state specific utility values is not reasonable as the trial-based utilities would have already accounted for exacerbations. Removal of exacerbation specific utility decrements from the model had only a minor impact on the ICER.

6.49 A summary of the key drivers of the model is presented in Table 13.

Table 13: Key drivers of the model

Description	Method/Value	Impact Base case: $[redacted][1]QALY gained
Case fatality rate (CFR)	15.6% per severe exacerbation. The Sub-Committees considered a reduction in the CFR input may be appropriate to account for the likely double counting of the mortality impact of severe exacerbations.	High, favoured dupilumab Removing the CFR from the base case increased the ICER to $[redacted][2]
Time horizon	35 years in the base case. The Sub-Committees considered a 10-year time horizon appropriate.	Moderate, favoured dupilumab Use of a 10-year time horizon increased the ICER to $[redacted][3]/QALY gained.
Duration of treatment effect of dupilumab	The treatment effect on FEV_1 was maintained for 2 years beyond the end of the trial period. The Sub-Committees considered that the assumption of a maintained treatment effect should be removed.	Moderate, favoured dupilumab Removing the maintained treatment effect increased the ICER to $[redacted][4]/QALY.
Exacerbation rates	Exacerbation rates in the comparator arm were from the year prior to randomisation. Exacerbation rates in the dupilumab arm were the rates for triple inhaled therapy times the relative risk of exacerbation observed during the study period	Moderate, favoured dupilumab Use of the exacerbation rates from the trials in comparator arm increased the ICER to $[redacted][4].

Source: Compiled during the evaluation.
CFR = case fatality rate; FEV_1 = forced expiratory volume in 1 second; ICER = incremental cost-effectiveness ratio; QALYs = quality adjusted life years.
The redacted values correspond to the following ranges:
[1] *$35,000 to < $45,000*
[2] *$75,000 to < $95,000*
[3] *$55,000 to < $75,000*
[4] *$45,000 to < $55,000*

6.50 The results of the stepped economic evaluation are presented in Table 14. In Step 2, adjusting the exacerbation rates for the effect of the COVID-19 epidemic reduced the ICER, largely due to an increase in the incremental benefit (reduction in exacerbations were more than doubled). Implementing the stopping rule (at the end of the trial period, 52 weeks) in Step 5 reduced the ICER from $95,000 to < $115,000 to $55,000 to < $75,000.

Table 14: Results of the stepped economic evaluation (discounted)

Step and component	Proposed medicine	Comparator	Increment
Step 1: trial-based costs and outcomes			
Costs	$[redacted]	$1,415	$[redacted]
Exacerbations	0.605	0.846	-0.241
Incremental cost/exacerbation avoided			$[redacted][1]
Step 2: Adjust exacerbation rates (pre-trial rates) for effect of COVID-19 epidemic[a]			
Costs	$[redacted]	$4,377	$[redacted]
Exacerbations	1.559	2.194	-0.635
Incremental cost/ exacerbation avoided			$[redacted][2]
Step 3: Limiting time horizon to one year and converting outcomes to QALYs			
Costs	$[redacted]	$6,330	$[redacted]
QALYG	0.82	0.81	0.01
Incremental cost/ extra QALY gained			$[redacted][3]
Step 4: 10-year time horizon			
Costs	$[redacted]	$41,402	$[redacted]
QALYG	5.05	4.63	0.41
Incremental cost/extra QALY gained			$[redacted][4]
Step 5: Implement stopping rule			
Costs	$[redacted]	$41,402	$[redacted]
QALYG	5.27	4.63	0.63
Incremental cost/extra QALY gained			$[redacted][5]
Step 6: Lifetime time horizon			
Costs	$[redacted]	$51,559	$[redacted]
QALYG	6.48	5.50	0.99
Incremental cost/extra QALY gained (base case)			$[redacted][6]

Source: Table 3.8-4, p173 of the submission.

ICER = Incremental cost-effectiveness ratio; QALY = quality-adjusted life year; QALYG = QALY gained.

[a] Rate of moderate exacerbations in the trials, uplifted by 2.5; Rate of severe exacerbations in the trials, uplifted by 3.5 to make the rates in the comparator arm similar to those observed in the year prior to the trials.

The redacted values correspond to the following ranges:

[1] *$45,000 to < $55,000*

[2] *$15,000 to < $25,000*

[3] *$955,000 to < $1,055,000*

[4] *$95,000 to < $115,000*

[5] *$55,000 to < $75,000*

[6] *$35,000 to < $45,000*

6.51 The results of key univariate and multivariate analyses (MVA) are summarised in Table 15. The Sub-Committees considered a revised base case was required to address a number of unsupported assumptions and advised it should include a 10-year time horizon and the removal of the 2 year (maintained) FEV_1 treatment effect beyond the trial period in the dupilumab arm. The Sub-Committees noted that these changes to the model increased the ICER to $55,000 to < $75,000/QALY. Removing the CFR (in addition to the above changes) increased the ICER to $255,000 to < $355,000/QALY. As noted in paragraph 6.46, the Sub-Committees considered that including a CFR of 15.6% was likely too optimistic, but also considered removing it may be too conservative. The Sub-Committees considered a reduction in the CFR input may be appropriate to account for the likely double counting of the mortality impact of severe exacerbations. The Sub-Committees noted that reducing the CFR for severe

exacerbations to 10% and further to 5% increased the ICER to $75,000 to < $95,000 per QALY gained and $115,000 to < $135,000 per QALY gained, respectively.

Table 15: Sensitivity analyses

Analyses	Incremental QALY	Incremental cost	ICER	% change to ICER
Base case	**0.99**	**$**	**$** [1]	-
Time horizon (base case: 35 years)				
10 years (A)	0.63	$	$ [2]	%
Discount rate (base case: 5%)				
0%	1.52	$	$ [3]	- %
3.5%	1.11	$	$ [1]	- %
Annual discontinuation rate of dupilumab from Year 2 (base case: 15%)				
9.3% (same as in Year 1)	1.15	$	$ [1]	%
FEV_1 Treatment Effect Duration (base case: maintained 2 years after trial period)				
No maintenance of FEV_1 treatment effect beyond trial period (B)	0.83	$	$ [1]	%
Baseline Exacerbation Rate in the comparator arm (base case: Year prior to randomisation)				
Pooled BOREAS and NOTUS (C)	0.90	$	$ [1]	%
Annual transition probabilities between COPD stage (base case: adjusted for type 2 inflammation 1.5x)				
Reduced by 20%	0.97	$	$ [1]	%
Reduced by 50%	0.93	$	$ [1]	%
Excess Mortality Due to Severe Exacerbation (base case: 15.6%)				
No excess mortality due to severe exacerbation (D)	0.37	$	$ [4]	%
Excess mortality due to severe exacerbation 5% (E) [b]	0.62	$	$ [2]	%
Excess mortality due to severe exacerbation 10 % (F) [b]	0.82	$	$ [1]	%
Multivariate analysis [a]				
10-year time horizon (A) No FEV_1 treatment effect beyond trial period (B) Baseline exacerbation rate in the comparator arm using trial data (C)	0.47	$	$ [4]	%
10-year time horizon (A) No FEV_1 treatment effect beyond trial period (B) Baseline exacerbation rate in the comparator arm using trial data (C) Removing CFR for severe exacerbation (D)	0.11	$	$ [5]	%
Sub-Committees' requested multivariate analyses [b]				
10-year time horizon (A) No maintenance of FEV_1 treatment effect beyond trial period (B)	0.54	$	$ [2]	%
10-year time horizon (A) No maintenance of FEV_1 treatment effect beyond trial period (B) CFR for severe exacerbation (10%) (F)	0.41	$	$ [4]	%
10-year time horizon (A) No maintenance of FEV1 treatment effect beyond trial period (B) CFR for severe exacerbation (5%)(E)	0.28	$	$ [6]	%
10-year time horizon (A) No maintenance of FEV_1 treatment effect beyond trial period (B) Removing CFR for severe exacerbation (D)	0.12	$	$ [5]	%

Source: Table 3.9-1, p177 of the submission
CFR = case fatality rate; FEV_1 = forced expiratory volume in 1 second; ICER = incremental cost-effectiveness ratio; QALY = quality adjusted life year.
[a] Compiled during the evaluation. [b] Complied during the preparation of the ESC DUSC ADV.
The redacted values correspond to the following ranges:
[1] *$35,000 to < $45,000*
[2] *$55,000 to < $75,000*
[3] *$25,000 to < $35,000*
[4] *$75,000 to < $95,000*
[5] *$255,000 to < $355,000*
[6] *$115,000 to < $135,000*

6.52 The ICERs for PBAC recommendations for related conditions include $40,000 - $45,000 per QALY for omalizumab for uncontrolled severe allergic asthma (omalizumab PSD, November 2010 PBAC Meeting) and $45,000 to < $55,000 per QALY gained for tezepelumab for non-eosinophilic and non-allergic severe uncontrolled asthma (paragraph 7.11, tezepelumab PSD, November 2025 PBAC Meeting). The net cost to the PBS/RPBS for omalizumab was estimated by the submission to be less than $10 million in any of the first 5 years (omalizumab PSD, November 2010 PBAC Meeting). The net cost to the PBS/RPBS for of listing tezepelumab was estimated by the submission to be $30 million to < $40 million in Year 6, and a total of $100 million to < $200 million in the first 6 years of listing (paragraph 6.84, tezepelumab PSD, November 2025 PBAC Meeting). The PBAC has previously suggested lower acceptable ICERs for other conditions with larger numbers of eligible patients and larger estimated net costs to the PBS/RPBS than those reported for omalizumab and tezepelumab. An ICER of less than $15,000 - $45,000 per QALY was accepted for evolocumab (paragraph 5.8, evolocumab PSD, November 2019 PBAC Meeting), an ICER in the order of $30,000 per QALY gained was considered appropriate in the PBAC's deferral of tirzepatide for the treatment of adult patients with inadequately controlled type 2 diabetes (paragraph 7.9, tirzepatide PSD, July 2025 PBAC Meeting), and an ICER of up to $25,000 per QALY gained for semaglutide for use in patients with established cardiovascular disease with obesity accepted (paragraph 7.12, semaglutide PSD, November 2025 PBAC Meeting).

Dupilumab cost/patient/year

Table 16: Drug cost per patient for Dupilumab and triple inhaled therapy

	Dupilumab Trial dose and duration	Dupilumab Model	Dupilumab Financial estimates	Triple therapy Trial dose and duration[j]	Triple therapy Model	Triple therapy Financial estimates[n]
Mean dose	300 mg	300 mg	300 mg	Triple therapy	Triple therapy	Triple therapy
Cost per dose	$[redacted][a]	$[redacted][a]	$[redacted]	NA	NA[k]	NA
Doses per month	2.17[b]	2.17[b]	2.17	NA	NA[k]	NA
Doses per year	26.07[c]	26.07[c]	26.07	NA	NA[k]	NA
Compliance	98%[d]	100%[h]	100%[h]	NA	100%[h]	NA
Mean duration	0.91 years[e]	4.17 years[i]	NA	NA	7.39 years[l]	NA
Cost/patient/month	$[redacted][f]	$[redacted][f]	$[redacted][f]	NA	$83.66[m]	NA
Cost/patient/year	$[redacted][g]	$[redacted][g]	$[redacted][g]	NA	$1,003.90	NA

Source: 'Drug Acqu and Admin' worksheet of the economic model workbook provided with the submission, Table 2.4-4, p60 of the submission; and compiled during the evaluation.

[a] Cost of the pack ($[redacted]) divided by doses in the pack (2)

[b] 1 dose every 14 days = 2.17 doses per month (30.41 days per month)

[c] Doses per month x 12

[d] Reported in trials (p60 of the submission)

[e] mean duration 332.83 days

[f] Cost per dose x doses per month

[g] Cost per dose x doses per year x compliance

[h] Submission's assumption

[i] Duration in the trial period (0.96 years) + Duration in the Markov period (3.21 years) - Undiscounted

[j] Formulation of triple therapy used in the key trials is not known

[k] Three different PBS listed triple therapy formulations were considered in the submission. It is not possible to present the combined doses

[l] Duration in the trial period (0.94 years) + Duration in the Markov period (6.45 years) - Undiscounted

[m] Weighted cost of fixed dose triple therapy formulations listed on PBS (Cell G:23, 'Drug Acqu and Admin' worksheet of the economic model workbook)

[n] Financial estimates did not include the cost of triple therapy

6.53 The annual cost of dupilumab is $[redacted] based on the effective price ($[redacted]/28 x 365.25) assuming 100% compliance. The dose applied in the economic model and the financial estimates was consistent with the trial dose. The annual cost of triple inhaled therapy in the model and the financial estimates was calculated as the weighted average of three triple inhaled therapies currently listed on the PBS (11379X – 63.1%, 12468F – 20.9%, 12672Y – 16.0%). The weights were estimated based on the market share of the respective triple inhaled therapies currently listed on the PBS.

Estimated PBS usage & financial implications

6.54 This submission was jointly considered by DUSC and ESC.

6.55 The submission used both epidemiological sources and PBS 10% sample data to estimate the number of patients eligible for treatment with dupilumab. The submission stated that the epidemiological approach underestimated the number of people on triple therapy compared to the PBS 10% sample and applied an average of the two approaches in the base case. The evaluation considered this methodology unconventional and likely to overestimate the eligible population. The submission tested the impact of using only one of the approaches in a sensitivity analysis. The PSCR stated that the two approaches to estimate the number of people on triple therapy were broadly consistent, and an average of the two was proposed as the most

reasonable estimate, while the sponsor acknowledged that some uncertainty remains, they considered that the base case presented provides robust estimates based on the best available data. The Sub-Committees considered that the estimates derived from the use of the epidemiological sources and the PBS data were uncertain and considered that an approach based on the actual treated prevalent population would provide more certain estimates.

6.56 The key inputs used to estimate the utilisation of dupilumab are presented in Table 17.

Table 17: Key inputs for financial estimates

Data	Value	Source	Comment
Eligible population			
Epidemiological approach			
Australian population aged 35 years and older	Yr 1: 15,572,275 to Yr 6: 16,962,091	ABS 3222.0 – medium series	The Sub-Committees considered this was reasonable.
Prevalence of treated COPD in Australia for people aged 35 years and older	2.7%	AIHW 2023a (NIHSI multi-source prevalence of COPD)	The Sub-Committees considered this was reasonable.
Proportion of patients with moderate or severe COPD	Moderate – [redacted]% Severe – [redacted]%	METIS survey – Sponsor commissioned clinician survey of 100 GPs and 46 Respiratory Physicians	GPs and Respiratory physicians were asked to report what proportion of their patients would qualify as having mild, moderate or severe COPD based on COPD-X definitions. The evaluators considered it was not clear if the participant feedback in METIS survey was representative of all COPD patients in Australia. The Sub-Committees agreed with the evaluation and considered that this estimate was uncertain.
Proportion of patients with moderate or severe COPD on triple therapy	Moderate – [redacted]% Severe – [redacted]% With growth rate of [redacted]% - Yr 1 and 2, [redacted]% - Yr 3, [redacted]% - Yr 4, 5, 6	Proportion of patients based on METIS survey. Growth rate based on PBS 10% sample which indicates a growth in the market with the introduction of single inhaler FDC triple therapy in 2018.	Triple therapy was assumed to grow at a stable rate of [redacted]% from Year 4. The evaluators considered there was no evidence that this growth will slow down or plateau in future. This makes the magnitude of the estimates uncertain. The Sub-Committees agreed with the evaluation and considered that this estimate was uncertain. The Sub-Committees noted that clinicians in the METIS survey were asked about patients not only on triple therapy but also patients with dual therapy (LAMA+LABA if ICS was contraindicated). The Sub-Committee considered that the inclusion of dual therapy due to contraindication of ICS may lead to an overestimate of patients on triple therapy.
Serum eosinophils ≥ 300 µL	33.7%	BOREAS CSR p42	The Sub-Committees noted that the 33.7% reported in the BOREAS CSR is the percentage of participants who failed to meet the inclusion criteria as they did NOT

Data	Value	Source	Comment
			have an BEC ≥ 300 cells/μL (Visit 1). As such, the Sub-Committees considered this input as a baseline measure was not appropriate. The Sub-Committees noted that the submission stated that in the peer-review literature estimates vary from 29% to 40%. The Sub-Committee also noted that the submission used the results of an Australian study of COPD in outpatient clinics (Hiles et al. 2021) in a sensitivity analysis. The Hiles et al. 2021 study estimated 29.4% of patients have an BEC ≥ 300 cells/μL. The Sub-Committee noted that this was consistent with the findings from the METIS survey in which clinicians estimated the percentage of patients with BEC ≥ 300 cells/μL in the last 12 months varied from 19% to 28% in moderate COPD and was estimated to be 30% in severe COPD.
Proportion of moderate and severe COPD patients at high risk of exacerbation	Moderate – [redacted]% Severe – [redacted]%	METIS survey	The evaluation considered it is not clear if the clinician estimates from the METIS survey was representative of all COPD patients in Australia. The Sub-Committees agreed with the evaluation that this estimate was uncertain.
PBS 10% sample approach			
Patients receiving triple therapy	Yr 1: [redacted]1 Yr 2: [redacted]1 Yr 3: [redacted]2 Yr 4: [redacted]2 Yr 5: [redacted]2 Yr 6: [redacted]2	PBS 10% sample used to determine the number of patients who were dispensed at least one script for triple therapy in the previous 12 months. [redacted]1 patients on triple therapy in 2025 with a growth rate of [redacted]% - Year 1 and 2, [redacted]% - Year 3, [redacted]% - Year 4, 5, 6.	While the assumption of a [redacted]% growth rate in the first two years of listing is reasonable, there is no evidence that this growth will slow down or plateau in future. The Sub-Committees considered that this estimate was uncertain. The Sub-Committees noted that the [redacted]1 patients reported by the submission to be on triple therapy in 2025 was based on [redacted]1 patients receiving single inhaler FDC triple therapy and [redacted]3 patients receiving open triple therapy. The Sub-Committees noted that based on the 100% PBS sample, the number of prevalent patients who had received at least one prescription for single inhaler FDC triple therapy in 2025 was 186,168 (see Table 19).
Serum eosinophils ≥ 300 μL	33.7%	BOREAS CSR p42	Same input as Epidemiological approach. See above for comment on this input.
Proportion at high risk of exacerbation	[redacted]%	Average of the proportion of moderate and severe COPD patients at high risk of exacerbation from Epidemiological	Same input as Epidemiological approach. See above for comment on this input.

Data	Value	Source	Comment
		approach (METIS survey)	
Average of Epidemiological and PBS 10% sample approaches			
Base case eligible population	Yr 1: [redacted][4] Yr 2: [redacted][3] Yr 3: [redacted][3] Yr 4: [redacted][3] Yr 5: [redacted][3] Yr 6: [redacted][3]	Eligible patient population determined by averaging both the epidemiological and the PBS 10% sample approaches	The evaluation considered this methodology is unconventional and is likely to overestimate the eligible population. The Sub-Committees considered that for the epidemiological approach, the proportion of the population who had used triple therapy in the preceding 3 months based on the METIS survey remained an area of uncertainty due to concerns around the representativeness of the survey to the PBS population. The Sub-Committees considered that the estimates derived from the use of the average of the epidemiological and PBS 10% sample approaches were uncertain and considered that a market share approach based on the actual treated prevalent population would provide more certain estimates.
Grandfather population			
Grandfather population	[redacted][5]	Sponsor forecasts. Grandfathered patients considered to be a subset of the eligible patient population and were assumed to have the same discontinuation rates as initiating patients.	
Treatment utilisation			
Uptake rate	Yr 1: [redacted]% Yr 2: [redacted]% Yr 3: [redacted]% Yr 4: [redacted]% Yr 5: [redacted]% Yr 6: [redacted]%	Prescribing rates reported by respiratory physicians from market research undertaken by the sponsor (INSIGHTS 2025).	There is a wide variation in the prescribing rates of dupilumab reported by the respiratory physicians (<[redacted]% to [redacted]%) in the INSIGHTS survey.
Persistence rates	Yr 1: 85.4%, Yr 2 to Year 6: 85.0%	It is assumed that 94.2% of initiating patients will meet the continuation criteria with a further 9.3% expected to discontinue by the end of the first year (94.2% x 90.7% = 85.4%) with 85% from subsequent years (Global advisory board and precedents).	Annual discontinuation rate is consistent with the economic model, although applied differently in the economic model. Used in the financial estimates to determine the split between initiating and continuing patients. Patients who discontinued treatment were not removed from the prevalent pool for subsequent years.

Data	Value	Source	Comment
% compliance	100%	13 scripts for one full year of treatment	The mean compliance with administration was high >98% in both BOREAS and NOTUS trials but trials may not reflect real world compliance. The Sub-Committees noted that the BOREAS and NOTUS trials had very high compliance rate (>98%) and considered that this is unlikely to reflect real world experience. The Sub-Committees considered a compliance rate of 93% may be more appropriate. The PBAC noted a compliance rate of 93% was consistent with that considered appropriate by DUSC in the consideration of tezepelumab for non-eosinophilic and non-allergic severe uncontrolled asthma population (Table 20, tezepelumab PSD, November 2025 PBAC meeting).
Costs			
Dupilumab	Published DPMQ - $1,755.99 Effective DPMQ - $[redacted]	Proposed published and effective price of dupilumab.	
Cost offset due to reduction in use of amoxycillin and prednisolone	Amoxicillin 250mg capsule, 20 (11998L) - $19.22 (DPMQ) Prednisolone 5 mg tablet, 60 (1917X) – $17.33 (DPMQ)	Frequency of use of amoxicillin and prednisolone derived from METIS survey was multiplied with the reduction in exacerbations to derive reduction in use of amoxicillin and prednisolone.	The submission assumed dupilumab will result in fewer moderate and severe exacerbations each year compared to triple inhaled therapy only. This was based on observations from the trial data (pooled BOREAS and NOTUS) and consistent with the estimates in the economic model for cycle 1.
Other cost offsets/additional costs	Specialist attendance - $101.30 (MBS item 104) GP attendance - $43.90 (MBS item 23) ED visit - $1,651.00 Ambulance - $914.00 Hospitalisation - $8,312.00 (AR-DRG E65A & E65B)	Cost of each item multiplied with reduction in resource due to reduction in exacerbations.	It is not appropriate to include cost offsets associated with GP and specialist visits as these are not likely to be realised. ED visit, ambulance and hospitalisation should not be included as they do not accrue a PBS or MBS cost.
Patient copayment	PBS – $8.60 RPBS – $4.10	Average of PBS and RPBS copayments based on dispensing data for PBS items 11379X, 12468F, 12672Y for triple inhaled therapy.	
Administration costs	$88.90	MBS item 82215 – nurse training for subcutaneous injection	Included only as one-off cost for initiating patients. Some patients may require assistance with administration more than once over their treatment duration.

Source: compiled during the evaluation based on Table 4.1-1, p180; Table 4.1-4, p183; Table 4.2-6, p192, Section 4.2 and Section 4.5 of the submission.
AR-DRG = Australian Refined Diagnosis Related Group; ABS = Australian Bureau of Statistics; AIHW = Australian Institute of Health and Welfare; COPD = chronic obstructive pulmonary disease; DPMQ = dispense price for maximum quantity; ED = Emergency Department; BEC = blood eosinophil count; FDC = fixed dose combination; GP = general physician; MBS = Medicare Benefits Schedule; PBS = Pharmaceutical Benefits Scheme; RP = respiratory physician; RPBS = Repatriation Pharmaceutical Benefits Scheme; Yr = Year.
The redacted values correspond to the following ranges:
[1] *100,000 to < 200,000*
[2] *200,000 to < 300,000*
[3] *30,000 to < 40,000*
[4] *20,000 to < 30,000*
[5] *500 to < 5,000*

6.57 A summary of the estimated use and financial implications is presented in Table 18.

Table 18: Estimated use and financial implications (effective price)

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Total
Eligible for dupilumab							
Epidemiological approach	[redacted][1]	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][3]
PBS 10% sample approach	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][4]
Average of both approaches	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][4]
Estimated extent of use							
Number of patients treated[a]	[redacted][b 5]	[redacted][6]	[redacted][6]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][3]
Number of scripts dispensed[c]	[redacted][3]	[redacted][3]	[redacted][4]	[redacted][4]	[redacted][7]	[redacted][7]	[redacted][8]
Estimated financial implications of dupilumab							
Cost to PBS/RPBS less copayments	$[redacted][9]	$[redacted][9]	$[redacted][10]	$[redacted][11]	$[redacted][11]	$[redacted][11]	$[redacted][12]
Estimated financial implications for other medicines							
Cost to PBS/RPBS less copayments	-$[redacted][13]	-$[redacted][13]	-$[redacted][13]	-$[redacted][13]	-$[redacted][13]	-$[redacted][13]	-$[redacted][13]
Net financial implications							
Net cost to PBS/RPBS	$[redacted][9]	$[redacted][9]	$[redacted][10]	$[redacted][10]	$[redacted][11]	$[redacted][11]	$[redacted][12]
Net cost to MBS[d]	$[redacted][14]	$[redacted][14]	$[redacted][14]	$[redacted][14]	$[redacted][14]	$[redacted][14]	$[redacted][14]
Net cost to PBS/RPBS/MBS	$[redacted][9]	$[redacted][9]	$[redacted][10]	$[redacted][11]	$[redacted][11]	$[redacted][11]	$[redacted][12]

Source: Table 4.2-4, p190; Table 4.2-5, p191; Table 4.2-11, p196; Table 4.3-1, p 197; Table 4.3-3, p198; Table 4.4-2, p199; Table 4.5-7, p203 of the submission.

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

[a] Uptake take: Year 1 – [redacted]%, Year 2 – [redacted]%, Year 3 – [redacted]%, Year 4 – [redacted]%, Year 5 – [redacted]%, Year 6 – [redacted]%.
Persistence – 85%

[b] Includes 500 to < 5,000 grandfathered patients.

[c] Assuming 13 scripts dispensed per patient per year as estimated by the submission.

[d] Excluding costs associated with GP and specialist visits.

The redacted values correspond to the following ranges:

[1] 20,000 to < 30,000
[2] 30,000 to < 40,000
[3] 100,000 to < 200,000
[4] 200,000 to < 300,000
[5] 5,000 to < 10,000
[6] 10,000 to < 20,000
[7] 300,000 to < 400,000
[8] 1,000,000 to < 2,000,000
[9] $100 million to < $200 million
[10] $200 million to < $300 million
[11] $300 million to < $400 million
[12] > $1 billion
[13] net cost savings
[14] $0 to < $10 million

6.58 The net cost to the PBS/RPBS of listing dupilumab was estimated to be $300 million to < $400 million in Year 6, and a total of > $1 billion over the first 6 years of listing.

6.59 The evaluation considered that some of the input parameters used to estimate the number of patients on treatment with dupilumab were uncertain, such as the assumed proportion of patients with BEC ≥ 300 cells/µL, proportion of patients with high risk of exacerbation and the uptake rate of dupilumab. These areas of uncertainty were tested in sensitivity analyses. The Sub-Committees noted that the estimates

were most affected by assumptions regarding the assumed uptake rate, proportion of patients with BEC ≥ 300 cells/µl and exacerbation risk.

6.60 The Sub-Committees noted the analysis of the 100% PBS sample undertaken by the Drug Utilisation Section, which reported the number of incident and prevalent patients and the scripts for PBS listed single inhaler triple therapies for COPD during 2023–2025 (Table 19). The Sub-Committees considered a market share approach based on the actual number of treated prevalent patients supplied triple therapy would likely provide more certain estimates for the utilisation of the single inhaler triple therapies. The Sub-Committees noted that there would also be an additional open triple inhaled therapy population.

Table 19: Number of incident and prevalent patients, and scripts for PBS listed single inhaler triple therapies for COPD

Year/Drug/Item Code	Incident patients	Prevalent patients	Scripts
Total 2023	**46,654**	**138,169**	**857,453**
Beclometasone + formoterol + glycopyrronium (item code 12468F)	11,133	27,473	148,005
Budesonide + glycopyrronium + formoterol (item code 12672Y)	10,021	20,164	100,709
Fluticasone furoate + umeclidinium + vilanterol (item code 11379X)	25,500	90,532	608,739
Total 2024	**48,179**	**160,545**	**965,113**
Beclometasone + formoterol + glycopyrronium (item codes 12468F and 14310E)	13,252	38,054	202,852
Budesonide + glycopyrronium + formoterol (item codes 12672Y and 14536C)	11,601	29,945	155,633
Fluticasone furoate + umeclidinium + vilanterol (item codes 11379X and 14346C)	23,326	92,546	606,628
Total 2025	**47,736**	**186,168**	**993,497**
Beclometasone + formoterol + glycopyrronium (item codes 12468F and 14310E)	13,952	48,438	228,186
Budesonide + glycopyrronium + formoterol (item codes 12672Y and 14536C)	12,309	40,543	190,492
Fluticasone furoate + umeclidinium + vilanterol (item codes 11379X and 14346C)	21,475	97,187	574,819

Source: Authorities data and prescriptions data was extracted on the 9 February 2026 from the prescription database and Authorities database maintained by the Department of Health, Disability and Ageing, processed by Services Australia from between 1 January 2023 and 31 December 2025, respectively. Data were extracted based on the date of supply. The number of incident patients, prevalent patients, and scripts dispensed was determined by counting the number of people supplied at least one PBS prescription using person specific numbers (non-identifying) in the data for the time period 1 January 2023 and 31 December 2025. Patient initiation was defined as the date of supply of the first PBS or RPBS prescription.

6.61 The Sub-Committees considered that revised financial estimates were required and suggested these could be provided in the pre-PBAC response. The Sub-Committees considered a market share approach based on the actual number of treated prevalent patients supplied triple therapy outlined in Table 19 with an additional estimate for the open triple inhaled therapy population would be appropriate. As outlined in Table 17, the Sub-Committees considered that there was no evidence that growth will slow down or plateau and advised that a linear projection to forecast the eligible population

would be appropriate. The Sub-Committees considered the percentage of patients with BEC ≥ 300 cells/µL from Hiles et al (2021) was likely appropriate as were assumptions employed in the model regarding the proportion at high risk of exacerbations. The Sub-Committees considered that compliance assumptions should be as outlined by the Sub-Committees in Table 17. The Sub-Committees considered that sensitivity analyses varying assumptions around the percentage of patients with BEC ≥ 300 cells/µL (based on range in METIS survey) along with those for compliance and uptake rates would also be informative.

6.62 The pre-PBAC response provided revised financial estimates which:

- Incorporated a linear projection, based on the 100% PBS data, to forecast the single triple inhaler therapy population. It was assumed that the open triple therapy population (based on the PBS 10% sample) remained stable (assumed to be [redacted]% in June 2025);
- Decreased the percentage of patients with BEC ≥ 300µL to 29.4% (Hiles et al. 2021);
- Retained the percentage of the population at high risk of exacerbations as [redacted]% based on the METIS survey; and
- Decreased compliance to 93%.

The pre-PBAC response stated that the uptake rate remained consistent with the submission base case. The Pre-PBAC Response reported the number of patients treated increased from 10,000 to < 20,000 (including 500 to < 5,000 grandfathered patients) in Year 1 to 40,000 to < 50,000 patients in Year 6. The net cost to the PBS/RPBS of listing dupilumab was reported as $400 million to < $500 million in Year 6, and a total of > $1 billion over the first 6 years of listing.

6.63 The PBAC noted that the PBS 10% sample data provided by the submission indicated that open triple therapy as a percentage of total triple therapy had reduced significantly across time with the introduction of single inhaler triple therapy. As such, the PBAC considered the assumption that the open triple therapy population remained stable was not reasonable. The PBAC considered the trend of decreasing open triple therapy should be accounted for in the financial model and considered that this would result in an additional open triple inhaled therapy population in Year 1 only. Furthermore, the PBAC considered the market share for the additional open triple inhaled therapy population in Year 1 should not exceed the 2025 level.

6.64 The PBAC noted that the uptake rate was applied directly to the prevalent pool of patients each year. This essentially resulted in patients who had discontinued treatment in previous years, starting treatment again. The PBAC advised that this resulted in an implausibly high number of patients initiating treatment over the 6 year estimates, i.e., it was estimated that 50,000 to < 60,000 patients initiated treatment over the 6 years which was more than the prevalent pool of eligible patients (40,000 to < 50,000 in year 1, 50,000 to < 60,000 in year 6). The PBAC considered that a cumulative approach to uptake should be applied. Assuming uptake increases

linearly, this would involve [redacted]% of the eligible population initiating treatment in Year 1 with [redacted]% applied in Year 2 to Year 6 to reach a cumulative total of [redacted]% in Year 6.

6.65 Both the submission base case and the pre-PBAC response revised estimates applied the annual discontinuation rate to inform the split between initiating and continuing patients, however as noted in the paragraph above, patients who discontinued treatment were not removed from the prevalent pool in subsequent years. The PBAC considered that rather than using the assumed discontinuation rate (20% annually) it may be more appropriate to use the proportion of patients continuing treatment from the economic model to inform annual treatment persistence. The PBAC noted that this approach accounted for treatment discontinuation due to any cause and mortality.

Quality Use of Medicines

6.66 The submission noted that healthcare professional education materials will be created to explain the benefits, risks, and appropriate patient selection for dupilumab in uncontrolled COPD with type 2 inflammation (BEC ≥ 300 cells/µL), aligned with the TGA-approved information and disseminated through multiple channels. The submission stated patient-focused resources will be developed to support an understanding of the condition, treatment, and potential side effects. The Sub-Committees noted that the submission assumed one nurse practitioner visit for 40 minutes for patient education on administration and then all future treatments are self-administered. The Sub-Committees considered that it is likely that repeat education on administration will be required for some patients. For those patients who can't self-administer, there was nothing to support administration except an acknowledgement patients may need health professional assistance to support administration. The Sub-Committees considered that patients will need continued support to ensure optimised inhaler technique before and after starting dupilumab.

Financial Management – Risk Sharing Arrangements

6.67 The submission proposed a risk sharing arrangement whereby the sponsor would rebate a maximum of [redacted]% of any expenditure (Commonwealth Payment) above the agreed utilisation estimates, with the remaining [redacted]% absorbed by the Commonwealth.

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

7 PBAC Outcome

7.1 The PBAC recommended the listing of dupilumab as an add-on maintenance treatment for adults with uncontrolled chronic obstructive pulmonary disease (COPD) and type 2 inflammation (defined by the submission as blood eosinophil count (BEC) ≥ 300 cells/µL). The PBAC was satisfied that dupilumab provides, for some patients, a significant improvement in efficacy over triple inhaled therapy alone. The PBAC noted that dupilumab plus triple inhaled therapy significantly reduced the annualised rate of moderate/severe acute exacerbations of COPD (AECOPD) and significantly

extended the time to first moderate/severe AECOPD compared to triple inhaled therapy alone. The PBAC considered that the incremental cost-effectiveness ratio (ICER) was high and uncertain, but that with revisions to the economic model and a price reduction dupilumab could be considered cost-effective. The PBAC noted the revised financial estimates provided in the dupilumab pre-PBAC response and considered that further amendments to the estimates were required. The PBAC considered that the remaining uncertainties could be managed by a risk sharing arrangement (RSA).

7.2 The PBAC noted and welcomed comments from individuals, health care professionals and organisations. The PBAC noted comments describing the significant impact COPD had on the daily lives of patients, impacting their ability to work and socialise, which led to a decline in mental health. The PBAC also noted the comments highlighted the unmet clinical need for this population, noting the lack of effective treatment options for patients who continue to experience exacerbations despite triple inhaled therapy and the resulting continued dependence on oral corticosteroids, which carry substantial toxicity. The PBAC noted the comments highlighted the importance of additional treatment options, such as dupilumab, to help manage disease burden, reduce reliance on oral corticosteroids, and ultimately improve long-term outcomes.

7.3 With respect to the proposed restriction, the PBAC proposed that:

- A Section 100, Highly Specialised Drug Program Authority Required (Written) listing was appropriate for both the Initial and Grandfathering treatment phases. A Section 100, Highly Specialised Drugs Program Authority Required (Telephone/Online) listing was appropriate for the continuing treatment phase. The initial treatment restriction should have 6 repeats with 5 repeats for the continuing and grandfathering treatment phases.
- Noting that the indication for use was uncontrolled COPD and that prescribing was restricted to respiratory physicians or general physicians experienced in the management of patients with COPD, initial treatment criteria requiring diagnosis based on FEV_1/FVC ratio or FEV_1 % predicted was not required.
- As per paragraph 3.3, a BEC of at least 300 cells per microlitre in the 12 months prior to commencing treatment was appropriate.
- For patients who had not achieved or who had not sustained a response to treatment, a re-trial after a 12-month break was considered appropriate.
- Clinical criteria specifying that patients must not have achieved adequate control with at least 3 months of an optimised triple inhaled therapy was required in both the initial and grandfathering treatment phases. Triple inhaled therapy was considered to consist of treatment with a long-acting muscarinic agonist (LAMA), long-acting beta-2 agonist (LABA) and inhaled corticosteroid (ICS).

- Patients must have experienced at least one severe COPD exacerbation, or at least two moderate COPD exacerbations in the 12 months prior to treatment. At least one of those exacerbations must have occurred while the patient was taking triple inhaled therapy.
- As per paragraph 3.5, each treatment phase should require dupilumab to be taken in combination with triple inhaled therapy.
- Both the continuing and grandfathering phases should include clinical criteria requiring patients who have received at least 24 weeks of treatment to have both achieved and sustained an adequate response. An adequate response is defined as maintenance (i.e. no change) or a reduction in the number of moderate and/or severe exacerbation/s compared to the baseline levels provided with the initial authority application.
- Should a second biologic be listed for this indication, flow on changes to the restriction in paragraph 8.1 as outlined in paragraph 8.2 were considered appropriate.
- Flow on changes to all PBS-subsidised biological medicine listed for nasal polyps, uncontrolled severe allergic asthma, and uncontrolled severe asthma to prevent concomitant therapy with another biologic listed for these indications including uncontrolled COPD as outlined in paragraph 8.3.

7.4 The PBAC considered that the proposed comparator of triple inhaled therapy was appropriate. The PBAC also considered that mepolizumab was a relevant near market comparator, and noted mepolizumab was also considered by the Committee for the same indication at its March 2026 meeting.

7.5 The PBAC noted that the submission was based on 2 randomised, double-blind, placebo-controlled trials comparing dupilumab + triple inhaled therapy to placebo + triple inhaled therapy alone in patients with uncontrolled COPD and type 2 inflammation, BOREAS (n=939) and NOTUS (n=935). The PBAC noted that dupilumab led to a statistically significant reduction in the annualised rate of moderate/severe AECOPD compared to placebo (BOREAS: relative risk [RR] = 0.705, 95% confidence interval [CI]: 0.58 to 0.86, p=0.0005; NOTUS: RR = 0.664, 95% CI: 0.54 to 0.82, p=0.0002; Pooled intention-to-treat population: RR = 0.687, 95 CI%: 0.60 to 0.79, p<0.0001). The PBAC noted that dupilumab delayed the time to first moderate or severe COPD exacerbation event compared to placebo in BOREAS (hazard ratio [HR] = 0.803, 95% CI: 0.658 to 0.980; p=0.0309) and NOTUS (HR = 0.714, 95% CI: 0.574 to 0.887; p=0.0024). The PBAC also noted that the improvement in pre-BD FEV_1 observed at Week 2 was maintained until around week 44 with a decline evident thereafter (see Figure 1). The PBAC considered that the claim of superior comparative effectiveness compared to triple inhaled therapy alone was reasonable.

7.6 The PBAC noted that treatment emergent adverse events (TEAEs) related to the investigational medicinal product were higher in the dupilumab arm in BOREAS (7.5%

versus 3.8%) and the pooled safety data (5.3% versus 3.9%) with the submission attributing this difference to a higher number of injection site reactions. Overall, the PBAC considered the claim of non-inferior comparative safety compared to triple inhaled therapy alone was reasonable. The PBAC noted the Sub-Committees considered that a longer duration of follow-up was needed to adequately capture the long-term safety of dupilumab in COPD patients.

7.7 The PBAC noted that 2 literature-based indirect treatment comparisons (ITCs) had been identified comparing dupilumab and mepolizumab (see paragraph 6.26). The PBAC noted the primary ITC analysis undertaken by Bhatt et al. (2025) found that dupilumab provided a numerically favourable but not statistically significant reduction (rate ratio = 0.82, 95% CI 0.66–1.01) in the rate of moderate or severe COPD exacerbations compared with mepolizumab. The PBAC noted that the ITC analysis undertaken by Suter et al. (2025) restricted trials to those that required patients to have a BEC 300 cells/µL at inclusion. Suter et al. (2025) reported both dupilumab and mepolizumab were associated with significant reductions in annual exacerbation rates versus placebo, with overlapping 95% confidence intervals. The PBAC recalled that it had previously accepted a claim of non-inferior comparative safety for dupilumab and mepolizumab in its consideration of dupilumab for uncontrolled severe eosinophilic or allergic asthma (see paragraph 6.26). Overall, the PBAC advised that the totality of the data suggested that mepolizumab and dupilumab have similar clinical effectiveness and safety, and that a claim of non-inferior comparative effectiveness and safety would be reasonable.

7.8 The PBAC noted that the submission presented a cost-utility analysis to support the cost-effectiveness of dupilumab plus triple inhaled therapy versus triple inhaled therapy alone. The PBAC acknowledged the key concerns raised by the Sub-Committees (paragraph 6.51). The PBAC noted that the Sub-Committees considered that the 2-year (maintained) FEV_1 treatment effect beyond the trial period in the dupilumab arm should be removed and agreed with the Sub-Committees that the decline in pre-BD FEV_1 from approximately Week 44 (Figure 1) supported this advice. The Sub-Committees also considered that 10 years was the most appropriate time horizon for this patient group. The PBAC also noted that the Sub-Committees considered a reduced case fatality rate (CFR) may be appropriate to account for the likely double counting of mortality due to severe exacerbations. The PBAC also considered that while the rate of exacerbation is regarded as an important clinical endpoint which is directly experienced by patients and represent important changes in symptoms and health status, when used to project longer-term outcomes, such as mortality and long-term decline, such measures function similar to an intermediate or surrogate measure.

7.9 The PBAC noted that the ICER ranged between $55,000 to < $75,000 per quality adjusted life year (QALY) gained and $255,000 to < $355,000 per QALY gained when inputs were adjusted according to the Sub-Committees' recommendations (Table 15). The PBAC noted that the Pre-PBAC Response considered that there was minimal

double counting of mortality related to severe exacerbations in the economic model. However, the PBAC noted in the context of the model structure, agreed with the Sub-Committees that the inclusion of a CFR of 15.6% and standardised mortality rates (SMRs) likely led to an overestimated risk of death due to exacerbations in the economic model. The PBAC considered a CFR of 10% was reasonable to include on top of the base case SMRs. The PBAC noted that, with the revisions to the economic model recommended by the Sub-Committees and a 10% CFR the ICER was $75,000 to < $95,000 per QALY gained. The PBAC considered that in light of uncertainties related to the model's reliance on surrogate endpoints and its unknown long-term clinical impact along with ICERs accepted in similar contexts (see paragraph 6.52), dupilumab would be cost-effective with a price reduction which achieved an ICER of less than $25,000 to < $35,000 per QALY gained.

7.10 The PBAC noted the currently near market comparator mepolizumab was also considered for the same indication at its March 2026 meeting, and that as per paragraph 7.7 the Committee considered a claim of non-inferior comparative effectiveness and safety was reasonable. The PBAC recommended that if both dupilumab and mepolizumab are listed on the PBS the following equi-effective doses would be appropriate for a cost-minimisation approach for the subsequent therapy listed:

- Mepolizumab 100 mg by subcutaneous injection every 4 weeks (13 doses over 1 year)
- Dupilumab 300 mg by subcutaneous injection every 2 weeks (26 doses over 1 year).

7.11 The PBAC noted that both epidemiological sources and PBS 10% sample data were used to estimate the number of patients eligible for dupilumab with an average of these two approaches applied in the submission base case. The PBAC agreed with its Sub-Committees that the resulting estimates were uncertain. The PBAC noted the analysis of the 100% PBS sample which reported the number of prevalent patients for PBS listed single inhaler triple therapies for COPD (Table 19). The PBAC agreed with its Sub-Committees that an approach based on the actual number of treated prevalent patients supplied triple therapy was appropriate and noted the additional suggested revisions to inputs outlined in paragraph 6.61.

7.12 The PBAC noted the pre-PBAC response provided revised financial estimates based on the number of treated prevalent patients supplied triple therapy with inputs as outlined in paragraph 6.62. As outlined in paragraph 6.63, the PBAC considered that the pre-PBAC response estimates should be amended to account for the reduction in open triple therapy observed across time with the inclusion of an additional open triple inhaled therapy population in Year 1 only. With this correction the PBAC considered the approach taken in the pre-PBAC response to estimate the total number of eligible patients was appropriate. The PBAC noted that grandfathered patients were appropriately not separately accounted for in the prevalence-based

approach used in the pre-PBAC response. The PBAC considered the assumption of an uptake rate of [redacted]% in Year 1 increasing to [redacted]% by Year 6 was optimistic but potentially reasonable. However, the PBAC considered the approach taken to applying the uptake rate in the pre-PBAC response estimates was not appropriate. As outlined in paragraph 6.64, the PBAC considered a cumulative approach to uptake should be applied. In addition, as outlined in paragraph 6.65, the PBAC considered that the proportion of patients continuing treatment from the economic model should be used to inform annual treatment persistence. The PBAC considered that, with these amendments and with the price reduction required to achieve cost effectiveness outlined in paragraph 7.9, it would be reasonable to accept the pre-PBAC response revised financial estimates as the basis of establishing a risk sharing arrangement.

7.13 The PBAC considered that the risk of use outside of the proposed patient population (particularly in patients not optimised on triple inhaled therapy) was high and that this along with the remaining uncertainties in the financial estimates could be managed through an RSA with a [redacted]% rebate for expenditure above the annual caps. Should the near market comparator mepolizumab be listed on the PBS before dupilumab is able to proceed to listing, it would be appropriate for dupilumab to join any established RSA with no increase in the caps.

7.14 The PBAC advised that dupilumab is not suitable for prescribing by nurse practitioners.

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

7.16 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met. Specifically, the PBAC found that in the circumstances of its recommendation for dupilumab:

a. The treatment is expected to provide a clinically relevant improvement in the rate and time to next moderate or severe exacerbation over inhaled triple therapy alone, however its effect beyond that observed in the clinical trials remains unclear, and no changes in long-term outcomes such as survival have been established;

b. The treatment is not expected to address a high and urgent unmet clinical need as there are therapies listed on the PBS that can be used in the management of exacerbations. However, the persistent clinical need for therapies that can reduce both exacerbations and reliance on oral corticosteroids in the management of exacerbations was acknowledged;

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

7.17 The PBAC advised that this submission would not be eligible for an Independent Review as it received a positive recommendation.

Outcome:
Recommended

8 Recommended listing

8.1 Add new listing (new indication) as follows:

Initial treatment

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
DUPILUMAB					
dupilumab 300 mg/2mL injection, 2 x 2 mL syringes	NEW (HSD PUBLIC) NEW (HSD PRIVATE) MP	1	2	6	Dupixent®
dupilumab 300 mg/2mL injection, 2 x 2 mL pen devices	NEW (HSD PUBLIC) NEW (HSD PRIVATE) MP	1	2	6	Dupixent®
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: The length of a break in therapy is measured from the date that the relevant PBS-subsidised medicine listed for this PBS indication is ceased during the most recent treatment cycle, until the date of the subsequent application for treatment under a new treatment cycle.					
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: 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					
Indication: Uncontrolled chronic obstructive pulmonary disease (COPD)					
Treatment Phase: Initial treatment (New patients; or Recommencement of treatment in a new treatment cycle following a break in PBS subsidised biological medicine therapy)					
Clinical criteria:					
Patient must not have received PBS-subsidised treatment with a biological medicine for this condition; **OR**					

Patient must have had at least a 12-month break from the most recently approved PBS-subsidised biological medicine for this condition
AND
Clinical criteria:
Patient must have a blood eosinophil count of at least 300 cells per microlitre in the 12 months prior to commencing treatment with this drug in this treatment cycle.
AND
Clinical criteria:
Patient must not have achieved adequate control with at least 3 months of an optimised triple inhaler therapy consisting of: (i) long-acting muscarinic antagonist (LAMA), (ii) a long-acting beta-2 agonist (LABA), (iii) an inhaled corticosteroid (ICS), 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 have experienced at least one severe COPD exacerbation, or at least two moderate COPD exacerbations in the 12 months prior to commencing treatment with this drug in this treatment cycle.
AND
Clinical criteria:
The treatment must be in combination with all of (i) LAMA, (ii) LABA, (iii) ICS in an optimised triple inhaler therapy
AND
Clinical criteria:
The treatment must not be used in combination with and within 4 weeks of another PBS-subsidised biological medicine prescribed for any of: (i) nasal polyps, (ii) uncontrolled severe allergic asthma, (iii) uncontrolled severe asthma, (iv) uncontrolled chronic obstructive pulmonary disease.
AND
Clinical criteria:
Patient must not receive more than 28 weeks of treatment under this restriction
Treatment criteria:
Must be treated by a medical practitioner who is either a (i) respiratory physician, (ii) general physician experienced in the management of patients with this condition.
Prescribing Instructions: For the purpose of administering this restriction, COPD exacerbations in the 12 months prior to starting treatment in this treatment cycle are defined as experiencing: (i) at least 1 severe COPD exacerbation which required hospitalisation AND/OR (ii) 2 or more moderate COPD exacerbations, of which at least: a) one required treatment with systemic corticosteroids and b) one required treatment with systemic corticosteroids or antibiotics. At least one of the moderate or severe COPD exacerbations must have occurred while the patient was taking all of (i) LAMA, (ii) LABA, and (iii) ICS in an optimised triple inhaler therapy.
Prescribing Instructions: The authority application must be via the Online PBS Authorities System, or in writing via HPOS form upload or mail and must include the following: (a) the blood eosinophil count and date; (b) details of the optimised triple inhaler therapy with the combination of LAMA, LABA and ICS (name of treatment, dosage, date of commencement, and duration of therapy); and (c) details of the number and severity of COPD exacerbation(s) experienced in the 12 months prior to commencing treatment with this drug in this treatment cycle including: (i) no. of moderate exacerbations requiring treatment with systemic corticosteroids (ii) no. of moderate exacerbations requiring treatment with antibiotics

(ii) no. of severe exacerbation/s which required hospitalisation The details of the number and the severity of COPD exacerbations are to inform the basis of determining if an adequate response to treatment has been achieved under the continuing treatment restriction. In addition to stating the above details in the authority application, document them in the patient's medical records.
Prescribing Instruction: If the application is submitted through HPOS form upload or mail, it must include: i) details of the proposed prescription; and ii) 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).

Continuing and Grandfather treatment:

MEDICINAL PRODUCT **medicinal product pack**	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
DUPILUMAB					
dupilumab 300 mg/2mL injection, 2 x 2 mL syringes	NEW (HSD PUBLIC) NEW (HSD PRIVATE) MP	1	2	5	Dupixent®
dupilumab 300 mg/2mL injection, 2 x 2 mL pen *devices*	NEW (HSD PUBLIC) NEW (HSD PRIVATE) MP	1	2	5	Dupixent®
Category / Program: ☒ Section 100 – Highly Specialised Drugs Program – Public (Code HB) / Private (Code HS)					
Prescriber type: ☒Medical Practitioners					
Restriction type: ☒ Authority Required – immediate/real time assessment by Services Australia (telephone/online application avenues)					
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					
Indication: Uncontrolled chronic obstructive pulmonary disease (COPD)					
Treatment Phase: Continuing treatment					
Clinical criteria:					
Patient must have received PBS-subsidised treatment with this biological medicine for this condition					
AND					
Clinical criteria:					
Patient must have both achieved and sustained an adequate response to this drug, defined as maintenance (i.e. no change) or reduction in the number of moderate and/or severe COPD exacerbation/s compared to the baseline levels provided with the initial PBS authority application.					
AND					
Clinical criteria:					
The treatment must be in combination with all of (i) LAMA, (ii) LABA, (iii) ICS in an optimised triple inhaler therapy					
AND					
Clinical criteria:					

The treatment must not be used in combination with and within 4 weeks of another PBS-subsidised biological medicine prescribed for any of: (i) nasal polyps, (ii) uncontrolled severe allergic asthma, (iii) uncontrolled severe asthma, (iv) uncontrolled chronic obstructive pulmonary disease.
Treatment criteria:
Must be treated by a medical practitioner who is either a (i) respiratory physician, (ii) general physician experienced in the management of patients with this condition.
Prescribing Instructions: The following must be provided in each continuing PBS authority application and be documented in the patient's medical records: details of the current number and severity of COPD exacerbations compared to baseline levels provided in the initial authority application of this treatment cycle including: (i) no. of moderate exacerbations requiring treatment with systemic corticosteroids (ii) no. of moderate exacerbations requiring treatment with antibiotics (ii) no. of severe exacerbation/s which required hospitalisation
Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).
Restriction Summary [New3] / Treatment of Concept: [New3A]: **Authority Required**
Restriction type: ☒ Authority Required – Authority Required (FULL assessment) in writing only via OPA/post/HPOS upload
Indication: Uncontrolled Chronic obstructive pulmonary disease (COPD)
Treatment Phase: Transitioning from non-PBS to PBS-subsidised supply- Grandfather arrangements
Clinical criteria:
Patient must have previously received non-PBS subsidised treatment with this biological medicine for this PBS indication prior to [listing date]
AND
Clinical criteria:
Patient must have had a blood eosinophil count of at least 300 cells per microlitre in the 12 months prior to commencing non-PBS subsidised treatment with this drug for this condition.
AND
Clinical criteria:
Patient must not have achieved, prior to commencing non-PBS subsidised treatment with this drug for this condition, adequate control with at least 3 months of optimised triple inhaled therapy consisting of: (i) long-acting muscarinic antagonist (LAMA),(ii) a long-acting beta-2 agonist (LABA), (iii) an inhaled corticosteroid (ICS), 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 have experienced at least one severe COPD exacerbation, or at least two moderate COPD exacerbations in the 12 months prior to commencing non-PBS subsidised treatment with this drug for this condition.
AND
Clinical criteria:
The treatment must be in combination with all of (i) LAMA, (ii) LABA, (iii) ICS in an optimised triple inhaler therapy
AND
Clinical criteria

Patient must have both achieved and sustained an adequate response to this drug, defined as maintenance (i.e. no change) or a reduction in the number of moderate and/or severe COPD exacerbation/s compared to the baseline levels provided with this authority application, if they received at least 24 weeks of treatment with this drug for this condition.
AND
Clinical criteria:
The treatment must not be used in combination with and within 4 weeks of another PBS-subsidised biological medicine prescribed for any of: (i) nasal polyps, (ii) uncontrolled severe allergic asthma, (iii) uncontrolled severe asthma, (iv) uncontrolled chronic obstructive pulmonary disease.
Treatment criteria:
Must be treated by a medical practitioner who is either a (i) respiratory physician (ii) general physician experienced in the management of patients with this condition.
Prescribing Instructions: For the purpose of administering this restriction, COPD exacerbations in the 12 months prior to commencing non-PBS subsidised treatment with this drug for this condition, are defined as experiencing: (iii) at least 1 severe COPD exacerbation which required hospitalisation AND/OR (iv) 2 or more moderate COPD exacerbations, of which at least: a) one required treatment with systemic corticosteroids and b) one required treatment with systemic corticosteroids or antibiotics. At least one of the moderate or severe exacerbations must have occurred while the patient was taking all of (i) LAMA, (ii) LABA, and (iii) ICS.
Prescribing Instructions: The authority application must be via the Online PBS Authorities System, or in writing via HPOS form upload or mail and must include the following: (a) the blood eosinophil count and date; (b) details of therapy with a combination of LAMA, LABA and ICS (name of treatment, dosage, date of commencement, and duration of therapy prior to commencing non-PBS subsidised treatment with this drug for this condition); (c) **Baseline exacerbation history:** details of the number and severity of COPD exacerbation(s) experienced in the 12 months immediately prior to commencement of this drug as non-PBS subsidised therapy for this condition including: (i) no. of moderate exacerbations requiring treatment with systemic corticosteroids (ii) no. of moderate exacerbations requiring treatment with antibiotics (iii) no. of severe exacerbation/s which required hospitalisation; and (d) **Assessment of response to treatment where applicable (for patients who have received at least 24 weeks of treatment):** details of the current number and severity of COPD exacerbations compared to baseline levels provided in this authority application including: (i) no. of moderate exacerbations requiring treatment with systemic corticosteroids (ii) no. of moderate exacerbations requiring treatment with antibiotics (iii) no. of severe exacerbation/s which required hospitalisation. The details of the number and the severity of COPD exacerbations are to inform the basis of determining if an adequate response to treatment has been achieved under the continuing treatment restriction. In addition to stating the above details in the authority application, document them in the patient's medical records.
Prescribing Instruction: If the application is submitted through HPOS form upload or mail, it must include: i) details of the proposed prescription; and ii) 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).
Administrative Advice: A Grandfathered patient may qualify for PBS-subsidised treatment under this restriction once only. For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the continuing treatment criteria.

Administrative Advice: This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.
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

8.2 Flow on changes to listing: Should a second biologic be listed for this indication, amend the treatment phase: Initial treatment to state: Initial treatment – *initial 1*, add initial 2 (change of treatment) restriction and the long Administrative Advice as follows.

MEDICINAL PRODUCT **medicinal product pack**	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
DUPILUMAB					
dupilumab 300 mg/2mL injection, 2 x 2 mL syringes	Initial item code (HSD PUBLIC) Initial item code (HSD PRIVATE) MP	1	2	6	Dupixent®
dupilumab 300 mg/2mL injection, 2 x 2 mL pen devices	Initial item code (HSD PUBLIC) Initial item code (HSD PRIVATE) MP	1	2	6	Dupixent®
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: 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
Indication: Uncontrolled chronic obstructive pulmonary disease (COPD)
Treatment Phase: Initial treatment – Initial 2 (Change of treatment)
Clinical criteria:
Patient must have received prior PBS-subsidised treatment with a biological medicine for this condition in this treatment cycle
AND
Clinical criteria:
Patient must have either: (i) not previously received this drug for this condition in the current treatment cycle, (ii) previously received this drug in the current treatment cycle and demonstrated/maintained an adequate clinical response.
AND
Clinical criteria:
The treatment must be in combination with all of (i) LAMA, (ii) LABA, (iii) ICS in an optimised triple inhaler therapy
AND
Clinical criteria:
The treatment must not be used in combination with and within 4 weeks of another PBS-subsidised biological medicine prescribed for any of: (i) nasal polyps, (ii) uncontrolled severe allergic asthma, (iii) uncontrolled severe asthma, (iv) uncontrolled chronic obstructive pulmonary disease.
AND
Clinical criteria:
Patient must not receive more than 28 weeks of treatment under this restriction
Treatment criteria:
Must be treated by a medical practitioner who is either a (i) respiratory physician, (ii) general physician experienced in the management of patients with this condition.
Prescribing Instructions: The authority application must be via the Online PBS Authorities System, or in writing via HPOS form upload or mail and must include the following: (a) details (date and duration of treatment) of prior biological medicine treatment; and (b) The reason for switching therapy (e.g. not achieving adequate response with prior biological therapy, partial response to prior therapy, adverse event to prior therapy) All supporting evidence must be documented in the patient's medical records
Prescribing Instruction: If the application is submitted through HPOS form upload or mail, it must include: (i) details of the proposed prescription; and (ii) 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).

Administrative Advice: **TREATMENT OF PATIENTS WITH UNCONTROLLED CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)** The following information applies to the prescribing under the Pharmaceutical Benefits Scheme (PBS) of the biological medicines for Uncontrolled COPD. 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 COPD'. A patient is eligible for PBS-subsidised treatment with only one biological medicine for 'Uncontrolled COPD' at any one time.

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 (first biologic for COPD listing date X/X/XXXX) is considered to have started a cycle of treatment.
Within the same treatment cycle, a patient cannot trial and not achieve response, or cease to respond to, the same PBS-subsidised biological medicine more than once.
Therefore, in cases where the patient does not achieve 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.
In cases where the patient does not achieve or sustain the response criteria to treatment two times, they are deemed to have completed a single treatment cycle. They must have at least a 12-month break in PBS-subsidised biological medicine therapy before they are eligible to recommence another new treatment cycle [further details are under 'Recommencement of treatment after a treatment break in PBS-subsidised therapy' below].
The length of the break in therapy is measured from the date the most recent treatment with a PBS-subsidised biological medicine is ceased until the date of the first application for recommencement of treatment with a biological medicine under the new treatment cycle.
There is no limit to the number of treatment cycles that a patient may undertake in their lifetime.

How to prescribe PBS-subsidised biological medicine treatment for 'Uncontrolled COPD'
(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 mandatory 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].
All applications for initial treatment will be limited to provide for a maximum of up to 28 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.

(2) Grandfather patients
A patient who commenced treatment with a biological medicine for 'Uncontrolled COPD' prior to [the relevant biological medicine's listing date, specified in the restrictions] and who continues to receive treatment at the time of application, may qualify for treatment under the 'Grandfather' treatment restriction.
A patient may only qualify for PBS-subsidised treatment under this restriction once. A maximum of 24 weeks of treatment will be authorised under this restriction. Following completion of the first PBS-subsidised course, further subsidised treatment must be prescribed under the continuing treatment restriction of the relevant biological medicine.

(3) 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.
(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 did not achieve response 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 ceased to respond to treatment with all 2 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 mandatory break in PBS-subsidised therapy of at least 12 months (in patients who have not achieved or ceased to sustain a response to treatment 2 times within a treatment cycle), must re-qualify through an Initial 1 restriction.

8.3 Flow on changes to all PBS-subsidised biological medicine listed for nasal polyps, uncontrolled severe allergic asthma, and uncontrolled severe asthma to prevent concomitant therapy with another biologic listed for these indications including uncontrolled COPD.

Amend the following clinical criterion with the addition of the text in italics:

Clinical criteria:
The treatment must not be used in combination with and within 4 weeks of another PBS-subsidised biological medicine prescribed for any of: (i) nasal polyps, (ii) uncontrolled severe allergic asthma, (iii) uncontrolled severe asthma, *(iv) uncontrolled chronic obstructive pulmonary disease*.

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

9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

10 Sponsor's Comment

The sponsor had no comment.