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6.11 DUPILUMAB, Injection 200 mg in 1.14 mL single dose prefilled syringe, Injection 200 mg in 1.14 mL single dose prefilled pen, Injection 300 mg in 2 mL single dose prefilled syringe, Injection 300 mg in 2 mL single dose prefilled pen, Dupixent®, Sanofi-Aventis Australia Pty Ltd

1 Purpose of Submission

1.1 In March 2022 the PBAC recommended expanding the listing of dupilumab for the treatment of severe atopic dermatitis (AD) to include patients aged less than 12 years. The Category 3 submission sought PBAC consideration of updated utilisation estimates and a revised Risk Sharing Arrangement (RSA) for the expanded listing of dupilumab. The proposed listing in the submission was for the treatment of chronic severe AD in children aged 6 months to 11 years who have had lesions for at least 6 months from the time of the initial diagnosis affecting either the whole body or the face/hands. The submission also requested minor amendments to the PBS restriction to allow prescribing by pre-filled syringe (PFS) or pre-filled pen (PFP), reduced pack numbers and revised administrative advice for measures of quality of life.

2 Background

Registration status

2.1 Dupilumab was registered by the TGA in June 2023 for the treatment of severe AD in children 6 months to 11 years, under the following indication:

> "Dupixent is indicated for the treatment of severe atopic dermatitis in patients aged 6 months to 11 years old who are candidates for chronic systemic therapy. Dupixent is not intended for episodic use".

2.2 Dupilumab was also registered by the TGA for the treatment of severe AD in children aged 6 to 11 years (August 2021), moderate to severe AD in adults (January 2018) and adolescents aged 12 and above (October 2019), as well as for the treatment of several other conditions (prurigo nodularis, asthma, chronic rhinosinusitis with nasal polyposis and chronic obstructive pulmonary disease).

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Previous PBAC consideration

2.3 Dupilumab is listed on the PBS with (i) a General Schedule Authority Required (Telephone/online PBS Authorities system) listing for chronic severe AD in patients aged 12 years and over, as well as (ii) a Section 100 Highly Specialised Drug (HSD) Authority Required (in writing only via post/HPOS upload) listing for uncontrolled severe asthma in patients aged 6 years and over, which was not the focus of this submission.

2.4 At its March 2022 meeting, the PBAC recommended the listing of dupilumab for the treatment of severe AD in patients aged less than 12 years. The PBAC considered that the clinical evidence suggests the magnitude of benefit in patients aged 6-11 years is similar to that in the adult/adolescent population and the cost-effectiveness was acceptable at the same price per month as for the adult/adolescent population (paragraph 7.1, dupilumab Public Summary Document [PSD], March 2022 PBAC meeting). Following the March 2022 recommendation, the sponsor submitted a Pricing Offer Package to the Department in June 2022, but this was subsequently withdrawn by the sponsor.

2.5 At its July 2024 meeting the PBAC provided further advice regarding the cost-effectiveness, estimated financial implications and RSA for dupilumab for AD in patients aged 12 years and older, in the context of the sponsor's request to otherwise delist dupilumab for this indication from the PBS. Following the PBAC's July 2024 recommendation, the current arrangements give effect to an effective unit price of $[redacted] for dupilumab for AD in patients aged 12+, with a [redacted].

2.6 At its March 2025 meeting, the PBAC recommended dupilumab PFP for severe AD in patients aged <12 years on a cost-minimisation basis to dupilumab PFS, noting that dupilumab PFS has not been listed on the PBS for the paediatric population (paragraph 6.1, dupilumab PSD, March 2025 PBAC meeting). Following the March 2025 recommendation, the sponsor submitted a Pricing Offer Package to the Department in November 2025 for dupilumab in children aged 6 months-11 years. The revised pricing proposal included a higher effective AEMP and substantially increased financial estimates that were not consistent with the PBAC's March 2022 advice and therefore could not be accepted by the Department. The sponsor was informed that a submission would be required for PBAC consideration of the changes.

2.7 Table 1 summarises the key differences between the March 2022 PBAC consideration and the current submission.

Table 1: Key differences in the March 2022 PBAC consideration and the current submission

Components	March 2022 PBAC consideration	July 2026 submission (current)
Requested PBS restriction	The PBAC considered (paras 7.3 and 7.4, dupilumab PSD March 2022): - baseline EASI score should be at least 20 (rather than 21) and the wording in the restrictions for the adolescent/adult population with respect to DLQI was sufficiently inclusive for use of CDLQI in the paediatric listing.	The current submission proposed the following changes: - baseline EASI score of at least 20. - administrative advice to include children's DLQI and IDQoL assessment, and a revised hyperlink for the EASI scoring tool.

<table>
<tr><th>Components</th><th>March 2022 PBAC consideration</th><th>July 2026 submission (current)</th></tr>
<tr><td></td><td>- existing 300 mg listings to be retained, but a prescribing instruction under Q4W regimen to allow no more than 3 repeats for initial treatment and no more than 2 repeats for continuing. The current maximum number of repeats (5) for 300 mg presentation was for Q2W dosing in adults. Children <30 kg is administered 300 mg Q4W, resulting in an extended treatment duration at the maximum number of repeats.
- for paediatrics <12 years, a minimum age was not required.</td><td>- reduced pack numbers for dupilumab 200 mg to three packs (one pack plus two repeats), consistent with 300 mg.
- additional restrictions for prescribing of dupilumab by PFS or PFP in patients aged ≥2 years, consistent with approved PI.
- Patient must be less than 12 years of age</td></tr>
<tr><td>Proposed DPMQ (EMP)</td><td>The proposed published and effective prices for patients aged 6-11 years are:
<table>
<tr><th>Freq</th><th>Popn</th><th>Dose</th><th>Effective EMP (DPMQ)</th><th>Published EMP (DPMQ)</th></tr>
<tr><td>Q4W</td><td>6-11 yo 15-<30 kg</td><td>300 mg PFS</td><td>$[redacted] ($[redacted])</td><td>$3,219.71 ($3,380.91)</td></tr>
<tr><td>Q2W</td><td>6-11 yo 30-<60 kg</td><td>200 mg PFS</td><td>$[redacted] ($[redacted])</td><td>$1,609.86 ($1,754.28)</td></tr>
<tr><td></td><td>6-11 yo ≥60 kg</td><td>300 mg PFS</td><td>$[redacted] ($[redacted])</td><td>$1,609.86 ($1,754.28)</td></tr>
</table>
The submission requested an EMP for 300 mg Q4W to be twice that for 200/300 mg Q2W, to maintain the same monthly treatment cost. There was no price proposed for patients aged <6 years.</td><td>The proposed published and effective prices for patients <12 years are:
<table>
<tr><th>Freq</th><th>Popn</th><th>Dose</th><th>Effective EMP (DPMQ)</th><th>Published EMP (DPMQ)</th></tr>
<tr><td>Q4W</td><td>0.5-5 yo 5-<15 kg</td><td>200 mg PFS/PFP</td><td>$[redacted] ($[redacted])</td><td>$1,609.86 ($1,757.10)</td></tr>
<tr><td></td><td>0.5-11 yo 15-<30 kg</td><td>300 mg PFS/PFP</td><td>$[redacted] ($[redacted])</td><td>$1,609.86 ($1,757.10)</td></tr>
<tr><td>Q2W</td><td>6-11 yo 30-<60 kg</td><td>200 mg PFS/PFP</td><td>$[redacted] ($[redacted])</td><td>$1,609.86 ($1,757.10)</td></tr>
<tr><td></td><td>6-11 yo ≥60 kg</td><td>300 mg PFS/PFP</td><td>$[redacted] ($[redacted])</td><td>$1,609.86 ($1,757.10)</td></tr>
<tr><td>Weighted</td><td>all</td><td>200/300 mg PFS/PFP</td><td>$[redacted] ($[redacted])</td><td>$1,609.86 ($1,757.10)</td></tr>
</table>
The effective prices by dose frequency were unchanged from March 2022, but the sponsor proposed a flat pricing structure for 200 and 300 mg (PFP/PFS) formulations. The submission requested an average weighted effective EMP of $[redacted], assuming a proportional split of 41%:59% for the Q2W:Q4W regimens.</td></tr>
<tr><td>Clinical evidence and clinical claim</td><td>The PBAC considered the claim of superior comparative effectiveness and inferior safety was reasonable (para 6.30 and 6.31, dupilumab PSD March 2022). The submission was based on one trial Study 1652 (AD-1652), comparing dupilumab + TCS to placebo + TCS in patients aged ≥6 to <11 years with severe AD inadequately controlled with topical therapies. Patients on dupilumab received either 300 mg Q4W or 100 mg Q2W (weight <30kg) or 200 mg Q2W (weight ≥30 kg).</td><td>The submission maintained its claim that in children aged 0.5-11 years with severe AD, dupilumab has superior efficacy compared to SoC and similar (non-inferior) safety profile, with the exception of injection site reactions and conjunctivitis. Data were presented from Study AD-1652 (re-presented), Study AD-1539 (LIBERTY AD PRESCHOOL) for patients aged <6 years and Study AD-1434 (LIBERTY AD PED-OLE). Clinical efficacy in patients 0.5-5 years (200 mg Q4W if ≥5 kg to <15 kg or 300 mg Q4W if ≥15 kg to <30 kg) was consistent with those aged 6-11 years.</td></tr>
<tr><td>Economic evaluation</td><td>The PBAC considered that in patients aged 6-11 years, the cost-effectiveness was acceptable at the same price per month as for the adult/adolescent population (para 7.1, dupilumab PSD March 2022).</td><td>The submission did not present an economic evaluation, given the PBAC previously accepted dupilumab was cost-effective in the proposed population, at the same price per month as for the adult/adolescent population.</td></tr>
<tr><td>Financial estimates</td><td>The financial estimates used an epidemiological approach. The PBAC considered (paras 7.13-7.17, dupilumab PSD March 2022):
- the estimates included patients 6-11 years, whereas the PBAC recommended listing in <12 years.</td><td>The financial estimates used an epidemiological approach. The main changes were:
- inclusion of patients 0.5-11 years, weighing 5-≥60 kg.</td></tr>
</table>

Components	March 2022 PBAC consideration	July 2026 submission (current)
	- a small increase in patient numbers was reasonable to account for use in those <6 years (although dose regimen has not been established for <15 kg). In children aged 4 or 5 years and ≥15 kg, uptake would be up to half the rate in 6-11 years. - it was not reasonable that no patients weigh ≥60 kg and use 300 mg Q2W regimen. However, this assumption did not impact the net financial cost as cost/month is equivalent for each dose regimen. - the financial estimates were sensitive to the uptake rates, which remains uncertain. - include 30.3% sustained response to reflect likely use in practice. - utilisation under the proposed continuing paediatric listing may be overestimated as older children would access dupilumab under adult/adolescent listing once they reach 12 years of age. - remove MBS offsets from reduced specialist visits and reduce offsets from primary care and phototherapy by ≥50%.	- revised prevalence assumptions with paediatric-specific estimates. - increased uptake rates based on real-world prescribing patterns in patients ≥12 years. - split of patient weights used WHO/CDC growth chart distributions. - assumed 30.3% sustained response - use of a weighted effective EMP/DPMQ. - removal of MBS cost of specialist visits and reduced rate of phototherapy by 50%.
RSA	The PBAC considered that 100% rebate would be required for expenditure exceeding the estimated financial cost (paragraph 7.18, dupilumab PSD March 2022).	The sponsor proposed an updated RSA structure to support the listing of dupilumab in patients aged 6 months to less than 12 years with severe AD, whereby the sponsor rebates a maximum of [redacted]% of any Commonwealth expenditure above the annual subsidisation cap.

Blue shading indicates previously seen by the PBAC.
Source: compiled during the evaluation.
AD=atopic dermatitis; EASI=Eczema Area and Severity Index; EMP=ex-manufacture price; Freq=frequency; IDQoL=Infant's Dermatology Quality of Life; PFP=pre-filled pen; PFS=pre-filled syringe; PI=product information; Popn=population; RSA=risk sharing agreement; SoC=standard of care; TCS=topical corticosteroids; QxW=every x week

3 Requested pricing

3.1 Table 2 summarises the recommended dose of dupilumab in children.

Table 2: Recommended dosing regimen of dupilumab in paediatrics aged <12 years (TGA PI)

Age (years)	Weight (kg)	Recommended dose	Scripts required		Device
			Initial (16w)	Continuing (24w)	
0.5 to 5	5 - <15	200 mg Q4W	2	3	PFP ≥2 years PFS ≥6 months
	15 - <30	300 mg Q4W	2	3	
6 to 11	15 - <30	600 mg (2x300 mg) load then 300 mg Q4W	2.5	3	PFP/PFS ≥6 years
	30 - <60	400 mg (2x200 mg) load then 200 mg Q2W	4.5	6	
	≥60	600 mg (2x300 mg) load then 300 mg Q2W	4.5	6	

Source: Table 1.4, p12 of the submission.
PFP=pre-filled pen; PFS=pre-filled syringe; PI=product information; TGA=Therapeutics Goods Administration; QxW=every x week;

3.2 The submission proposed a Special Pricing Arrangement (SPA), with a weighted average effective ex-manufacturer price (EMP) of $[redacted] (DPMQ $[redacted]), assuming a proportional split of 41%:59% across the Q2W and Q4W dosing regimens. The effective prices by dose frequency were unchanged from the March 2022 submission (and subsequent pricing proposals in June 2022 and November 2025); with monthly EMP for Q4W ($[redacted]) being twice that of Q2W ($[redacted]) to maintain equivalent annual

treatment cost on both dose regimens. The submission proposed a flat pricing structure with the same price for the 200 and 300 mg (PFP/PFS) formulations.

3.3 The proposed weighted effective price was higher than the weighted price proposed in the June 2022 pricing package ($[redacted]) based on proportional split of 53.42%:46.58% across Q2W:Q4W dosing and the November 2025 pricing package ($[redacted] based on proportional split of 42.1%:57.9%. The revised weighting was based on the split of packs in the financial estimates. The submission reported that pack use modelling was based on CDC/WHO growth chart weight distributions. The pre-PBAC response clarified that the CDC values were applied for all populations and provided a worksheet including the calculations. The weighted price also relies on assumptions applied in the financial estimates (e.g. the same uptake rates in patients <6 years and those 6-11 years).

3.4 The PBAC previously considered dupilumab would be cost-effective at the same price per month for children as for the adolescent/adult population (paragraph 7.1, dupilumab PSD March 2022 PBAC meeting). However, the proposed cost per month is higher than that of PBS-listed dupilumab in adolescent/adult patients aged ≥12 years ($[redacted]). The submission did not include a modelled economic evaluation to account for the difference between the proposed price of dupilumab for children and the current price in adolescent/adults.

3.5 The submission stated that "for the paediatric population, the commercial realities of the current reimbursement environment necessitate a pricing model that is both appropriate to the characteristics of the paediatric cohort and financially sustainable over the long term, noting that the pricing parameters for this indication are already at their feasible limit within the prevailing geopolitical context". The submission also noted that several other AD therapies have received positive PBAC recommendations in the 12+ population but have not proceeded with PBS listing and it is unclear whether sponsors of these treatments will seek PBS listing for paediatric AD patients.

3.6 The sponsor also stated that since 2022 understanding of the burden of AD in children and the impact of early intervention have progressed significantly, indicating that there are ongoing benefits for paediatric patients that were not incorporated into the previous submission. These include: potential reduction in "atopic march" and disease modification (attenuating effect on the acquisition of new allergies), impact on growth and bone mass density, impact on pain, and impact on QoL for patients and carers.

4 Requested listing

4.1 The submission requested eligibility and response criteria for patients under 12 years that were similar to the recommended listing at the March 2022 and March 2025 PBAC meetings. The submission stated that some amendments were considered necessary and proposed a separate listing for children under 12 years rather than amend the current listing in adolescents and adults. An abridged version of the requested listing has been presented below with unchanged aspects shaded in blue.

MEDICINAL PRODUCT medicinal product pack	Dispensed Price for Max Qty	Max. qty packs	Max. qty units	№.of Rpts	Available brands
DUPILUMAB					
dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes	Effective: $[redacted]; Published: $1,757.10	1	2	2	Dupixent
dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL pen devices	Effective: $[redacted]; Published: $1,757.10	1	2	2	Dupixent
dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes	Effective: $[redacted]; Published: $1,757.10	1	2	2	Dupixent
dupilumab 300 mg/2 mL injection, 2 x 2 mL pen devices	Effective: $[redacted]; Published: $1,757.10	1	2	2	Dupixent
Restriction Summary 12498 / Treatment of Concept: 12497					
Category / Program: ☒ GENERAL - General Schedule (Code GE)					
Prescriber type: ☒Medical Practitioners					
Restriction type: ☒Authority Required (telephone/online PBS Authorities system)					
Administrative Advice: Pharmaceutical benefits that have the form dupilumab injection 200 mg/1.14 mL, 2 x 1.14 mL syringes and pharmaceutical benefits that have the form dupilumab injection 200 mg/1.14 mL, 2 x 1.14 mL pen devices are equivalent for the purposes of substitution					
Administrative Advice: Pharmaceutical benefits that have the form dupilumab injection 300 mg/2 mL, 2 x 2 mL syringes and pharmaceutical benefits that have the form dupilumab injection 300 mg/2 mL, 2 x 2 mL pen devices are equivalent for the purposes of substitution.					
Administrative Advice: Instructions on the use of the Eczema Area and Severity Index and copyright details can be found here: https://www.homeforeczema.org/research/easi-for-clinical-signs.aspx					
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.					
Administrative Advice: An increase in the number of repeats up to a total of 5 may be sought only where the patients is greater than 30 kg and receiving treatment on a fortnightly (Q2W) basis.					
Administrative Advice: Special Pricing Arrangements apply.					
Indication: Chronic severe atopic dermatitis					
Treatment Phase: Initial treatment of the whole body					
Clinical criteria:					
Patient must have a Physicians Global Assessment (PGA) (5-point scale) baseline score of at least 4 as evidence of severe disease despite treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor), for at least 28 days **AND**					
Patient must have an age appropriate Dermatology Life Quality Index (DLQI), children's DLQI, or Infants Dermatology Quality of Life (IDQoL) baseline score (of any value) measured following treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor), for at least 28 days **AND**					
The condition must have had lesions for at least 6 months from the time of the initial diagnosis of chronic severe atopic dermatitis affecting either of: (i) the whole body, (ii) face/hands **AND**					
Patient must have an Eczema Area and Severity Index (EASI) baseline score of at least 20 despite treatment with daily topical therapy (corticosteroid of medium to high potency/calcineurin inhibitor), for at least 28 days **AND**					
The treatment must be the sole PBS-subsidised biological medicine for this PBS indication **AND**					
Patient must not have experienced an inadequate response to this biological medicine in this PBS indication					
Treatment criteria:					
Must be treated by a dermatologist; **OR**					
Must be treated by a clinical immunologist					
Population criteria:					
Patient must be less than 12 years of age					
Prescribing Instructions:					
State each of the qualifying (i) PGA, (ii) EASI and (iii) DLQI/cDLQI/IDQoL scores in the authority application. Acceptable scores can be:					

(a) current scores; or (b) past scores, including those previously quoted in a PBS authority application for another drug listed for this indication. The EASI and DLQI/cDLQI/IDQoL baseline measurements are to form 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. Document the details of the medium to high potency topical corticosteroids (or calcineurin inhibitors) initially trialled in the patient's medical records.
Treatment Phase: Continuing or resuming treatment of the whole body
Clinical criteria:
Patient must have received PBS-subsidised treatment with this biological medicine for the treatment of chronic severe atopic dermatitis affecting the whole body **AND**
Patient must have achieved an adequate response within the first 16 weeks of treatment; OR
Patient must have maintained an adequate response to their most recent course of PBS-subsidised treatment with this biological medicine for this PBS indication if this is the second or subsequent Continuing treatment authority application; OR
Patient must have temporarily ceased treatment for reasons other than lack of response (e.g, vaccination with live vaccines, adverse-effect investigation), thereby being unable to achieve/maintain an adequate response immediately prior to this authority application AND
The treatment must be the sole PBS-subsidised biological medicine for this PBS indication AND
Prescribing Instructions:
For the purposes of this restriction, an adequate response to treatment is defined as: (a) An improvement/maintenance in the Eczema Area and Severity Index (EASI) score of at least 50% compared to baseline; and (b) An improvement/maintenance in Dermatology Life Quality Index (DLQI), children's DLQI (cDLQI), or Infant's Dermatology Quality of Life (IDQoL) score of at least 4 points compared to baseline Where an initial baseline (post-topical corticosteroid, pre-biological medicine) DLQI score was not measured for a patient who had commenced treatment through a clinical trial, early access program or through private, non-PBS-subsidised supply, an absence of worsening in the current DLQI/cDLQI/IDQoL score compared to that measured at the time of the 'Grandfather listing' authority application will suffice as an adequate response for requirement (b) above. State each of the current EASI and DLQI/cDLQI/IDQoL scores for this authority application.

Source: Table ES.3, ppv-vii and Table 1.5, p13 of the submission and Appendix 3 of the submission.

4.2 The submission noted that both the 200 mg and 300 mg presentations of dupilumab are required for dosing regimens every two weeks (Q2W) and every four weeks (Q4W), but the number of prescriptions required differs by weight (200 or 300 mg Q4W for patients <30 kg, 200 mg or 300 mg Q2W for patients ≥30kg). For both presentations, the submission proposed a maximum quantity of three packs (one pack plus two repeats) for initial and continuing treatment. This provides at least 20 weeks of initial treatment and 24 weeks of continuing treatment for patients <30 kg, but only 10 weeks of initial treatment and 12 weeks of continuing treatment for patients ≥ 30kg. To account for this, the submission proposed Administrative Advice permitting up to five repeats for patients ≥ 30kg, which would provide up to 22 weeks of initial treatment and 24 weeks of continuing treatment for those patients. This approach differs from the recommendation at the March 2022 PBAC meeting for a maximum of five repeats in conjunction with prescriber directions to seek a lower number of repeat prescriptions in patients <30 kg (page 38, dupilumab PSD March 2022 PBAC Meeting). The pre-PBAC response indicated that the sponsor was also supportive of the March 2022 approach (five repeats).

4.3 The requested restriction required patients to be less than 12 years of age, without a minimum age for access to treatment, consistent with the March 2022 PBAC

recommendation. As patients must have had lesions for at least 6 months from the time of the initial diagnosis, patients would be eligible from 6 months of age in practice, which was consistent the TGA indication and the new trial evidence from Study AD 1549.

4.4 The submission proposed minor amendments to the requested restriction to explicitly include the Infant's Dermatology Quality of Life (IDQoL) assessment and a children's Dermatology Life Quality Index (cDLQI), in addition to the standard DLQI. The IDQoL is a validated, age-appropriate tool specifically designed for infants and toddlers under four years of age and, like DLQI and cDLQI, was developed by Cardiff University, employs the same 0–30 scoring range, and measures the same underlying construct of dermatology-related QoL. However, this may complicate assessments of response as a patient grows and utilises different assessment tools (IDQoL to cDLQI to DLQI). The continuing restriction requires patients to have improved in quality of life by score of at least 4 points compared to baseline.

4.5 The submission also included an updated active hyperlink for the Eczema Area and Severity Index (EASI) scoring tool to support consistent disease-severity assessment. The sponsor also requested that the same updates to the hyperlink be applied to the 12-years-and-over restriction for alignment.

4.6 Following the March 2025 PBAC recommendation, the PFP device is now registered. Duplicate PBS restrictions are required to allow prescribing of either the PFS or PFP device types. Consistent with Product Information (PI), administrative advice states that the PFP may only be supplied to patients aged ≥2 years. A-flagging between PFS and PFP presentations will support flexible dispensing.

4.7 The submission did not propose any additional criteria for the <12 years population to ensure treatment in the most appropriate population or stopping rules to manage discontinuation of patients with resolution of AD. The pre-PBAC response maintained that feedback from clinicians indicated that they routinely assess the need for dose extension and ongoing treatment in an individualised way. The response noted that cessation of treatment would only be considered following a period of dose extension during which disease control is maintained. The pre-PBAC response suggested that a prescriber note regarding treatment cessation would provide the requisite flexibility without compromising individualised patient care.

5 Consideration of the evidence

Sponsor hearing

5.1 There was no hearing for this item.

Consumer inputs

5.2 The PBAC noted and welcomed the input from individuals (136), health care professionals (59) and organisations (7) via the Office of Health Technology Assessment Consultation Hub. The PBAC also recalled input received from individuals,

health care professionals and organisations in relation to the dupilumab submission considered at its March 2022 meeting and noted that the issues identified were largely unchanged.

5.3 Input from health care professionals was predominantly from dermatologists (30), immunologists/allergists (10), and nurse practitioners working in paediatric dermatology settings (3). Severe dermatitis was described by health care providers and individuals as having broad and substantial effects including: intense itch; pain; sleep disruption; irritability; poor concentration; recurrent skin infections; school and developmental impacts; and significant psychosocial burden. Some contributors also noted hospital admissions, as well as negative effects on growth and nutritional impacts. Contributors described dupilumab as a highly effective treatment for appropriately selected children with severe, refractory atopic dermatitis, particularly where conventional therapy has failed. For patients treated via compassionate access programs contributors noted that outcomes mirror those seen in older patients, with significant reductions in disease severity, improved quality of life, and decreased reliance on systemic immunosuppressants. Contributors (mainly parents) noted that when symptoms are better controlled, children are able to sleep through the night, which has a direct impact on their energy levels, behaviour, emotional wellbeing and ability to participate in school and daily activities. One contributor noted a possible additional benefit of dupilumab is the potential to treat multiple allergic co-morbidities such as eczema, asthma and eosinophilic oesophagitis, concurrently. A small number of contributors raised caveats, including limited data on the youngest infants, the fact that not all children achieve complete control, and uncertainty about whether early treatment may lead to longer-term remission.

5.4 Contributors described dupilumab as having a favourable safety profile compared with existing systemic treatment options for severe paediatric atopic dermatitis, which can also be highly burdensome. A small number also noted uncertainty about long-term safety in young children and suggested ongoing surveillance.

5.5 Contributors described current access to dupilumab for children aged under 12 years as inequitable, inconsistent and often dependent on compassionate access or individual hospital approvals, and identified barriers for rural and regional families. The cost of dupilumab on private prescription was described as prohibitive, and many contributors indicated treatment was unaffordable without PBS-subsidy. Contributors noted current treatment options are inefficient and costly due to ongoing GP visits; specialist appointments; prescriptions; and management of complications (such as infections).

5.6 A smaller number of contributors also emphasised the importance of strict eligibility criteria, specialist prescribing restrictions, and robust gatekeeping to ensure cost-effective use and to avoid inappropriate prescribing, noting that a broad PBS listing could create substantial public cost and risk inappropriate or premature use in children who may respond to optimised conventional management.

5.7 Input was also received from (5) medical organisations and (2) consumer organisations.

5.8 Medical Organisations (Children's Health Queensland, Australasian Society of Clinical Immunology and Allergy, Australian College of Dermatologists, Royal Children's Hospital Melbourne and National Paediatric Medicines Forum) all expressed support for the proposed PBS listing. The main issues raised in the input from medical organisations included:

- The impact of AD on patient quality of life and development for younger patients.
- The current treatment landscape may unintentionally result in some children becoming extremely unwell and experiencing prolonged periods of poorly controlled disease before advanced treatment pathways are explored.
- Severe disease can lead to emergency presentations and hospital admissions for infections or uncontrolled flares, which carry substantial costs for the healthcare system.
- Robust clinical trial data and post-marketing experience demonstrate that dupilumab is safe and effective in children as young as six months of age and can reduce hospitalisations.
- Evidence from overseas experience indicates that early use of dupilumab in younger children can reduce atopic march (including the development of asthma) and have a disease modifying effect, reducing the possibility of chronicity.
- In many cases dupilumab in children can be weaned after approximately 2 years of therapy, with the skin then remaining clear or nearly clear. Effective treatment in the younger age group should eventually reduce the numbers of adolescent and adult patients requiring long term therapy.
- The PBS listing for dupilumab for children 6 months to 11 years should include set criteria for use and limited prescribers (i.e. not be widely available) to ensure supply is directed most appropriately for children in need.
- The importance of equitable access for younger patients, noting the distressing experience of waiting until age 12 to access treatment.

5.9 Input from Consumer organisations Eczema Support Australia and Allergy & anaphylaxis Australia was also supportive of the proposed listing and emphasized the ongoing unmet need experienced by children with severe eczema and their families. The input also provided additional patient perspectives of the impact of AD, and described the effectiveness of dupilumab in treating severe AD and importance of equitable access.

Clinical trials

5.10 The submission presented new clinical evidence for patients aged 6 months to <6 years, which was not available at the time of the March 2022 submission. The new

data included results from one randomised control trial (RCT) comparing dupilumab plus topical corticosteroids (TCS) to placebo plus TCS in patients aged 6 months to <6 years (LIBERTY-AD-PRESCHOOL - 'Study AD-1539') and updated results of an open-label study for patients aged ≥0.5 to <12 years (LIBERTY-AD-PED-OLE - 'Study AD-1434' [0.5y to 12y cohort]).

5.11 The March 2022 submission presented clinical evidence for patients aged ≥6 to <12 years, based on one RCT comparing dupilumab plus TCS to placebo plus TCS in patients aged ≥6 to <12 years (LIBERTY-AD-PEDS – 'Study AD-1652') and results from an open-label extension study (LIBERTY-AD-PED-OLE - 'Study AD-1434' [6y to 12y cohort]). Based on the available evidence, the PBAC considered that the magnitude of benefit in patients aged 6-11 years is similar to that in the adult/adolescent population, and supported the listing of dupilumab for patients aged less than 12 years with severe AD (paragraph 7.1, dupilumab PSD March 2022 PBAC meeting).

5.12 Table 3 presents details of the trials presented in the submission. As a Category 3 submission, no evaluation of the clinical evidence was undertaken.

Table 3: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
LIBERTY-AD-PEDS (Study AD-1652) NCT03345914	A randomised, double-blind, placebo-controlled study to investigate the efficacy and safety of dupilumab administered concomitantly with topical corticosteroids in patients ≥6 years to <12 years of age, with severe atopic dermatitis.	Nov 2019
	Paller AS, Siegfried EC, Thaçi D, Wollenberg A, Cork MJ, Arkwright PD, Gooderham M, Beck LA, Boguniewicz M, Sher L, Weisman J, O'Malley JT, Patel N, Hardin M, Graham NMH, Ruddy M, Sun X, Davis JD, Kamal MA, Khokhar FA, Weinreich DM, Yancopoulos GD, Beazley B, Bansal A, Shumel B. Efficacy and safety of dupilumab with concomitant topical corticosteroids in children 6 to 11 years old with severe atopic dermatitis: A randomized, double-blinded, placebo-controlled phase 3 trial.	J Am Acad Dermatol. 2020. 83(5):1282-1293.
LIBERTY-AD-PRESCHOOL (Study AD-1539) NCT03346434	A Phase 2/3 Study Investigating the Pharmacokinetics, Safety, and Efficacy of Dupilumab in Patients Aged ≥6 Months to <6 Years with Severe Atopic Dermatitis. R668-AD-1539 - Final CSR for Part A	DCO: 09 Sep 2019
	A Phase 2/3 Study Investigating the Pharmacokinetics, Safety, and Efficacy of Dupilumab in Patients Aged ≥6 Months to <6 Years with Moderate-to-Severe Atopic Dermatitis. R668-AD-1539 - Part B Final CSR	DCO: 09 Jul 2021
	Paller AS, Simpson EL, Siegfried EC, Cork MJ, Wollenberg A, Arkwright PD, Soong W, Gonzalez ME, Schneider LC, Sidbury R, Lockshin B, Meltzer S, Wang Z, Mannent LP, Amin N, Sun Y, Laws E, Akinlade B, Dillon M, Kosloski MP, Kamal MA, Dubost-Brama A, Patel N, Weinreich DM, Yancopoulos GD, O'Malley JT, Bansal A; participating investigators. Dupilumab in children aged 6 months to younger than 6 years with uncontrolled atopic dermatitis: a randomised, double-blind, placebo-controlled, phase 3 trial.	Lancet. 2022. 400(10356):908-919.
	Paller AS, Pinter A, Wine Lee L, Aschoff R, Zdybski J, Schnopp C, Praestgaard A, Bansal A, Shumel B, Prescilla R, Bastian M. Efficacy and Safety of Dupilumab Treatment with Concomitant Topical Corticosteroids in Children Aged 6 Months to 5 Years with Severe Atopic Dermatitis.	Adv Ther. 2024. 41(3):1046-1061.
LIBERTY-AD-PED-OLE (Study AD-1434) NCT02612454	An Open-Label Extension Study to Assess the Long-Term Safety and Efficacy of Dupilumab in Patients ≥6 Months to <18 Years of Age with Atopic Dermatitis – CSR results from a third-step analysis conducted on data from patients aged ≥6 months to <6 years old at time of screening into the OLE. Study dates: 15 Oct 2015 to 31 Jul 2021.	Nov 2021
	– CSRs results from a second-step analysis conducted on data from patients aged ≥6 to <12 years old. Study dates: 15 Oct 2015 to 22 Jul 2019	Nov 2019
	– CSR results from a first-step analysis conducted on data from patients aged ≥12 to <18 years old. Study dates: 15 Oct 2015 to 21 Apr 2018	Sep 2018

Blue shading indicates previously seen by the PBAC.
Source: Section 2.1, pp20-21 of the submission.

Comparative effectiveness

5.13 Table 4 summarises the efficacy outcomes at Week 16 in Study AD-1652 and Study AD-1539 – overall trial population and by weight.

Table 4: Efficacy outcomes at Week 16 in Study AD-1652 and Study AD-1539 – overall trial population and by weight groups (baseline IGA=4)

Efficacy outcome	Study AD-1652 (aged 6-11 years)			Study AD-1539 (aged 0.5-5 years)[a]		
	N	n (%)	Difference (95%CI) vs PBO (%)	N	n (%)	Difference (95%CI) vs PBO (%)
IGA 0 or 1, Wk 16 (ITT)						
DUPI 100/200 mg Q2W[b]	122	36 (29.5)	**18.1 (8.28, 27.97)**	-	-	-
DUPI 300 mg Q4W (Study AD-1652), 200/300 mg Q4W (Study AD-1539)[c]	122	40 (32.8)	**21.4 (11.36, 31.45)**	63	9 (14.3)	**12.6 (3.28, 21.82)**
PBO	123	14 (11.4)	-	62	1 (1.7)	-
IGA 0 or 1, Wk 16 (<30kg)						
DUPI 100 mg Q2W[b]	63	13 (20.6)	(p=0.2663)	-	-	-
DUPI 200 mg Q4W[c]	-	-	-	18	2 (11.1)	11.1 (−3.4, 25.6)
DUPI 300 mg Q4W[c]	61	18 (29.5)	**(p=0.0277)**	45	9 (20.0)	**17.6 (5.1, 30.2)**
PBO (≥5 to <15 kg in Study AD-1539)	-	-	-	18	0	-
PBO (<30 kg in Study AD-1652 or ≥15 to <30 kg in Study AD-1539)	61	8 (13.1)	-	44	1 (2.4)	-
IGA 0 or 1, Wk 16 (≥30kg)						
DUPI 200 mg Q2W[b]	59	23 (39.0)	**(p=0.0002)**	-	-	-
DUPI 300 mg Q4W	61	22 (36.1)	**(p=0.005)**	-	-	-
PBO	62	6 (9.7)	-	-	-	-
EASI-75, Wk 16 (ITT)						
DUPI 100/200 mg Q2W[b]	122	82 (67.2)	**40.4 (28.95, 51.82)**	-	-	-
DUPI 300 mg Q4W (Study AD-1652), 200/300 mg Q4W (Study AD-1539)[c]	122	85 (69.7)	**42.8 (31.54, 54.14)**	63	29 (46.0)	**38.9 (24.79, 52.92)**
PBO	123	33 (26.8)	-	62	4 (7.2)	-
EASI-75, Wk 16 (<30kg)						
DUPI 100 mg Q2W[b]	63	38 (60.3)	**(p=0.0003)**	-	-	-
DUPI 200 mg Q4W[c]	-	-	-	18	10 (55.6)	**49.7 (24.1, 75.2)**
DUPI 300 mg Q4W[c]	61	46 (75.4)	**(p<0.0001)**	45	28 (62.2)	**47.9 (30.3, 65.6)**
PBO (≥5 to <15 kg in Study AD-1539)	-	-	-	18	1 (5.9)	-
PBO (<30 kg in Study AD-1652 or ≥15 to <30 kg in Study AD-1539)	61	17 (27.9)	-	44	6 (14.3)	-
EASI-75, Wk 16 (≥30kg)						
DUPI 200 mg Q2W[b]	59	44 (74.6)	**(p<0.0001)**	-	-	-
DUPI 300 mg Q4W	61	39 (63.0)	**(p<0.0001)**	-	-	-
PBO	62	16 (25.8)	-	-	-	-

Blue shading indicates data previously seen by the PBAC.

Source: Table 2.12, p35 of the submission, Table 6, dupilumab PSD March 2022 PBAC meeting.

AD=atopic dermatitis; CI=confidence interval; DUPI=dupilumab; EASI=Eczema Area and Severity Index; IGA=Investigator's Global Assessment; ITT=intention-to-treat; PBO=placebo; QxW=every x week; wk=week;

a In Study AD-1539, similar statistical analysis for the overall population was used for the severe AD (IGA=4) subpopulation. The analysis was prespecified, but the endpoints were not included in the statistical testing hierarchy, therefore, nominal p-values are provided.

b In Study AD-1652, patients either received DUPI Q2W with 100 mg (baseline weight <30kg) or 200 mg (baseline weight ≥30 kg).

c In Study AD-1539, patients either received DUPI 200 mg Q4W (baseline weight ≥5 kg to <15 kg) or 300 mg Q4W (baseline weight ≥15 kg to <30 kg).

5.14 The results from Study AD-1539 (aged 6 months to <6 years) were broadly consistent with Study AD-1652 (aged 6 to <12 years). In patients with severe AD (IGA=4), there was greater improvement in primary and secondary outcomes including IGA and EASI outcomes and quality of life measures (such as Children's Dermatology Life Quality Index (CDLQI) and IDQoL) for dupilumab + TCS compared to placebo + TCS at Week 16 (p<0.05). Long-term data from Study AD-1434 indicated that improvement in disease

severity (IGA and EASI) and quality of life (CDLQI and IDQoL) at Week 16 were maintained to Week 52. The results for patients aged 6 months to <6 years were consistent with those aged 6 to 12 years.

Comparative harms

5.15 In Study AD-1539, the incidence of AEs was similar between groups at Week 16, however patients treated with dupilumab had a higher incidence of conjunctivitis. The safety results were obtained under trial conditions in which patients were administered sham injections in the placebo arm; therefore, additional injection reactions are to be expected for dupilumab treatment in clinical practice compared with placebo. Overall, the safety profile of paediatric patients aged 6 months to <6 years treated with dupilumab through Week 16 was consistent with those in adults and older children (aged 6-17 years) with AD. Long-term data of dupilumab treatment to Week 52 from open-label extension Study AD-1434 was generally consistent with the safety data to Week 16.

Clinical claim

5.16 In paediatric patients aged 6 months to 11 years, with severe AD not adequately controlled with topical therapies, the submission described dupilumab as superior in terms of effectiveness compared to placebo and similar in terms of safety, with the exception of injection site reactions and conjunctivitis compared with placebo. The clinical claim was unchanged from the March 2022 submission.

5.17 Based on evidence from Study AD-1652 (patients aged ≥6 to 11 years), the PBAC previously considered that the claim of superior comparative effectiveness was reasonable (paragraphs 7.7 and 6.30, dupilumab PSD March 2022 PBAC meeting). For safety, the PBAC previously noted conjunctivitis and injection site reactions occurred more frequently in the dupilumab arms of Study AD-1652 and considered a claim of inferior safety was reasonable (paragraph 7.9, dupilumab PSD March 2022 PBAC meeting).

5.18 The PBAC considered that the claim of superior comparative effectiveness for paediatric patients aged 6 months to 11 years was reasonable.

5.19 The PBAC considered that a claim of inferior safety for paediatric patients aged 6 months to 11 years was appropriate.

Estimated PBS usage and financial implications

5.20 This submission was considered by the joint DUSC and ESC Sub-committees ('the Sub-committees').

5.21 The submission applied an epidemiological approach to the financial estimates, consistent with the March 2022 submission. Table 5 summarises the inputs for the

financial estimates for the current submission and March 2022 submission, June 2022 and November 2025 pricing proposals.

Table 5: Key inputs for the financial estimates - current submission, March 2022 submission, June 2022 and November 2025 pricing proposals

Component	March 2022 submission	June 2022 pricing proposal	November 2025 pricing proposal	Current (July 2026) submission	
Epidemiology					
Population	Aged 6-11 yrs (ABS 3222.0 Series B 2022 to 2027)	Aged 2-11 yrs (ABS 3222.0 Series B 2023 to 2028)	Aged 0-11 yrs (ABS 3222.0 Series B 2026 to 2031)	Aged 0.5-11 yrs (ABS 3222.0 Series B 2026 to 2031)	
Prevalence of AD	9% (Metis 2019a)	9% (Metis 2019a)	20% (ESA 2023)	20% (ESA 2023)	
Eligible patients					
Severe AD	5% (Metis 2019a)	Unchanged	Unchanged	Unchanged	
Uncontrolled with existing therapy	100% (assumed)	Unchanged	Unchanged	Unchanged	
EASI score ≥21	95% (sponsor's adult early access program)	Unchanged	Unchanged	Unchanged	
Weight distribution (6-11 yrs)	15-<30kg: 52% 30-<60kg: 48% ≥60kg: 0% (Study AD-1652)	Unchanged	Unchanged	15-<30kg: 54.77% 30-<60kg: 44.67 ≥60kg: 0.57% (CDC growth charts)	
Weight distribution (<6 yrs)	NA	Age 2-5 yrs ≥15kg: 60.38% Excluded (<15 kg): 39.62% (CDC growth charts)	Age 0-5 yrs 5-<15kg: 50% 15-<30kg: 41.67% Excluded (<5kg or <6 months): 8% (CDC growth charts)	Age 0-5 yrs 5-<15kg: 50.17% 15-<30kg: 41.5% Excluded (<5kg or <6 months): 8% (CDC growth charts)	
Utilisation					
Uptake and treatment					
Initiating (6-11 yrs)	Yr 1: [redacted]% Yr 2: [redacted]% Yr 3: [redacted]% Yr 4: [redacted]% Yr 5: [redacted]% Yr 6: [redacted]%	Unchanged	Yr 1: [redacted]% Yr 2: [redacted]% Yr 3: [redacted]% Yr 4: [redacted]% Yr 5: [redacted]% Yr 6: [redacted]%	Initiation Yr 1: [redacted]% Yr 2: [redacted]% Yr 3: [redacted]% Yr 4: [redacted]% Yr 5: [redacted]% Yr 6: [redacted]%	Total Yr 1: [redacted]% Yr 2: [redacted]% Yr 3: [redacted]% Yr 4: [redacted]% Yr 5: [redacted]% Yr 6: [redacted]%
Initiating (<6 yrs)	NA	Age 2-5 yrs: half the uptake of 6-11 yrs	Age 0-5 yrs: same uptake as 6-11 yrs	Age 0-5 yrs: same uptake as 6-11 yrs	
Response (Yr 1) and persistence	Wk 16: 76.9% (Study 1652) Wk 42: 73.6% (CHRONOS) Responders at Wk 42 become continuing patients in the following year.	Unchanged	Unchanged	Unchanged	
Sustained response[e]	SA only[f] Permanent remission: 30.3%[f] Relapse (24-week break): 33.3% No sustained remission (no break): 36.4% (Study AD-1434)	Base case; unchanged rates	Base case; unchanged rates	Base case; unchanged rates	

Component	March 2022 submission	June 2022 pricing proposal	November 2025 pricing proposal	Current (July 2026) submission
Scripts/yr – initial (Yr 1)	Q2W / Q4W Non-response: 6 / 4 response: 13.5 / 7	Unchanged	Q2W / Q4W Non-response: 6 / 3 response: 13.5 / 7	Q2W / Q4W Non-response: 6 / 3 response: 13.5 / 7
Scripts/yr – continuing (with sustained response)	Q2W: 13.04; Q4W: 6.52	Q2W: 9.89; Q4W: 4.95	Q2W: 9.89; Q4W: 4.95	Q2W: 9.89; Q4W: 4.95
Grandfathered patients	[redacted][1]	[redacted][1]	[redacted][2]	[redacted][2]
Cost of medicines				
Dupilumab DPMQ (effective)	Q2W: $[redacted] Q4W: $[redacted]	Weighted average: $[redacted][a]	Weighted average: $[redacted][b]	Weighted average: $[redacted][c]
Co-pay	$29.01 (PBS item 1964J)	$20.97 (PBS item 1964J)	$22.28 (PBS item 1964J)	$15.75 (Dupilumab paediatric asthma items[d])

Blue shading indicates data previously seen by the PBAC.
Source: Table 4.1, pp45-46 of the submission.
AD=atopic dermatitis; CDC=Centers for Disease Control and Prevention; ESA=Eczema Support Australia; EASI=Eczema area and severity index; NA=not applicable; SA=sensitivity analysis; QxW=every x week; yr=year;

a Same effective EMP for Q2W $[redacted] and Q4W $1[redacted] but weighted using proportional split of Q2W 53.42%:Q4W 46.58%. The pricing proposal used patient weight distributions from WHO/CDC Growth Charts for the 2–5 age group and trial-based weight split for 6-11 age group to model the pack use per patient to inform the projected Q2W/Q4W dosing split over six years.

b Same effective EMP for Q2W $[redacted] and Q4W $[redacted] but weighted using proportional split of Q2W 42.1%:Q4W 57.9%. The pricing proposal used patient weight distributions from WHO/CDC Growth Charts for the 0.5–5 age group and trial-based weight split for 6-11 age group to model the pack use per patient to inform the projected Q2W/Q4W dosing split over six years.

c Same effective EMP for Q2W $[redacted] and Q4W $[redacted], but weighted using proportional split of Q2W 41%:Q4W 59%. The submission used patient weight distributions from WHO/CDC Growth Charts for the 0.5–11 age group to model the pack use per patient to inform the projected Q2W/Q4W dosing split over six years.

d PBS items: 15041P, 14959H, 15032E, 14964N, 15021N, 15011C, 14986R, 14988W, 14961K, 14987T, 14978H, 14963M, 14999K, 14962L, 14960J, 14965P, 15043R, 15012D, 15033F, 15022P, 14977G, 15034G, 15042Q, 15000L.

e The submission assumed a proportion of patients that enter remission will relapse after a mean 24 weeks (and miss approximately one cycle (six months) of dosing. Hence, the average "scripts/year" was reduced when sustained remission was included.

f The PBAC considered the financial estimates should include 30.3% sustained response (as in the sensitivity analysis) to better reflect likely use of dupilumab in practice (para 7.15, dupilumab PSD March 2022).

The redacted values correspond to the following ranges:

[1] *< 500*

[2] *500 to < 5,000*

5.22 The following minor issues were identified in the submission overview:

- The submission assumed the number of initial scripts would allow for 20-24 weeks of initial treatment for the 'Week 16 non-responders', which was inconsistent with the requested restriction in which patients were assessed for response after 16 weeks of initial treatment.
- The assumed population split of grandfather patients by age and weight continuing dupilumab (52%:48% for age 6-11 years, 15-30 kg : >30 kg; and 54.55%:45.45% for age <6 years, 5-15 kg : 15-30 kg) could not be verified and was inconsistent with the estimated population split by CDC growth chart weight-for-age distribution (54.8%:45.2% for age 6-11 years, 15-30 kg : >30 kg and 58.5%:41.5% for aged <6 years, 5-15 kg : 15-30 kg).

- The submission applied the average weight percentiles of all children from 0 to 11.5 months then assumed 50% of patients aged <1 year (or 8.3% of patients <5 years) would not be eligible for dupilumab (due to being aged <6 months or <5 kg). However, the average weight percentiles of children from 6.5 to 11.5 months are >5 kg, equating to 100% eligibility in patients 6 months to 5 years. Correcting for this calculation error had minimal impact on the estimated utilisation. Based on the requested restriction, it was reasonable that patients <6 months would not be eligible for treatment.
- The model included cost offsets for the MBS item 23 (Primary care consultations). This item should not be included in the financial estimates.

5.23 Table 6 summarises the estimated patient numbers and costs for the PBS listing of dupilumab for the treatment of severe AD in paediatric patients.

Table 6: Estimated use and financial implications (effective prices)

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use in paediatric patients with severe AD (aged 0.5 to 11 years)						
Eligible patients	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Patients receiving dupilumab	[redacted][2]	[redacted][3]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][5]
Initiating	[redacted][2]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Continuing	[redacted][6]	[redacted][2]	[redacted][2]	[redacted][3]	[redacted][3]	[redacted][4]
Number of scripts dispensed	[redacted][1]	[redacted][7]	[redacted][8]	[redacted][9]	[redacted][9]	[redacted][9]
Q2W	[redacted][4]	[redacted][5]	[redacted][1]	[redacted][10]	[redacted][11]	[redacted][11]
Q4W	[redacted][5]	[redacted][1]	[redacted][11]	[redacted][7]	[redacted][12]	[redacted][13]
Estimated financial implications for dupilumab						
Cost to PBS/RPBS [a] ($)	[redacted][14]	[redacted][15]	[redacted][16]	[redacted][16]	[redacted][16]	[redacted][17]
Net financial implications						
Net cost to PBS/RPBS ($)	[redacted][14]	[redacted]	[redacted][16]	[redacted][16]	[redacted][16]	[redacted][17]
Net cost to MBS ($)	-[redacted][18]	-[redacted][18]	-[redacted][18]	-[redacted][18]	-[redacted][18]	-[redacted][18]
Net cost to Government ($)	[redacted][14]	[redacted]	[redacted][16]	[redacted][16]	[redacted][16]	[redacted][17]
March 2022 submission (aged 6-11 years)						
Eligible patients	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
Net cost to PBS/RPBS ($)	[redacted][18]	[redacted][19]	[redacted][19]	[redacted][19]	[redacted][19]	[redacted][19]
June 2022 pricing proposal (aged 2-11 years)						
Eligible patients	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]
Net cost to PBS/RPBS ($)	[redacted][18]	[redacted][19]	[redacted][19]	[redacted][19]	[redacted][19]	[redacted][19]
November 2025 pricing proposal (aged 0-11 years)						
Eligible patients	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Net cost to PBS/RPBS ($)	[redacted][14]	[redacted]	[redacted][16]	[redacted][16]	[redacted][16]	[redacted][17]

Blue shading indicates data previously seen by the PBAC.

Source: Table 4.11, p55 of the submission, UCM_Workbook_Paed_AD_July_2026_FINAL (1).xlsx, March 2022 – PBAC submission.xlsx, November 2022 – Post PBAC Pricing Package (UCM vB 20221124).xlsx, November 2025 – Pricing Package.xlsx.

MBS=Medical Benefits Scheme; PBS=Pharmaceutical Benefits Scheme; RPBS=Repatriation Pharmaceutical Benefits Scheme.

a Without subtracting co-payments

The redacted values correspond to the following ranges:

[1] 30,000 to < 40,000
[2] 500 to < 5,000
[3] 5,000 to < 10,000
[4] 10,000 to < 20,000
[5] 20,000 to < 30,000
[6] < 500
[7] 60,000 to < 70,000
[8] 80,000 to < 90,000
[9] 100,000 to < 200,000
[10] 40,000 to < 50,000
[11] 50,000 to < 60,000
[12] 70,000 to < 80,000
[13] 90,000 to < 100,000
[14] $50 million to < $60 million[15] $90 million to < $100 million
[16] $100 million to < $200 million
[17] $200 million to < $300 million[18] $0 to < $10 million
[19] $10 million to < $20 million

5.24 The total cost to the PBS/RPBS for listing dupilumab for the treatment of severe AD in paediatric patients (aged 6 months to 11 years) was estimated to be $200 million to < $300 million in Year 6, and a total of $800 million to < $900 million in the first 6 years of listing. Annual costs for dupilumab were [redacted] to [redacted] times higher than in the June 2022 proposal and the total cost over 6 years represented a [redacted]% increase from the March 2022 submission (estimated to be $70 million to < $80 million in the first 6 years of

listing for patients aged 6 to 11 years only). The total costs estimated in year 6 of the estimates ($200 million to < $300 million) were similar to the total agreed caps for dupilumab and upadacitinib in the 12+ population ($200 million to < $300 million in 2026-2027, up to $200 million to < $300 million in 2028-2029) despite being for a much smaller population. The Sub-Committees considered that the rationale provided to support the significant increase in cost from the June 2022 Pricing Proposal to the current increase was poorly supported.

5.25 The net cost to the PBS/RPBS and the Government health budget was high and likely to be overestimated due to the following issues identified in the submission overview and by the Sub-Committees:

- The Sub-Committees considered that the estimates should account for the natural history of the disease with an annual remission rate of around 30% from one year of age. The submission overview noted that the assumed uptake rates (%-%) were uncertain and applied directly to the prevalent pool of patients each year, resulting in patients who discontinued in the previous years starting treatment again i.e. it was estimated that 40,000 to < 50,000 patients initiated dupilumab over the 6 years, which was more than the prevalent pool of eligible patients (30,000 to < 40,000 in Year 1 and 30,000 to < 40,000 in Year 6). Non-responders and patients with sustained response should have been removed from the prevalent pool of patients.
- The submission overview noted that the submission applied the assumed increasing uptake rates to the prevalent pool of patients but also modelled persistence over time for patients who initiate treatment in previous years, resulting in a much higher proportion of prevalent patients on treatment than implied by the uptake rates (i.e., % uptake rate in Year 6, but % of prevalent patients on treatment in Year 6). The Sub-Committees considered that uptake estimates of up to % of the prevalent population are high for this population and may be overestimated. The pre-PBAC response considered that uptake is likely to continue to increase over several years after PBS listing with increased clinician familiarity, mature referral pathways and confidence in long-term outcomes.
- The submission overview and the Sub-Committees noted that the estimates included 500 to < 5,000 grandfathered patients in addition to the prevalent population, which would double count these patients. These patients should instead be subtracted from the eligible population. The pre-PBAC acknowledged that grandfathered patients should be removed from the eligible prevalent population.
- The submission assumed a higher prevalence rate (20%), based on estimates in children aged <14 years reported in Eczema Support Australia (ESA) 2023. The

estimates from the ESA report were based on the publication Zeleke 2023[1], which reported values from various sources, some of which were lifetime prevalence rates that are not applicable to estimating the annual prevalent population. A systematic review by Migliavaca 2024[2] noted the worldwide point prevalence of AD was 11.1% in children and adolescents, with the proportion of severe cases ranging 1.9-7.2%, whereas Volke 2022[3] reported annual prevalence in high income countries (such as Australia) was 16.3% in children aged 0-5 years and 9.4% in those aged 6-12 years. Other evidence from Australia reported the current (2-year) prevalence of AD was 6.5-13.8% in children aged 0-14 years (Chidwick 2020[4]) or for data from the HealthNuts study (Melbourne) the current prevalence decreased from 26.6% in children 1 year old to <15% for patients aged 10 years (Zeleke 2023[5]). The Sub-Committees also considered the prevalence is likely to have been overestimated in children over two years of age. The Sub-Committees noted that current prevalence rates from Australian sources ranged from ~6.5% (in patients aged 10-14, Chidwick et al 2020) to 17% from the HealthNuts study (Zeleke et al, 2022). The Sub-Committees considered a prevalence of 13% would be more appropriate for the financial estimates; noting that a prevalence of 17% would represent the upper limit as it was from a study population with a higher prevalence of the disease as compared to other regions of Australia. The pre-PBAC response acknowledged the uncertainty in prevalence estimates for AD in children and stated that adopting a point estimate of less than 20% may understate the number of children with severe AD who are eligible for treatment.

- The Sub-Committees considered that use of dupilumab in patients with comorbid severe asthma should be considered in estimates, with these patients removed to avoid double-counting. The pre-PBAC response argued that as the asthma restriction is limited to a narrow, highly selected group only a small subset of children with both conditions would qualify under the asthma indication.

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[2] Migliavaca CB, Lazzarini R, Stein C, Escher GN, de Gaspari CN, Dos Santos HWG, Myers DE, Lemeshow AR, Pinheiro MRT, Falavigna M, Pachito DV. Prevalence of Atopic Dermatitis: A Systematic Review and Meta-Analysis. Dermatitis. 2025. 36(6):575-582.

[3] Volke A, Toompere K, Laisaar KT, Oona M, Tisler A, Johannson A, Kallavus K, Lang K, Kiisk E, Uusküla A. 12-month prevalence of atopic dermatitis in resource-rich countries: a systematic review and meta-analysis. Sci Rep. 2022. 12(1):15125.

[4] Chidwick K, Busingye D, Pollack A, Osman R, Yoo J, Blogg S, Rubel D, Smith S. Prevalence, incidence and management of atopic dermatitis in Australian general practice using routinely collected data from MedicineInsight. Australas J Dermatol. 2020. 61(3):e319-e327.

[5] Zeleke BM, Lowe AJ, Dharmage SC, Lopez DJ, Koplin JJ, Peters RL, Soriano VX, Tang MLK, Walters EH, Varigos GA, Lodge CJ, Perret JL, Abramson MJ. Epidemiology of eczema in South-Eastern Australia. Australas J Dermatol. 2023. 64(1):e41-e50.

- The Sub-Committees considered the number of prescriptions per person per year is likely to have been overestimated given the 2023 DUSC analysis of dupilumab for severe atopic dermatitis[6] indicated that in the adult (12+) population 8.4 prescriptions per person per year were used. The Sub-Committees noted that continuation rates accounted for patients with sustained remission (without relapse) and the Sub-Committees considered they were uncertain. However, the Sub-Committees considered that rates of continuation would be captured if reduced scripts per patient per year were applied, consistent with DUSC's 2023 analysis of dupilumab utilisation in AD. The pre-PBAC response considered that this adjustment would underestimate scripts because (1) it includes patients initiating treatment later in the year, (2) discontinuation is already captured in the model, and (3) adult/adolescent utilisation may not be representative of the paediatric population.
- The submission overview noted that the proposed weighted effective price ($[redacted]), based on the same EMPs by dose forms as requested in the March 2022 submission, was higher than the weighted price ($[redacted]) calculated using the current effective price for dupilumab in adolescent/adult patients (EMP $[redacted]).
- The assumed Q2W:Q4W proportional split (41%:59%) was uncertain. Following the March 2022 recommendation of dupilumab in patients aged less than 12 years, the in-principle agreement by the Department was a weighted price calculated at the effective EMP level based on script volumes as per the utilisation and cost model at the time, which constituted a weighting of 53.42%:46.58% across the dosing regimens (based on the dosing in the trial). The split of script numbers is also impacted by assumptions regarding uptake in patients <6 years vs 6-11 years. Using the weighting from the March 2022 estimates at the current effective price of dupilumab (to give a weighted price of $[redacted]) would reduce the net financial impact by [redacted]%.
- Evidence by Wheller 2025[7] from an Australian paediatric hospital indicated of the children aged 6 months to 11 years (N=102) with moderate to severe AD treated with dupilumab, 2% were aged 6 months to 2 years, 24.5% were 3-5 years, 73.5% were aged 6 to 11 years. This was not consistent with the split of patients in the financial estimates where 53% of initiating patients were 6-11 years and uptake rates were assumed to be the same for patients <6 years and 6-11 years.

5.26 Sensitivity analyses showing the impact of some of these assumptions are shown in Table 7.

[6] Analysis of dupilumab for severe atopic dermatitis, September 2023 | Pharmaceutical Benefits Scheme (PBS)

[7] Wheller L, Fordham S, Cao M, Zappala T, Casey G, Jibreal H, Wall N, Dore A. A Real-World Retrospective Cohort Study on the Use of Dupilumab for Severe Atopic Dermatitis in Patients Aged 6 Months to 16 Years. Australas J Dermatol. 2026. 67:89-95.

Table 7: Sensitivity analyses for dupilumab utilisation and financial estimates

	2027	2028	2029	2030	2031	2032	%
Base case[a] ($)	[redacted][1]	[redacted][2]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][4]	[redacted]%
Base case (fixed 4c)[b] ($)	[redacted][1]	[redacted][2]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][4]	
A: Remove GF patient from prevalence							
Remove GF ($)	[redacted][1]	[redacted][2]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][4]	-[redacted]%
B: Revision of scripts per person to 8.4 for 30kg+ and 4.2 for <30kg (base case: 9.89)							
Revision Rx per person ($)	[redacted][1]	[redacted][2]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][4]	-[redacted]%
C: Revised prevalence to 17% (base case: 20%)							
Prevalence 17%($)	[redacted][5]	[redacted][6]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	-[redacted]%
D: Revised prevalence to 13% (base case: 20%)							
Prevalence 13% ($)	[redacted][5]	[redacted][7]	[redacted][2]	[redacted][3]	[redacted][3]	[redacted][3]	-[redacted]%
E: DUPI 12+ script cost (base case: $[redacted])							
$[redacted][c] ($)	[redacted][5]	[redacted][6]	[redacted][8]	[redacted][3]	[redacted][3]	[redacted][3]	-[redacted]%
F: Revised uptake to [redacted]% for Yr 4-6 (initiation) (base case yr 4: [redacted]%, yr 5: [redacted]%, yr 6: [redacted]%)							
20.5% uptake yr 4-6 ($)	[redacted][1]	[redacted][2]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	-[redacted]%
Multivariate sensitivity analyses							
A + D ($)	[redacted][9]	[redacted][1]	[redacted][2]	[redacted][3]	[redacted][3]	[redacted][3]	-[redacted]%
A+D+E[d] ($)	[redacted][9]	[redacted][5]	[redacted][7]	[redacted][2]	[redacted][3]	[redacted][3]	-[redacted]%

Abbreviations: GF = grandfather

Notes:

a base case model 'UCM_Workbook_Paed_AD_July_2026_FINAL (1)'

b activates worksheet 4c. Impact – affected (eff) in the base case model 'UCM_Workbook_Paed_AD_July_2026_FINAL (1)' so the offset is calculated properly at the effective price level. This was applied in all sensitivity analyses.

c Weighted price for DUPI based on the current price for 12+ population.

d Weighted price for DUPI based on the current price for 12+ population in this scenario is $[redacted]

The redacted values correspond to the following ranges:

[1] *$50 million to < $60 million*

[2] *$80 million to < $90 million*

[3] *$100 million to < $200 million*

[4] *$200 million to < $300 million*

[5] *$40 million to < $50 million*

[6] *$70 million to < $80 million*

[7] *$60 million to < $70 million*

[8] *$90 million to < $100 million*

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

Risk-sharing arrangements

5.27 The sponsor proposed to rebate a maximum of [redacted]% of any Commonwealth expenditure above the agreed utilisation estimates.

5.28 The PBAC previously considered that a [redacted]% rebate would be required for expenditure exceeding the estimated financial cost for dupilumab to address the potential for use

outside the intended population, and to address the potential continuing use in patients who do not have adequate response or where patients' disease has resolved and no longer requires treatment. The PBAC also previously noted that a separate cap for the paediatric population would require separate PBS listings for the paediatric and adolescent/adult populations.

5.29 The pre-PBAC response acknowledged that there is uncertainty in population size, uptake rates, and treatment duration, given current PBS listings exclude children aged <12 years and are therefore not captured in the PBS data. The pre-PBAC response suggested that residual uncertainty in the estimates should be managed through the RSA.

6 PBAC Outcome

6.1 The PBAC recalled that it previously recommended dupilumab for severe atopic dermatitis in paediatric patients aged less than 12 years at its March 2022 meeting. The PBAC considered the current submission, which proposed significant changes to the utilisation estimates and Risk Sharing Arrangements (RSA) previously considered, did not support a cost-effective listing and therefore did not provide an appropriate basis for the PBAC to vary its March 2022 recommendation. The PBAC considered that the proposed price (which was higher than for the current PBS listing for dupilumab for atopic dermatitis in patients aged 12 years or more), the increase in the financial estimates, and proposed parameters for the RSA in this submission, were not acceptable. Thus, the PBAC advised that its March 2022 recommendation remained unchanged. The PBAC also provided further advice regarding the restriction.

6.2 The PBAC noted the high number of consultation inputs received from consumers (mainly parents), health care providers and organisations in relation to the proposed listing. The PBAC acknowledged that there is a high clinical need for treatments for severe atopic dermatitis in paediatric patients, noting the disease has a significant impact on many aspects of quality of life and broader impacts on development for younger patients. The PBAC acknowledged the importance of expanding eligibility to enable equitable access to younger patients.

6.3 The PBAC noted that clinical guidelines state that dupilumab is the preferred treatment for patients with severe atopic dermatitis, who have not responded to daily topical therapy (corticosteroid/calcineurin inhibitor) and that few other treatments are available for patients aged <12 years. Other systemic options for this population include cyclosporine, methotrexate, and phototherapy, where it is accessible. The PBAC noted that currently some of the most severely affected patients are managed in public hospitals and are able to access dupilumab though hospital formularies. The PBAC also noted that a substantial number of patients are currently accessing subsidised treatment via a compassionate access program. Patients may also access dupilumab via private prescription, though costs are prohibitive. The PBAC noted the inherent inequity in these existing arrangements.

6.4 The PBAC noted that the submission did not propose any additional restriction criteria for the <12 years population to restrict treatment to the most severely affected paediatric population with the highest need. In the context of the price requested for dupilumab, and noting the very large number of patients expected to receive treatment in the revised financial estimates, the PBAC considered that it may be preferable to explore mechanisms to limit treatment to patients with the highest need.

6.5 The PBAC noted that the submission did not propose any restriction criteria (i.e. stopping rules) to manage discontinuation of dupilumab in paediatric patients with resolution of AD. The PBAC noted that paediatric patients have high rates of resolution or substantial improvement of atopic dermatitis with or without treatment and considered that it would be both clinically inappropriate and cost-ineffective for patients to receive ongoing treatment after resolution without a trial of treatment cessation.

6.6 The PBAC noted that the current submission proposed a price per month for paediatric patients that was higher than the current price in the adolescent/adult population (aged 12+). The PBAC maintained its advice that dupilumab would be cost-effective at the same price per month for children as for the adolescent/adult population (paragraph 7.1, dupilumab PSD March 2022 PBAC meeting). The PBAC considered that there was no clear evidence provided to support or quantify any additional benefits for paediatric patients and that at the higher proposed price, use of dupilumab in the paediatric population was not acceptably cost-effective. The PBAC also noted that it was uncertain whether the proposed weighting of Q2W and Q4W dosing was reasonable, as it relied on assumptions applied in the financial estimates (e.g. the same uptake rates in patients <6 years and those 6-11 years). The PBAC noted that its March 2022 advice in relation to pricing already provides for a higher unit price in the paediatric population than in the adolescent/adult population, reflecting the lower average dosing frequency in children.

6.7 The PBAC noted that the current submission included revised financial estimates with annual costs for dupilumab that were [redacted] to [redacted] times higher than in the sponsor's June 2022 proposal. The total cost to the PBS/RPBS for listing dupilumab for the treatment of severe atopic dermatitis in paediatric patients (6 months to 11 years) was estimated to be $800 million to < $900 million in the first 6 years of listing, which was more than [redacted] times that requested in the March 2022 submission (for patients aged 6 to 11 years only). The PBAC considered that the revisions to the inputs informing the financial estimates were not reasonable. Specifically, the PBAC considered that the assumed prevalence (20%) was not supported by the available evidence, which indicated that the prevalence of AD in Australia is likely to be between 6.5% and 17%, with rates at the lower end of the range in older paediatric patients. The PBAC considered that the assumed uptake rates (up to [redacted]% of the prevalent population), appeared to be overestimated and unlikely to be consistent with the expected rates of resolution of AD and cessation of treatment that would be clinically appropriate in the paediatric

population, which did not appear to be adequately captured in the estimates. The PBAC considered, that these issues, along with other issues identified in the submission overview and by the Sub-Committees (see paragraph 5.25) resulted in financial estimates that were likely to be substantially overestimated.

6.8 The submission proposed RSA of financial caps with a rebate of [redacted]% for expenditure above the utilisation estimates. The PBAC considered that the submission did not provide sufficient justification to support this rebate percentage. The PBAC noted that the pre-PBAC response acknowledged that there is uncertainty in population size, uptake rates, and treatment duration for children aged <12 years, and suggested that residual uncertainty should be managed through the RSA. The PBAC considered that the RSA proposed in the submission did not address uncertainty in the utilisation estimates and did not adequately address the potential for use outside the intended population, or the potential continuing use in patients who do not have adequate response or where patients' disease has resolved and no longer requires treatment. Further, the submission did not address the role of the RSA in the 12+ population [redacted] or how this would be accounted for in deriving a cost-effective price for <12 years population.

6.9 Overall, the PBAC considered that the price proposed, the changes to the financial estimates, and the proposed parameters for the RSA were not acceptable. Thus, the PBAC advised that its March 2022 recommendation for dupilumab remained unchanged.

6.10 The PBAC considered that if the sponsor is unable to progress the intent of the March 2022 PBAC recommendation, an alternative approach may be to explore mechanisms to limit treatment to patients with the highest need. The PBAC noted that, depending on the approach, the way forward could include either:

- Reduce the price, substantially reduce the financial estimates, and revise the RSA proposal, so that the listing is cost-effective and the economic and financial risks associated with the listing are adequately managed; or
- Propose revisions to the restriction criteria, allowed prescriber types, restriction authority level, and RSA caps for the paediatric population reflecting a more limited population and requirements for trial of treatment cessation. If a higher cost per month is requested for the paediatric population compared with the adolescent/adult population, a justification for the price based on cost-effectiveness would be required.

6.11 The PBAC provided further advice regarding the restriction that should be applied to the March 2022 recommendation, should it progress. The PBAC advised that:

- revisions to the requested restriction to explicitly include the Infant's Dermatology Quality of Life (IDQoL) assessment and a children's Dermatology Life Quality Index (cDLQI), in addition to the standard DLQI, appeared reasonable.

- it would be reasonable to allow prescribing of either the PFS or PFP device types, with administrative advice to note that the PFP should only be given to patients aged ≥2 years.
- the hyperlink the Eczema Area and Severity Index (EASI) scoring tool in proposed and existing listings can be updated.
- the proposed maximum quantity of three packs (one pack plus two repeats) for initial and continuing treatment, with administrative advice permitting up to five repeats for patients ≥ 30kg, was reasonable.

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

Outcome:
Not recommended

7 Context for Decision

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

8 Sponsor's Comment

The sponsor had no comment.