

6.13 DUPILUMAB,

**Injection 200 mg in 1.14 mL single dose autoinjector,
Injection 300 mg in 2 mL single dose autoinjector,
Dupixent[®],
Sanofi-Aventis Australia Pty Ltd**

1 Purpose of Submission

- 1.1 The Category 4 submission requested listing for two new forms of dupilumab: 200 mg in 1.14 mL and 300 mg in 2 mL single dose autoinjector (hereafter referred to as dupilumab AI) under the same circumstances as the currently listed dupilumab 200 mg in 1.14 mL and 300 mg in 2 mL single dose pre-filled syringe (hereafter referred to as dupilumab PFS).

2 Background

- 2.1 Dupilumab PFS is currently listed on the PBS as a General Schedule Authority Required listing for chronic severe atopic dermatitis (AD) and a Section 100 (Highly Specialised Drugs Program) Authority Required listing for uncontrolled severe asthma in patients aged 12 years and older.
- 2.2 At its March 2022 meeting, the PBAC recommended the Authority Required listing of dupilumab PFS for the treatment of children aged 6 to 11 years with chronic severe AD. As of the November 2022 PBAC meeting, dupilumab PFS had not been listed on the PBS for this indication.

Registration status

- 2.3 Dupilumab AI was registered on the Australian Register of Therapeutic Goods (ARTG) on 3 June 2022. The TGA approved Product Information (PI) states that dupilumab AI is not intended for use in children below 12 years of age, and that the PFS is the appropriate presentation for children 6 to 11 years of age with AD.

Previous PBAC consideration

- 2.4 Dupilumab AI has not been previously considered by the PBAC.

For more detail on PBAC's view, see section 6 PBAC outcome.

3 Requested listing

- 3.1 The submission requested the listing of dupilumab AI under the same conditions as the existing listings for dupilumab PFS.

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- 3.2 Listing of the AI form for the treatment of children aged 6 to 11 years with chronic severe AD was not requested, to be consistent with the TGA approved PI.
- 3.3 The PBAC considered that a caution should be added to the AI form to highlight that it should not be prescribed to children 6-11 years, e.g., ‘the pre-filled pen is not intended for use in children below 12 years of age. For children below 12 years of age with atopic dermatitis, the pre-filled syringe is the appropriate presentation for this population’.
- 3.4 The PBAC considered that the following administrative advice should be added to the listing: ‘Pharmaceutical benefits that have the form dupilumab injections 200 mg/1.14 mL, 2 x 1.14 mL and 300 mg/2 mL, 2 x 2 mL syringes and pharmaceutical benefits that have the form dupilumab injections 200 mg/1.14 mL, 2 x 1.14 mL and 300 mg/2 mL, 2 x 2 mL pen devices, respectively, are equivalent for the purposes of substitution’.

Add new medicinal product pack as follows:

MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	No.of Rpts	Available brands
General Schedule					
DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes	12292Y	1	2	5	Dupixent
DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL pen devices	NEW	1	2	5	Dupixent
Section 100 – Highly Specialised Drugs Program - (Public Hospital)					
DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes	12293B	1	2	8	Dupixent
DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL pen devices	NEW	1	2	8	Dupixent
Section 100 – Highly Specialised Drugs Program - (Private Hospital)					
DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes	12294C	1	2	5	Dupixent
DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL pen devices	NEW	1	2	5	Dupixent
Section 100 – Highly Specialised Drugs Program - (Public Hospital)					
DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes	12302L	1	2	5	Dupixent
DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL pen devices	NEW	1	2	5	Dupixent
Section 100 – Highly Specialised Drugs Program - (Private Hospital)					

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DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes	12310X	1	2	8	Dupixent
DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL pen devices	NEW	1	2	8	Dupixent
Caution [chronic severe atopic dermatitis indication only]		Pen device is not intended for use in children below 12 years of age. For children below 12 years of age with atopic dermatitis, syringe is the appropriate form for this population			
Administrative Advice [New]		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.			

MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
General Schedule					
DUPILUMAB dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes	12291X	1	2	5	Dupixent
DUPILUMAB dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL pen devices	NEW	1	2	5	Dupixent
Section 100 – Highly Specialised Drugs Program - (Public Hospital)					
DUPILUMAB dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes	12309W	1	2	8	Dupixent
DUPILUMAB dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL pen devices	NEW	1	2	8	Dupixent
Section 100 – Highly Specialised Drugs Program - (Private Hospital)					
DUPILUMAB dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes	12313C	1	2	8	Dupixent
DUPILUMAB dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL pen devices	NEW	1	2	8	Dupixent
Section 100 – Highly Specialised Drugs Program - (Private Hospital)					
DUPILUMAB dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes	12316F	1	2	5	Dupixent
DUPILUMAB dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL pen devices	NEW	1	2	5	Dupixent
Section 100 – Highly Specialised Drugs Program - (Public Hospital)					
DUPILUMAB dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes	12318H	1	2	5	Dupixent

DUPILUMAB	NEW	1	2	5	Dupilumab
dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL pen devices					
Caution [chronic severe atopic dermatitis indication only]					
Pen device is not intended for use in children below 12 years of age. For children below 12 years of age with atopic dermatitis, syringe is the appropriate form for this population					
Administrative Advice [New]					
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.					

- 3.5 The submission proposed that dupilumab AI should not be considered equivalent to dupilumab PFS at the pharmacy level (i.e., ‘a’-flagged in the Schedule) due to the requirement for appropriate training in the use of each form.
- 3.6 Historically, the PBAC has not recommended ‘a’-flagging between AI and PFS forms of the same drug (e.g. etanercept November 2021, adalimumab July 2020, certolizumab March 2017).
- 3.7 In November 2020, the PBAC recommending ‘a’-flagging between different adrenaline autoinjector devices (adrenaline Public Summary Document (PSD), November 2020 PBAC meeting). In this instance, the PBAC considered that ‘a’-flagging would assist in the timely dispensing of adrenaline during shortages, and was satisfied that differences in administration techniques would be appropriately managed.

For more detail on PBAC’s view, see section 6 PBAC outcome.

4 Comparator

- 4.1 The submission nominated dupilumab 200 mg in 1.14 mL and 300 mg in 2 mL PFS as the comparator. The PBAC considered that, although dupilumab PFS was an appropriate comparator, there are also other appropriate comparators, including upadacitinib (for chronic severe AD) which was recommended on a cost-minimisation basis with dupilumab (upadacitinib PSD, July 2021 PBAC meeting); and mepolizumab, omalizumab and benralizumab (for uncontrolled severe asthma), noting that the original recommendation for dupilumab was on the basis of cost-minimisation to the least costly of these medicine (dupilumab PSD, November 2020 PBAC meeting).

For more detail on PBAC’s view, see section 6 PBAC outcome.

5 Consideration of the evidence

Clinical trials

5.1 The submission presented two clinical trials as evidence to demonstrate that dupilumab AI is non-inferior to dupilumab PFS in terms of effectiveness and safety. Details of the trials are summarised in Table 1.

Table 1: Trials presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
R668-AD-1607 (NCT03050151)	An open-label, randomized, actual use study of dupilumab autoinjector device in patients with atopic dermatitis Part A CSR– 8 February 2018 Part B CSR – 8 October 2018	8 February 2018 and 8 October 2018
Cohen 2022	Cohen et al. Pharmacokinetics of subcutaneous dupilumab injection with an autoinjector device or prefilled syringe	Clin Pharmacol Drug Dev. 2022, 11(5):675-681

Source: Table 2-1 of the submission

5.2 As a Category 4 submission, no evaluation of the clinical evidence was undertaken.

Clinical claim

5.3 The submission claimed non-inferior comparative effectiveness and safety of dupilumab AI compared with dupilumab PFS.

5.4 The TGA Delegate confirmed that, while separate and distinct goods under subsection 16(1) of the *Therapeutic Goods Act*, dupilumab 200 mg in 1.14 mL AI and 300 mg in 2 mL AI are the same as registered medicines dupilumab 200 mg in 1.14 mL PFS and 300 mg in 2 mL PFS, respectively, except for the container type, packaging and AUST R numbers.

Economic analysis

5.5 The submission presented a cost-minimisation approach comparing dupilumab AI to dupilumab PFS for the respective indications at the published and effective approved ex-manufacturer prices (AEMP). It was assumed that there would be no differences in administration complexity, setting of care, treatment uptake, adherence, and the utilisation of other healthcare resources between these forms of dupilumab.

5.6 The submission estimated the equi-effective doses to be:

- 200 mg in 1.14 mL dupilumab AI = 200 mg in 1.14 mL dupilumab PFS
- 300 mg in 2 mL dupilumab AI = 300 mg in 2 mL dupilumab PFS

5.7 While not a matter for the PBAC, the submission stated that Section 99ACB of the Act, which pertains to first new brand price reductions for brands of pharmaceutical items that are not combination items, does not apply to dupilumab AI, as the exemption criteria specified in subsection (3A) have been met.

5.8 As a Category 4 submission, the economic analysis has not been independently evaluated.

Estimated PBS utilisation and financial implications

- 5.9 The submission adopted a market share approach to estimate the net financial impact of listing the AI form of dupilumab. The submission assumed that dupilumab AI is expected to substitute for dupilumab PFS on a 1:1 basis at the same published and effective prices. As such, the submission estimated the requested listing of dupilumab AI to be cost neutral to the PBS/RPBS.
- 5.10 The submission noted the existing Deeds of Agreement in place for the PFS form of dupilumab and acknowledged that the AI form would be subject to the same Deed arrangements.
- 5.11 As a Category 4 submission, the financial estimates have not been independently evaluated.

Sponsor hearing

- 5.12 There was no hearing for this item.

Consumer comments

- 5.13 The PBAC noted and welcomed input from Asthma Australia via the Consumer Comments facility on the PBS website. Asthma Australia noted that the existing dupilumab PFS requires careful assembly and administration, which may be difficult for some users, and comes with a risk of injury, contamination, or maladministration. Asthma Australia also reported that some consumers have expressed concern about the invasiveness of the PFS. Asthma Australia considered that the AI, which in contrast to the PFS is all-in-one device, will allow seamless administration and safe handling of the medicine.

6 PBAC Outcome

- 6.1 The PBAC recommended the listing of two new forms of dupilumab: 200 mg in 1.14 mL and 300 mg in 2 mL single dose AI under the same circumstances as the currently listed dupilumab 200 mg in 1.14 mL and 300 mg in 2 mL single dose PFS.
- 6.2 The PBAC recommended the listing on a cost-minimisation basis compared to the lowest-cost comparator in each of the relevant indications.
- 6.3 The PBAC considered that, although dupilumab PFS was an appropriate comparator, there were also other appropriate comparators, such as upadacitinib (for chronic severe AD) and mepolizumab, omalizumab and benralizumab (for uncontrolled severe asthma).
- 6.4 The PBAC considered that the submission's claim that dupilumab AI had non-inferior comparative effectiveness and safety compared with dupilumab PFS was appropriate.
- 6.5 The PBAC noted that the TGA Delegate had confirmed that dupilumab 200 mg in 1.14 mL AI and 300 mg in 2 mL AI were the same as registered medicines dupilumab

200 mg in 1.14 mL PFS and 300 mg in 2 mL PFS, respectively, except for the container type, packaging and AUST R numbers.

- 6.6 The PBAC noted that the submission had estimated the following equi-effective doses, and considered that they were appropriate:
- 200 mg in 1.14 mL dupilumab AI = 200 mg in 1.14 mL dupilumab PFS
 - 300 mg in 2 mL dupilumab AI = 300 mg in 2 mL dupilumab PFS
- 6.7 The PBAC noted that there would be no net financial implications to the PBS/RPBS from listing dupilumab AI as it is expected to substitute for dupilumab PFS on a 1:1 basis and will be cost-minimised to the lowest-cost comparator.
- 6.8 The PBAC noted that its March 2022 recommendation to list dupilumab PFS on the PBS for children aged 6 to 11 years with chronic severe AD had not yet proceeded to listing.
- 6.9 The PBAC considered that, should the listing for dupilumab PFS for children aged 6 to 11 with chronic severe AD occur, a caution should be added to the AI form to highlight that it should not be prescribed to children 6-11 years, e.g., ‘the pre-filled pen is not intended for use in children below 12 years of age. For children below 12 years of age with atopic dermatitis, the pre-filled syringe is the appropriate presentation for this population’.
- 6.10 The PBAC considered that, under Section 101(4AACD) of the *National Health Act 1953*, the AI and PFS forms of the same strength of dupilumab should be considered equivalent for the purposes of substitution (i.e., ‘a’-flagged to each other in the Schedule).
- 6.11 The PBAC noted the sponsor’s request that dupilumab AI not be ‘a’-flagged to dupilumab PFS due to the requirement for appropriate training in the use of each form. However, the PBAC was satisfied that this training could be adequately managed by prescribers and pharmacists.
- 6.12 The PBAC considered that the following administrative advice should be added to the listing: ‘Pharmaceutical benefits that have the form dupilumab injections 200 mg/1.14 mL, 2 x 1.14 mL and 300 mg/2 mL, 2 x 2 mL syringes and pharmaceutical benefits that have the form dupilumab injections 200 mg/1.14 mL, 2 x 1.14 mL and 300 mg/2 mL, 2 x 2 mL pen devices, respectively, are equivalent for the purposes of substitution’.
- 6.13 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because dupilumab AI is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over dupilumab PFS, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health*

(Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022 for Pricing Pathway A were not met.

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

Outcome:

Recommended

7 Recommended listing

7.1 Add new medicinal product pack as follows:

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General Schedule					
DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes	12292Y	1	2	5	Dupixent
DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL pen devices	NEW	1	2	5	Dupixent
Section 100 – Highly Specialised Drugs Program - (Public Hospital)					
DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes	12293B	1	2	8	Dupixent
DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL pen devices	NEW	1	2	8	Dupixent
Section 100 – Highly Specialised Drugs Program - (Private Hospital)					
DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes	12294C	1	2	5	Dupixent
DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL pen devices	NEW	1	2	5	Dupixent
Section 100 – Highly Specialised Drugs Program - (Public Hospital)					
DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes	12302L	1	2	5	Dupixent
DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL pen devices	NEW	1	2	5	Dupixent
Section 100 – Highly Specialised Drugs Program - (Private Hospital)					
DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL syringes	12310X	1	2	8	Dupixent
DUPILUMAB dupilumab 300 mg/2 mL injection, 2 x 2 mL pen devices	NEW	1	2	8	Dupixent

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Concept ID (for internal Dept. use)	
Caution [chronic severe atopic dermatitis indication only]	Pen device is not intended for use in children below 12 years of age. For children below 12 years of age with atopic dermatitis, syringe is the appropriate form for this population
Administrative Advice [New]	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.

MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
General Schedule					
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Section 100 – Highly Specialised Drugs Program - (Public Hospital)					
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DUPILUMAB dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL pen devices	NEW	1	2	8	Dupixent
Section 100 – Highly Specialised Drugs Program - (Private Hospital)					
DUPILUMAB dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes	12316F	1	2	5	Dupixent
DUPILUMAB dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL pen devices	NEW	1	2	5	Dupixent
Section 100 – Highly Specialised Drugs Program - (Public Hospital)					
DUPILUMAB dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL syringes	12318H	1	2	5	Dupixent
DUPILUMAB dupilumab 200 mg/1.14 mL injection, 2 x 1.14 mL pen devices	NEW	1	2	5	Dupixent
Concept ID (for internal Dept. use)					

Caution [chronic severe atopic dermatitis indication only]	Pen device is not intended for use in children below 12 years of age. For children below 12 years of age with atopic dermatitis, syringe is the appropriate form for this population
Administrative Advice [New]	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.

This restriction will be similar to the listed dupilumab syringes' restriction. The restriction is yet to be finalised and may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

8 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.

9 Sponsor's Comment

The sponsor had no comment.