

5.12 Alirocumab, Injection 300 mg in 2 mL single dose autoinjector, Praluent[®], Sanofi-Aventis Australia Pty Ltd

1 Purpose of Submission

- 1.1 The Category 4 submission requested the listing of alirocumab (Praluent[®]) 300 mg in 2 mL single dose autoinjector (hereafter referred to as alirocumab AI) under the same circumstances as the PBS-listed alirocumab 75 mg in 1 mL and 150 mg in 1 mL subcutaneous injection pre-filled pens (hereafter referred to as alirocumab PFP) for the treatment of familial heterozygous hypercholesterolaemia (he-FH) and non-familial hypercholesterolaemia (non-FH)

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

Component	Description
Population	Familial heterozygous hypercholesterolaemia (he-FH) and Non-familial hypercholesterolaemia (non-FH) Relevant criteria currently under revision as an outcome of the July 2022 PBAC meeting
Intervention	Alirocumab 300 mg in 2 mL pre-filled autoinjector pen (without activation button)
Comparator	Alirocumab 2 x 150 mg in 1 mL pre-filled pen (with activation button)
Outcomes	Bioequivalence, effectiveness and safety, dose adherence and patient satisfaction
Clinical claim	Non-inferiority

Source: Table 1-1, p7 of the submission.

2 Background

Registration status

- 2.1 Alirocumab AI was registered by the Therapeutic Goods Administration (TGA) on 17 May 2022 for treatment of primary hypercholesterolaemia (he-FH and non-FH) and prevention of cardiovascular events.

Previous PBAC consideration

- 2.2 Alirocumab was recommended by the PBAC at its March 2019 meeting for treatment of he-FH and at its March 2020 meeting for the treatment of non-FH.
- 2.3 Alirocumab is currently listed on the PBS for treatment of he-FH and non-FH as Authority Required (Telephone/Online) for initial treatment and Authority Required (Streamlined) for continuing treatment.
- 2.4 Alirocumab AI had not been previously considered by the PBAC.

3 Requested listing

- 3.1 The submission requested the listing of alirocumab AI under the same conditions as the existing listings for alirocumab PFP (item codes: 12604J, 12607M, 12608N and 12613W). As such, the restrictions have not been reproduced in full below.
- 3.2 The submission stated there are expected changes to the restriction criteria as a result of the PBAC July 2022 recommendation relating to evolocumab (injection 140 mg in 1 mL single use pre-filled pen and injection 420 mg in 3.5 mL single use pre-filled pen). The recommended restriction changes were to lower the qualifying LDL cholesterol threshold from 2.6 millimoles/L to 1.8 millimoles/L and expand the treatment criteria to include treatment in consultation with a specialist physician (section 8.3, alirocumab Public Summary Document (PSD), July 2022 PBAC meeting). This expanded listing would require a reduction to the current prices of alirocumab. At the time of consideration, the sponsor had not yet lodged a listing proposal with the Department to progress the amendments to expand the eligible population.

Add new medicinal product pack as follows:

Initial treatment: Authority Required (Telephone/online)

MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
ALIROCUMAB Alirocumab injection 75 mg in 1 mL single use pre-filled pen	12613W	1	2	5	Praluent
ALIROCUMAB Alirocumab injection 150 mg in 1 mL single use pre-filled pen	12604J	1	2	5	Praluent
ALIROCUMAB Alirocumab injection 300 mg in 2 mL pen device	NEW	1	1	5	Praluent

Continuing treatment: Authority Required (Streamlined)

MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
ALIROCUMAB Alirocumab injection 75 mg in 1 mL single use pre-filled pen	12607M	1	2	5	Praluent
ALIROCUMAB Alirocumab injection 150 mg in 1 mL single use pre-filled pen	12608N	1	2	5	Praluent
ALIROCUMAB Alirocumab injection 300 mg in 2 mL pen device	NEW	1	1	5	Praluent

4 Comparator

- 4.1 The submission nominated alirocumab 150 mg in 1 mL PFP as the main comparator.
- 4.2 In its pre-PBAC response, the sponsor re-iterated this view, stating that alirocumab 150 mg in 1 mL PFP is the most appropriate comparator as it has the same drug and manner of administration as alirocumab AI, and that the choice of device would be secondary to a clinical decision about which PCSK9 inhibitor to prescribe.
- 4.3 The PBAC recalled that it considered evolocumab an appropriate comparator in previous considerations of alirocumab:
 - March 2019 – alirocumab PFP for he-FH and non-FH (paragraph 4.20, alirocumab Public Summary Document (PSD), March 2020 PBAC Meeting)
 - March 2020 – alirocumab non-FH (paragraph 4.10, alirocumab Public Summary Document (PSD), March 2020 PBAC Meeting)

The PBAC considered that, although alirocumab 150 mg in 1 mL PFP was an appropriate comparator, evolocumab was also an appropriate comparator.

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

5 Consideration of the evidence

Sponsor hearing

- 5.1 There was no hearing for this item.

Consumer comments

- 5.2 The PBAC noted and welcomed input from health care professionals (5) via the Consumer Comments facility on the PBS website. The comments described a range of benefits associated with alirocumab AI, including fewer side effects due to decreased injection frequency and easier and more convenient administration compared to alirocumab PFP.

Clinical claim

- 5.3 The submission claimed non-inferior comparative effectiveness and safety of alirocumab AI compared with alirocumab PFP.
- 5.4 The TGA Delegate confirmed that alirocumab AI is bioequivalent to the registered alirocumab PFP. The Delegate noted that alirocumab AI may provide a benefit for the patient by providing an option to administer a single injection for a monthly dose of 300 mg of alirocumab. The Delegate noted the human factor data suggests a comparable useability between the two devices. The Delegate noted that the safety data appeared to be comparable between the devices, however it was limited by the low number of subjects.

Clinical trials

- 5.5 The submission presented the results of clinical trial MSC14864, and an associated report, as evidence to demonstrate that alirocumab AI is non-inferior to alirocumab PFP in terms of effectiveness and safety. Details of the trials are summarised in Table 2.

Table 2: Trial presented in the submission and associated report presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
MSC14864 NCT03415178	Usability Study of the Commercial Auto-injector Device and the New Auto-injector Device (SYDNEY) in Patients with High or Very High CV Risk with Hypercholesterolemia Not Adequately Controlled with Their Lipid-Modifying Therapy	Unpublished
Frias, Koren et al. 2020	The SYDNEY Device Study: A Multicenter, Randomized, Open-label Usability Study of a 2-mL Alirocumab Autoinjector Device	Clinical Therapeutics 2020;42(1): pages 94-107

Source: Table 2-1, p11 of the submission.

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

Economic analysis

- 5.7 The submission presented a cost-minimisation analysis of alirocumab AI compared with alirocumab PFP for the respective indications at the published dispensed price per maximum quantity (DPMQ) (Table 3). It was assumed that there would be no differences in setting of care, utilisation adherence, persistence, effectiveness, safety or use of other healthcare resources between these strengths or devices of alirocumab.

Table 3: Cost-minimisation analysis presented by the submission

Treatment regimen (Initial and continuing treatment)	Published DPMQ (23 October 2022)	
	1 x 300 mg/2 mL device (proposed)	2 x 150 mg/1 mL devices (current)
300 mg SC Q4W	\$498.31	\$498.31

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

alirocumab 1 x 300 mg in 2 mL AI pen device = alirocumab 2 x 150 mg in 1 mL PFP devices

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

Estimated PBS usage and financial implications

5.10 The submission adopted a market share approach to estimate the net financial impact of listing the AI form of alirocumab. The submission assumed that alirocumab AI is expected to substitute for alirocumab PFP at the same price. As such, the submission estimated the requested listing of alirocumab AI to be nil cost to the PBS/RPBS (Table 4).

5.11 The submission noted that there are expected changes to the cost of alirocumab as a result of the PBAC July 2022 recommendation relating to evolocumab (injection 140 mg in 1 mL single use pre-filled pen and injection 420 mg in 3.5 mL single use pre-filled pen). However, as the listing for alirocumab AI is requested at the same price as alirocumab PFP, any changes in the price of alirocumab PFP will also apply to alirocumab AI and will therefore have no bearing on the estimated net financial implications. The PBAC noted that the potential changes to the cost of alirocumab is a separate matter to the requested addition of the new strength and is addressed in paragraph 3.2.

5.12 The submission noted the existing Deed of Agreement in place for alirocumab and acknowledged that the AI form would be subject to the same Deed arrangements.

5.13 As a Category 4 submission, the financial estimates have not been independently evaluated.

Table 4: Estimated financial implications of alirocumab AI

	2023(\$)	2024(\$)	2025(\$)	2026(\$)	2027(\$)	2028(\$)
PBS						
New listing	1	1	1	1	3	4
Changed listing	2	2	2	2	2	2
Net cost	1	1	1	1	1	1
RPBS						
New listing	1	1	1	1	1	1
Changed listing	2	2	2	2	2	2
Net cost	1	1	1	1	1	1
PBS/RPBS						
Net cost	1	1	1	1	1	1

Source: Table 4-4, p30 of the submission.

The redacted values correspond to the following ranges:

¹ \$0 to <\$10 million

² Net cost saving

³ \$10 million to <\$20 million

⁴ \$20 million to <\$30 million

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

6 PBAC Outcome

6.1 The PBAC recommended the listing of alirocumab AI under the same circumstances as alirocumab PFP.

- 6.2 The PBAC noted the sponsor's view that the appropriate main comparator for alirocumab is two pens of alirocumab 150 mg in 1 mL PFP devices. The PBAC agreed that alirocumab PFP was an appropriate comparator and also considered that evolocumab was also a relevant comparator.
- 6.3 The PBAC considered that the submission's claim that alirocumab AI had non-inferior comparative effectiveness and safety compared with alirocumab PFP was reasonable.
- 6.4 The PBAC noted that the TGA Delegate confirmed that alirocumab AI is bioequivalent to the registered alirocumab PFP.
- 6.5 The PBAC noted that the submission had estimated the following equi-effective doses, and considered that they were appropriate:
- alirocumab 300 mg AI pen device = alirocumab 300 mg PFP device
- 6.6 The PBAC noted that there would be no additional cost to the PBS/RPBS from listing alirocumab AI as it is expected to substitute for alirocumab PFP and will be cost-minimised to the lowest-cost comparator.
- 6.7 The PBAC noted that this submission is not eligible for an Independent Review because it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

Add new medicinal product pack as follows:

Initial treatment: Authority Required (Telephone/online)

MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
ALIROCUMAB Alirocumab injection 75 mg in 1 mL single use pre-filled pen	12613W	1	2	5	Praluent
ALIROCUMAB Alirocumab injection 150 mg in 1 mL single use pre-filled pen	12604J	1	2	5	Praluent
ALIROCUMAB Alirocumab injection 300 mg in 2 mL pen device	NEW	1	1	5	Praluent
Benefit Type 55680: Authority Required					
Prescriber Types Medical Practitioners					
Restriction Summary [11990] / TOC: [12008] Authority Required					

[21155]	Indication: Familial heterozygous hypercholesterolaemia
Restriction Summary 12053 / ToC: 12054: Authority Required	
[25657]	Indication: Non-familial hypercholesterolaemia

Continuing treatment: Authority Required (Streamlined)

MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
ALIROCUMAB Alirocumab injection 75 mg in 1 mL single use pre-filled pen	12607M	1	2	5	Praluent
ALIROCUMAB Alirocumab injection 150 mg in 1 mL single use pre-filled pen	12608N	1	2	5	Praluent
ALIROCUMAB Alirocumab injection 300 mg in 2 mL pen device	NEW	1	1	5	Praluent
Benefit Type 53778: Authority Required: Streamlined					
Prescriber Types Medical Practitioners					
Restriction Summary 12009 / ToC: 12011: Authority Required: Streamlined					
[21155]	Indication: Familial heterozygous hypercholesterolaemia				
Restriction Summary 12044 / ToC: 12010: Authority Required: Streamlined					
[25657]	Indication: Non-familial hypercholesterolaemia				

This restriction will be similar to the currently listed alirocumab pre-filled pen. 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.