

**5.30 Fremanezumab,
Solution for injection 225 mg in 1.5 mL single dose
autoinjector,
Ajovy®,
Teva Pharma Australia Pty Ltd**

1 Purpose of Submission

- 1.1 The Committee Secretariat submission requested listing a new form of fremanezumab 225 mg in 1.5 mL autoinjector (hereafter referred to as fremanezumab AI) under the same circumstances as the PBS-listed fremanezumab 225 mg in 1.5 mL pre-filled syringes (hereafter referred to as fremanezumab PFS).

2 Background

- 2.1 Fremanezumab PFS is currently listed on the Pharmaceutical Benefits Scheme (PBS) as an Authority Required (STREAMLINED) listing for chronic migraine.
- 2.2 A submission to add a new listing with an increased maximum quantity for fremanezumab (Ajovy®) is also being considered by the Pharmaceutical Benefits Advisory Committee (PBAC) in March 2022 (Agenda item 6.12). Should this be recommended, the sponsor has requested the additional maximum quantity listing to be applied to both fremanezumab PFS and fremanezumab AI.

Registration status

- 2.3 Fremanezumab AI was registered on the Australian Register of Therapeutic Goods (ARTG) on 2 June 2021 for the same indication as fremanezumab PFS.

Previous PBAC consideration

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

3 Requested listing

- 3.1 The submission requested a new Authority Required (STREAMLINED) listing for the AI that is consistent with the existing listing for fremanezumab 225 mg / 1.5 mL PFS (initial and continuing listings with item codes 12611R and 12603H respectively).

Add new medicinal products as follows:

MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
FREMANEZUMAB					
fremanezumab 225 mg/1.5 mL injection, 1.5 mL pen device	NEW	1	1	5	Ajovy
fremanezumab 225 mg/1.5 mL injection, 1.5 mL pen device	NEW	1	1	2	Ajovy
fremanezumab 225 mg/1.5 mL injection, 1.5 mL syringe	12603H	1	1	5	Ajovy
fremanezumab 225 mg/1.5 mL injection, 1.5 mL syringe	12611R	1	1	2	Ajovy

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

4 Comparator

4.1 The submission proposed fremanezumab PFS as the comparator. This was appropriate.

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 the input from individuals (18), a health care professional and an organisation via the Consumer Comments facility on the PBS website. The comments described a range of benefits of treatment with fremanezumab AI including the improved ability to self-administer. Individuals also mentioned that listing the AI form will save patients the cost of visiting a health care professional for administration, because they can self-administer the AI form.

5.3 The PBAC noted the comments from Migraine Australia indicating its full support of an AI presentation to allow more autonomy for patients and ease of use during cognitive difficulties.

Clinical trials

5.4 The Therapeutic Goods Administration (TGA) has confirmed bioequivalence between fremanezumab AI and fremanezumab PFS.

5.5 As a Committee Secretariat submission, no evaluation of the clinical evidence was undertaken.

Comparative effectiveness

- 5.6 The submission requested that the AI be considered equally effective as the PFS based on the TGA approved bioequivalence.

Comparative harms

- 5.6 The submission presented information from clinical trials to support its claim that fremanezumab administered via the AI or PFS as a single injection to the abdomen was well tolerated, with some small differences in incidence of adverse events (AE) observed between the AI and PFS treatments and generally mild reactions reported in both groups.
- 5.7 The submission noted the incidence of AE considered by the investigator to be treatment-related was somewhat higher in the AI group (36%) compared with the PFS group (24%).
- 5.8 The submission claimed, based on the key study TV48125-BE-10145 that no meaningful differences were observed between the AI and PFS, with injection site reactions as the most commonly occurring AEs. Treatment-related AEs were mainly of mild severity (AI 32%, PFS 22%) with few treatment-related AEs of moderate severity reported (AI 4%, PFS 2%). A topical redness was reported by some patients at 20 minutes post-dose (AI 24%, PFS 14%), which had largely abated after 1 hour post dose (absent in 94% in AI group and 95% in PFS group).

Clinical claim

- 5.7 The submission claimed non-inferior comparative effectiveness and non-inferior comparative safety of fremanezumab AI compared with fremanezumab PFS.
- 5.8 The PBAC considered that the claim of non-inferior comparative effectiveness was reasonable.
- 5.9 The PBAC considered that the claim of non-inferior comparative safety was reasonable.

Economic analysis

- 5.10 The submission presented a cost-minimisation analysis of fremanezumab AI compared with fremanezumab PFS as a comparison of drug costs only. The sponsor stated that the equi-effective doses are fremanezumab PFS 1 mg = fremanezumab AI 1 mg.
- 5.11 As a Committee Secretariat submission, the economic analysis has not been independently evaluated.

Estimated PBS utilisation and financial implications

- 5.12 The requested dispensed price for maximum quantity (DPMQ) (\$559.10) is equivalent to the DPMQ of fremanezumab PFS listed on the PBS on 1 August 2021.

- 5.13 The submission claimed that this listing is not expected to grow the market and given the price is cost-minimised, the listing of fremanezumab AI is expected to be cost neutral.

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

6 PBAC Outcome

- 6.1 The PBAC recommended the Authority Required (STREAMLINED) listing of fremanezumab (Ajovy®) 225 mg in 1.5 mL AI under the same circumstances as the PBS-listed fremanezumab (Ajovy®) 225 mg in 1.5 mL PFS. The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of fremanezumab AI would be acceptable if it were cost-minimised to fremanezumab PFS for the treatment of chronic migraine.
- 6.2 The PBAC recalled its March 2022 recommendation to amend the existing listing of fremanezumab PFS (for continuing therapy only). The PBAC considered it appropriate to flow this restriction change on to fremanezumab AI such that the continuing treatment for fremanezumab AI will have a maximum quantity of three and one repeat.
- 6.3 The PBAC noted the equi-effective doses are fremanezumab PFS 1mg = fremanezumab AI 1 mg.
- 6.4 The PBAC noted that the TGA determined that fremanezumab AI is bioequivalent to fremanezumab PFS. The PBAC advised that, under section 101(4AACD) of the *National Health Act 1953*, in the Schedule of Pharmaceutical Benefits, fremanezumab AI and fremanezumab PFS should be treated as equivalent ('a'-flagged) to each other for the purposes of substitution.
- 6.5 The PBAC noted that the listing of fremanezumab AI on the PBS is expected to have no change in the overall net cost to the government.
- 6.6 While not a matter for the PBAC, it noted that the listing of fremanezumab AI would trigger a first new brand reduction under Division 3A, Part VII of the *National Health Act 1953*, unless the Minister considers fremanezumab AI is a new presentation and it lists prior to 1 August 2026.
- 6.7 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because fremanezumab AI is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over fremanezumab 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 2009* for Pricing Pathway A were not met.
- 6.8 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

7.1 Add new medicinal product pack (fremanezumab AI) to the existing listings of fremanezumab PFS (12611R and 12603H) with schedule equivalence ('a'-flagged) as follows:

MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max.qty packs	Max.qty units	No.of Rpts	Available brands
FREMANEZUMAB					
fremanezumab 225 mg/1.5 mL injection, 1.5 mL pen device	NEW	3	3	1	Ajovy ^a
fremanezumab 225 mg/1.5 mL injection, 1.5 mL pen device	NEW	1	1	2	Ajovy ^a
fremanezumab 225 mg/1.5 mL injection, 1.5 mL syringe	12603H	43	43	51	Ajovy ^a
fremanezumab 225 mg/1.5 mL injection, 1.5 mL syringe	12611R	1	1	2	Ajovy ^a
Restriction Summary: / ToC:					
Concept ID	Category / Program:				
	GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction Type –				
	<input checked="" type="checkbox"/> Authority Required: Streamlined [New]				
	Administrative Advice:				
	No increase in the maximum quantity or number of units may be authorised.				
	Administrative Advice:				
	No increase in the maximum number of repeats may be authorised.				
	Administrative Advice:				
	Special Pricing Arrangements apply.				
	Indication: Chronic migraine				
	Treatment Phase: Initial treatment				
	Treatment criteria:				
	Must be treated by a neurologist				
	AND				
	Treatment criteria:				
	Patient must not be undergoing concurrent treatment with the following PBS benefits: (i) botulinum toxin type A listed for this PBS indication, (ii) another drug in the same pharmacological class as this drug listed for this PBS indication				
	AND				
	Clinical criteria:				
	Patient must have experienced an average of 15 or more headache days per month, with at least 8 days of migraine, over a period of at least 6 months, prior to commencement of treatment with this medicine for this condition				
	AND				
	Clinical criteria:				

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	Patient must have experienced an inadequate response, intolerance or a contraindication to at least three prophylactic migraine medications prior to commencement of treatment with this drug for this condition
	AND
	Clinical criteria:
	Patient must be appropriately managed by his or her practitioner for medication overuse headache, prior to initiation of treatment with this drug,
	AND
	Population Criteria
	Patient must be aged 18 years or older
	Prescribing instructions: Prophylactic migraine medications are propranolol, amitriptyline, pizotifen, candesartan, verapamil, nortriptyline, sodium valproate or topiramate.
	Prescribing instructions: Patient must have the number of migraine days per month documented in their medical records.
Restriction Summary / ToC:	
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction Type – <input checked="" type="checkbox"/> Authority Required: Streamlined [New]
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Indication: Chronic migraine
	Treatment Phase: Continuing treatment
	Treatment criteria:
	Must be treated by a specialist neurologist or in consultation with a specialist neurologist
	AND
	Treatment criteria:
	Patient must not be undergoing concurrent treatment with the following PBS benefits: (i) botulinum toxin type A listed for this PBS indication, (ii) another drug in the same pharmacological class as this drug listed for this PBS indication
	AND
	Clinical criteria:
	Patient must have previously received PBS-subsidised treatment with this drug for this condition,
	AND
	Clinical criteria:
	Patient must have achieved and maintained a 50% or greater reduction from baseline in the number of migraine days per month,
	AND
	Clinical criteria:

	Patient must continue to be appropriately managed for medication overuse headache.
	Prescribing instructions: Patient must have the number of migraine days per month documented in their medical records.

This restriction 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.