

An addendum to this public summary document has been included at the end of the document.

**6.03 FREMANEZUMAB,
Solution for injection 225 mg in 1.5 mL single dose
pre-filled syringe
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 submission requested a Category 2 General Schedule Authority Required (STREAMLINED) listing of fremanezumab for the treatment of high frequency episodic migraine (HFEM) in patients who have had an inadequate response, intolerance, or a contraindication to at least three prophylactic migraine medications.
- 1.2 The listing was requested on the basis of a cost-minimisation approach (CMA) versus galcanezumab. The key components of the clinical issue addressed in the submission are presented in Table 1.

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

Component	Description
Population	Adult patients with high frequency episodic migraine (HFEM), defined as patients having an average 8 to 14 headache days per month, and who have had an inadequate response, intolerance, or a contraindication to at least three prophylactic migraine medications
Intervention	Fremanezumab
Comparator	Galcanezumab
Outcomes	Mean change from baseline in the number of monthly migraine days ≥50% response rate in terms of monthly migraine days Treatment emergent adverse events
Clinical claim	Fremanezumab is non-inferior to galcanezumab in terms of efficacy and safety in HFEM patients who have an inadequate response, intolerance, or a contraindication to at least three prophylactic migraine medications

Source: Table 1-1, p1 of the submission.

2 Background

Registration status

- 2.1 Fremanezumab (pre-filled syringe) was registered on the Australian Register of Therapeutic Goods on 20 September 2019 for the preventive treatment of migraine in adults. The pre-filled pen device suitable for patient self-administration was registered on 2 June 2021.

Previous PBAC consideration

- 2.2 Fremanezumab has not previously been considered for the proposed PBS population, i.e., patients with HFEM (8 to 14 monthly migraine days) who have failed/tried ≥ 3 prophylactic migraine medications.
- 2.3 Fremanezumab was recommended for chronic migraine at the March 2020 PBAC meeting based on a cost-minimisation approach to Botox (para 6.1, Fremanezumab Public Summary Document [PSD], March 2020 PBAC meeting). It was listed on the PBS on 1 August 2021.
- 2.4 The proposed comparator, galcanezumab (GALC), was recommended by the PBAC in March 2022 for patients with HFEM (8 to 14 migraine days per month) who have failed/tried ≥ 3 prophylactic migraine medications. The PBAC considered galcanezumab would be cost-effective for the HFEM patient population at a price no higher than the current effective price for patients with chronic migraine (para 7.1, Galcanezumab PSD, March 2022 PBAC meeting). Galcanezumab was not listed on the PBS for HFEM at the time of PBAC consideration.

3 Requested listing

- 3.1 Suggestions and additions proposed by the Secretariat are added in italics and suggested deletions are crossed out with strikethrough.

MEDICINAL PRODUCT medicinal product pack	Dispensed Price for Max. Qty	Max. qty packs	Max. qty units	No. of Rpts	Available brands	
FREMANEZUMAB						
Initial						
fremanezumab, 225 mg/1.5 mL injection, 1.5 mL syringe	\$559.07 published price \$ effective price	1	1	2	Ajoyv	
fremanezumab, 225 mg/1.5 mL injection, 1.5 mL pen device ^a		1	1	2		
Continuing						
fremanezumab, 225 mg/1.5 mL injection, 1.5 mL syringe	\$1603.93 published price \$ effective price	3	3	1		
fremanezumab, 225 mg/1.5 mL injection, 1.5 mL pen device ^a		3	3	1		
^a The application for quarterly doses was recommended at the March 2022 PBAC meeting, but was not PBS listed at the time of PBAC consideration.						

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
Restriction type: <input checked="" type="checkbox"/> Authority Required (Streamlined) [<i>amendment to existing code</i>]
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.

*Public Summary Document – November 2022 PBAC Meeting with Out of Session Addendum
August 2023*

Administrative Advice: Special Pricing Arrangements apply.
Episodicity:-
Severity: Chronic and High Frequency Episodic Migraine
Condition: Migraine
Indication: <i>Treatment-resistant</i> 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 at least 8 days of migraine headache days per month, over a period of at least 6 months, prior to commencement of treatment with this medicine for this condition
AND
Clinical criteria: 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
AND
Prescribing instructions: Prophylactic migraine medications are propranolol, amitriptyline, pizotifen, candesartan, verapamil, nortriptyline, sodium valproate or topiramate.
AND
Prescribing instructions: Patient must have the number of migraine days per month documented in their medical records.

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
Restriction type: <input checked="" type="checkbox"/> Authority Required (Streamlined) <i>[amendment to existing code]</i>
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.

Public Summary Document – November 2022 PBAC Meeting with Out of Session Addendum
August 2023

Episodicity:-
Severity: Chronic and High Frequency Episodic Migraine
Condition: Migraine
Indication: <i>Treatment-resistant</i> migraine
Treatment Phase: Continuing treatment
Treatment criteria: Must be treated by a neurologist or in consultation with 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 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
AND
Prescribing instructions: Patient must have the number of migraine days per month documented in their medical records.

Source: Tables 1-8 to 1-10, pp10-12 of the submission, and Table 3-1, p102 of the submission.

Effective DPMQs using the markups that applied from 1 July 2022 for initial and continuing criteria are \$■ and \$■, respectively.

- 3.2 The submission requested a maximum quantity of one 225 mg pre-filled syringe (or autoinjector pen) with two repeats under the initial treatment restriction, providing up to 3 months of treatment. For the continuing treatment restriction, a maximum quantity of three 225 mg pre-filled syringes (or autoinjector pens) with one repeat was requested, providing up to 6 months of treatment. This is consistent with the current fremanezumab listing for chronic migraine, and the recommendations made by the PBAC for fremanezumab (quarterly dosing) in March 2022.
- 3.3 Fremanezumab is currently subject to a Special Pricing Arrangement (SPA) for chronic migraine, with a published Approved Ex-Manufacturer Price (AEMP) of \$488.89 (published Dispensed Price for Maximum Quantity (DPMQ) of \$559.07). The proposed published DPMQ for the quarterly dose listing for patients on continuing treatment (675 mg, given as 3 x 225 mg injections) is \$1603.93.
- 3.4 The proposed restriction includes patients with treatment-resistant chronic and high frequency episodic migraine and would replace the current chronic migraine listing.
- 3.5 The PBAC previously considered that it would be appropriate to amend the phrase ‘migraine days’ to ‘migraine headache days’ in the restriction for galcanezumab in

order to align the clinical criteria with the definitions used in the CONQUER trial (para 3.5, Galcanezumab PSD, March 2022 PBAC meeting). The proposed restriction criteria included the phrase ‘migraine headache days’. While this is consistent with the galcanezumab submission, the evaluation noted it is not consistent with the evidence presented in the submission for fremanezumab where the primary outcome in the FOCUS trial was the change from baseline in the number of monthly migraine days. The PBAC noted the difference in terminology; however, considered it would be appropriate to use the phrase ‘migraine headache days’ in the fremanezumab restriction in order to align the terminology with that recommended for galcanezumab.

4 Population and disease

- 4.1 Migraine is a distinct neurological condition characterised by recurrent episodes of headache that are typically unilateral, pulsating, and associated with moderate or severe pain. The headaches could be exacerbated by routine physical activity and are often associated with other symptoms such as photophobia, phonophobia, nausea, and vomiting. Migraine episodes can significantly impair functional ability at work or school, at home, and in social situations (American Headache Society Consensus Statement 2018).
- 4.2 The submission positioned fremanezumab as an additional option to galcanezumab for use in patients with treatment-resistant HFEM. This subgroup has been previously considered by the PBAC (para 7.1, Galcanezumab PSD, March 2022 PBAC meeting). It is unclear whether HFEM represents a clinically distinct subgroup of migraine. In some cases, it may not be possible to make a definitive diagnosis separating HFEM patients from the episodic migraine population due to the subjective nature of migraine diagnosis and severity, increasing the chance of use in patients with less frequent migraine. The PBAC considered that there would be a risk of use outside the restriction as the HFEM population may not be well defined.
- 4.3 Fremanezumab is a humanised monoclonal antibody that binds the calcitonin gene-related peptide. The recommended dose of fremanezumab is 225 mg monthly (FREM M) or 675 mg every three months (FREM Q) by subcutaneous injection.

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

5 Comparator

- 5.1 The submission nominated galcanezumab as the main comparator because it was recommended by the PBAC for the proposed population (para 7.1, Galcanezumab PSD, March 2022 PBAC meeting). The PBAC agreed with the ESC that galcanezumab was the appropriate comparator, although the PBAC noted it was not currently PBS listed for the proposed population.

- 5.2 The PBAC previously considered fremanezumab and galcanezumab to be non-inferior in terms of safety and efficacy for patients with chronic migraine (para 7.4, Fremanezumab PSD, November 2019 PBAC meeting).

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

6 Consideration of the evidence

Sponsor hearing

- 6.1 There was no hearing for this item.

Consumer comments

- 6.2 The PBAC noted that no consumer comments were received for this item but recalled the comments received previously regarding this population (para 7.2, Galcanezumab PSD, March 2022 PBAC meeting).

Clinical trials

- 6.3 No head-to-head trials comparing fremanezumab to galcanezumab for patients with migraine were identified.
- 6.4 The submission was based on an indirect comparison of two randomised trials:
- FOCUS: A phase III, multi-center, placebo-controlled randomised trial comparing fremanezumab versus placebo in patients with chronic and episodic migraine who have failed 2-4 prior prophylactic treatments (N=838; N=91 for HFEM subgroup).
 - CONQUER: A phase III, multi-center, placebo-controlled randomised trial comparing galcanezumab versus placebo in patients with chronic and episodic migraine who have failed 2-4 prior prophylactic treatments (N=462; N=80 for HFEM subgroup).
- 6.5 An indirect comparison was conducted between fremanezumab and galcanezumab using placebo as the common comparator, based on the HFEM subgroups which were defined post-hoc.
- 6.6 The FOCUS trial was previously considered by the PBAC as part of the November 2019, March 2020, and March 2022 fremanezumab submissions for chronic migraine. The CONQUER trial for galcanezumab was assessed in the November 2020 and March 2022 PBAC meetings for chronic migraine and HFEM, respectively.
- 6.7 In the FOCUS trial, patients were assigned to one of two fremanezumab dosing arms (quarterly, 675 mg and monthly, 225 mg) or matched placebo. The HFEM subgroups in the FOCUS trial comprised 25 patients in the fremanezumab quarterly dosing group, 36 patients in the fremanezumab monthly dosing group, and 30 patients in the placebo group. The HFEM subgroup of CONQUER included 48 patients in the galcanezumab arm and 32 patients in the placebo control.

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

Table 2: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
FOCUS (NCT03308968)	<p>A Multicenter, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled Study with an Open-Label Period to Evaluate the Efficacy and Safety of Fremanezumab for the Prophylactic Treatment of Migraine in Patients with Inadequate Response to Prior Preventive Treatments.</p> <p>Spierings EL, Kärppä M, Ning X, Cohen JM, Campos VR, Yang R, Reuter U. Efficacy and safety of fremanezumab in patients with migraine and inadequate response to prior preventive treatment: subgroup analyses by country of a randomized, placebo-controlled trial.</p> <p>Ashina M, Cohen JM, Galic M, Campos VR, Barash S, Ning X, Kessler Y, Janka L, Diener HC. Efficacy and safety of fremanezumab in patients with episodic and chronic migraine with documented inadequate response to 2 to 4 classes of migraine preventive medications over 6 months of treatment in the phase 3b FOCUS study.</p> <p>Pazdera L, Cohen JM, Ning X, Campos VR, Yang R, Pozo-Rosich P. Fremanezumab for the preventive treatment of migraine: subgroup analysis by number of prior preventive treatments with inadequate response</p> <p>Ferrari MD, Diener HC, Ning X, Galic M, Cohen JM, Yang R, Mueller M, Ahn AH, Schwartz YC, Grozinski-Wolff M, Janka L. Fremanezumab versus placebo for migraine prevention in patients with documented failure to up to four migraine preventive medication classes (FOCUS): a randomised, double-blind, placebo-controlled, phase 3b trial.</p>	<p>March 2019</p> <p>The Journal of Headache and Pain. 2021 Dec;22(1):1-2</p> <p>The Journal of Headache and Pain. 2021 Dec;22(1):1-3</p> <p>Cephalalgia. 2021 Sep;41(10):1075-88</p> <p>The Lancet. 2019 Sep 21;394(10203):1030-40</p>
CONQUER (NCT03559257)	<p>Mulleners, W. M., Kim, B. K., Láinez, M. J., Lanteri-Minet, M., Pozo-Rosich, P., Wang, S., ... & Detke, H. C. (2020). Safety and efficacy of galcanezumab in patients for whom previous migraine preventive medication from two to four categories had failed (CONQUER): a multicentre, randomised, double-blind, placebo-controlled, phase 3b trial.</p> <p>Okonkwo R, Tockhorn-Heidenreich A, Stroud C, Paget MA, Matharu MS, Tassorelli C. Efficacy of galcanezumab in patients with migraine and history of failure to 3–4 preventive medication categories: subgroup analysis from CONQUER study.</p>	<p>The Lancet Neurology. 2020 Oct 1;19(10):814-2</p> <p>The Journal of Headache and Pain. 2021 Dec;22(1):1-1</p>

Source: Table 2-5, p17 of the submission.

6.9 The key features of the randomised trials are summarised in Table 3.

6.10 The key primary and secondary outcomes were change in monthly migraine days and the proportion of patients achieving a $\geq 50\%$ reduction in monthly migraine days. The PBAC previously considered these outcomes (Table 1, Galcanezumab PSD, March 2022 PBAC meeting; para 6.15, Galcanezumab PSD, November 2020 PBAC meeting; Table 1, Fremanezumab PSD, November 2019 PBAC meeting).

6.11 There was a slight difference in the definition of monthly migraine days in both trials. The primary outcome was change from baseline in monthly migraine days (MMDs) in FOCUS, while it was change from baseline in monthly migraine headache days

(MMHDs) in CONQUER. This difference was due to variability in the duration of migraine for it to be counted as a typical migraine episode. The term MMDs has been used herein for consistency.

Table 3: Key features of the included evidence

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)	
Fremanezumab vs. placebo						
FOCUS (full trial population)	838	R, DB, MC (12 weeks with 12-week open-label extension)	Low ^a	- ≥4 migraine days per month - 2 to 4 prior treatment failures	<u>Primary outcome:</u> change from baseline in MMD or MMHD <u>Secondary outcome:</u> ≥50% response rate in terms of MMD or MMHD <u>Safety:</u> Treatment emergent adverse events	
FOCUS (HFEM ≥3 prior therapies subgroup)	91		High ^b	- 8 to 14 migraine days per month - 3 to 4 prior treatment failures		
Galcanezumab vs. placebo						
CONQUER (full trial population)	462	R, DB, MC (12 weeks with 12-week open-label extension)	Low ^a	- ≥4 migraine headache days per month - 2 to 4 prior treatment failures		
CONQUER (HFEM ≥3 prior therapies subgroup)	80		High ^c	- 8 to 14 monthly migraine headache days per month - 3 to 4 prior treatment failures		

Source: Table 2-8, p24 of the submission.

DB= double blind; HFEM= high frequency episodic migraine; MC= multi-centre; MMD= monthly migraine days; MMHD= monthly migraine headache days; R= randomised

^a The risk of bias was considered low in the full trial populations, in line with the November 2019 submission for fremanezumab and July 2019 submission for galcanezumab.

^b The submission did not comment on the risk of bias in the HFEM subgroup, however, the submission considered it to be low in the whole trial population. Given that the HFEM subgroup was not pre-specified in the trials, the risk of bias was considered high during the evaluation.

^c The ESC previously cautioned about the high risk of bias in the HFEM subgroup of the CONQUER trial (para 6.30, Galcanezumab PSD, March 2022 PBAC meeting).

^d The primary outcome in FOCUS was monthly migraine days compared with monthly migraine headache days in CONQUER. The term MMDs has been used herein for consistency.

6.12 The submission considered the overall risk of bias in the full trial populations of FOCUS and CONQUER to be low. This was consistent with the previous risk of bias considerations for the full trial populations of fremanezumab (Table 3, Fremanezumab PSD, November 2019 PBAC meeting) and galcanezumab (Table 3, Galcanezumab PSD, November 2020 PBAC meeting).

6.13 As results for the HFEM subgroups presented in the submission were conducted post-hoc, they were considered to be at high risk of bias. The ESC previously cautioned about the high risk of bias in the HFEM subgroup of the CONQUER trial (para 6.30, Galcanezumab PSD, March 2022 PBAC meeting). The Pre-Sub-Committee Response (PSCR) stated that the PBAC made positive recommendations based on subgroup analyses with ≥3 prior treatments previously for Botox and for galcanezumab, despite acknowledging that there was a high risk of bias with the post-hoc analyses. The ESC considered that this response was reasonable.

- 6.14 While both trials had similar eligibility criteria and baseline patient characteristics, there were some differences:
- The definition of what constituted a failed prior therapy in terms of therapy exposure and contraindications to a prior therapy differed between the trials. While both trials required patients to have failed/tried 2-4 prophylactic migraine medications, the FOCUS trial defined failure as an inadequate response to 3 months of treatment, safety/tolerability issues or contraindications to medications. The CONQUER trial defined failure as two months of therapy or safety/tolerability issues. Contraindications to prior therapies did not count as medication failure in CONQUER.
 - Another key difference was the duration that a migraine needed to last in order to qualify as a typical migraine episode for the study inclusion criteria. While the FOCUS trial required the migraine to last ≥ 4 hours for a migraine day to be recorded, the migraine had to be of only ≥ 30 minutes duration to be recorded as a migraine in the CONQUER trial. The migraine qualifying criterion was more stringent in the FOCUS trial compared with the CONQUER trial, and the ESC considered this more stringent criterion appropriate.
 - The FOCUS trial excluded people who had the most severe, unremitting headaches, clinically significant comorbidities (e.g., major cardiovascular disease) or clinically significant psychiatric issues. Therefore, people enrolled in the FOCUS trial were on average healthier than those who may be eligible for fremanezumab in clinical practice. The CONQUER trial excluded patients with an abnormal electrocardiogram, patients at serious cardiovascular risk, or those with a history of clinically significant cardiovascular disease. The TGA delegate previously noted that there are theoretical concerns suggesting that interfering with calcitonin gene-related peptide could modify processes relevant to protection against ischaemia, increasing the risk of cardiovascular events (p71, AusPAR Emgality galcanezumab Eli Lilly Australia Pty Ltd, September 2019). The ESC noted the exclusion criteria in the FOCUS and CONQUER trials and considered the differences in exclusion criteria were not a major concern given that these therapies are unlikely to be used in patients with severe ischaemic heart disease or severe psychotic illness in clinical practice.
- 6.15 Patients were allowed to use acute medication to treat acute migraine attacks, as needed in both trials. However, the use of other preventive migraine medications was not permitted. This may not be fully representative of patients eligible for fremanezumab or galcanezumab in clinical practice.
- 6.16 The submission nominated a difference of at least two headache days between the active treatment and placebo arms as a minimal clinically important difference (MCID). The PBAC previously accepted that a reduction of 2-3 headache days per month could be considered a clinically important benefit in the context of submissions

for chronic migraine (section 12, Botox PSD, July 2012 PBAC meeting; para 6.16, Galcanezumab PSD, July 2019 PBAC meeting). The March 2022 galcanezumab submission for HFEM also applied an MCID of at least 2 days.

- 6.17 For the indirect comparison of fremanezumab versus galcanezumab, the nominated MCID of two days was also chosen as the relevant non-inferiority margin. The PBAC considered this was reasonable, being consistent with non-inferiority margins nominated previously for chronic migraine (para 7.6, Fremanezumab PSD, November 2019 PBAC meeting; para 6.16, Galcanezumab PSD, July 2019 PBAC meeting).

Comparative effectiveness

- 6.18 Table 4 shows the results for the key primary outcome for all episodic migraine and the proposed PBS population of HFEM with ≥ 3 prior prophylactic migraine treatments.

Table 4: Change from baseline in monthly migraine days in all episodic migraine and HFEM subgroups in the FOCUS and CONQUER trials over 12 weeks

Trial ID	Treatment groups	FREM Q/FREM M/GALC			Placebo			LSM difference vs. placebo (95% CI)
		N	Baseline mean (SD)	LSM change (SE)	N	Baseline mean (SD)	LSM change (SE)	
All EM population								
FOCUS	FREM Q	107	9.4 (2.67)	-3.7 (0.44)	111	9.1 (2.61)	-0.7 (0.43)	-3.1 (-3.93, -2.19)
	FREM M	110	9.5 (2.73)	-3.8 (0.45)				-3.1 (-4.00, -2.25)
CONQUER	GALC	137	9.5 (3.0)	-2.88 (0.34)	132	9.2 (2.7)	-0.31 (0.34)	-2.6 (-3.41, -1.72)
Subgroup of patients with HFEM ≥ 3 prior treatment failures (proposed PBS population)								
FOCUS	FREM Q	25	10.6 (1.88)	-3.9 (1.03)	30	10.9 (1.74)	0.0 (0.85)	-3.9 (-6.10, -1.68)
	FREM M	36	11.0 (1.76)	-4.7 (0.98)				-4.7 (-6.76, -2.70)
CONQUER	GALC	48	NR	-4.19 (0.58)	32	NR	-1.76 (0.73)	-2.4 (-4.08, -0.79)

Source: Tables 2-24, 2-25, 2-28, 2-29; pp54, 56, 63 & 65 of the submission. Table 7, p11 of galcanezumab PSD, March 2022 PBAC meeting. CI = confidence interval; EM= episodic migraine; FREM= fremanezumab; GALC= galcanezumab; HFEM= high frequency episodic migraine; LSM= least squares mean; M= monthly (225 mg); MMDs= monthly migraine days; N= number of patients; NR=not reported; PBO= placebo; Q= quarterly (675 mg); SD = standard deviation; SE= standard error.

Bold values indicate statistical significance ($p < 0.05$).

- 6.19 Compared with the corresponding placebo arms, treatment with fremanezumab and galcanezumab in the individual trials resulted in statistically significant improvements in the change from baseline in the number of MMDs in the episodic migraine and HFEM subpopulations ($p < 0.05$, with the mean differences being more than the proposed MCID).
- 6.20 In the HFEM ≥ 3 prior treatment group, the upper limit of the 95% confidence interval for the change in MMDs (FREM Q versus placebo: -1.68 days and GALC versus placebo: -0.79 days) was less than the proposed MCID of at least two days for both the FREM Q versus placebo and the GALC versus placebo comparisons. The upper limit of the 95% confidence interval for FREM M compared to placebo (-2.70 days) was greater than the proposed MCID.
- 6.21 Results from the indirect comparisons of the key primary outcome of change in MMDs in various subgroups are presented in Table 5.

Table 5: Comparative summary of the primary outcome of change from baseline in monthly migraine days in the FOCUS and CONQUER trials over 12 weeks

Population	Indirect comparison Difference of means: FREM minus GALC	
	<u>FREM Q MINUS GALC</u> Estimate (95 % CI), p-value	<u>FREM M MINUS GALC</u> Estimate (95 % CI), p-value
All EM (2-4 prior prophylactic treatments)	-0.49 (-1.70, 0.72) 0.426	-0.56 (-1.77, 0.65) 0.363
EM ≥3 prior therapies	-1.04 (-3.32, 1.24) 0.370	-1.00 (-3.22, 1.22) 0.377
HFEM (2 to 4 prior therapies)	-0.69 (-2.17, 0.79) 0.361	-0.81 (-2.28, 0.66) 0.279
HFEM ≥3 prior therapies (proposed PBS population)	-1.47 (-4.18, 1.24) 0.288	-2.27 (-4.84, 0.30) 0.084

Source: Tables 2-24, 2-25, 2-28, 2-49; pp54, 56, 63 & 87 of the submission.

MMDs= monthly migraine days; CI= confidence interval; EM= episodic migraine; FREM= fremanezumab; GALC= galcanezumab; HFEM= high frequency episodic migraine; M= monthly; PBO= placebo; PBS=Pharmaceutical Benefits Scheme; Q= quarterly.

- 6.22 There were no statistically significant differences for any of the included indirect comparisons for the key primary outcome of change in MMDs (all $p > 0.05$). However, there was a trend in favour of fremanezumab versus galcanezumab for all subgroups. The indirect comparisons suggested non-inferiority for both the quarterly and monthly schedules of fremanezumab compared with galcanezumab, as the corresponding upper 95% confidence intervals, 1.24 and 0.30, were less than the non-inferiority margin of two migraine days per month.
- 6.23 Table 6 presents the results from the indirect comparisons for the key secondary outcome of the proportion of patients with a $\geq 50\%$ reduction in MMDs separately for all episodic migraine patients and the proposed population.

Table 6: Comparative summary of the key secondary outcome of $\geq 50\%$ response in monthly migraine days in the FOCUS and CONQUER trials over 12 weeks

Population	FOCUS		CONQUER	Indirect comparisons	
	FREM Q vs. placebo	FREM M vs. placebo	GALC vs. placebo	FREM Q vs. GALC Estimate (95% CI), p-value	FREM M vs. GALC Estimate (95% CI), p-value
All EM population					
Risk difference	0.37	0.33	0.25	0.122 (-0.03, 0.273) 0.115	0.082 (-0.07, 0.23) 0.286
Risk ratio	4.72	4.31	2.44	1.93 (0.93, 4.02) 0.077	1.77 (0.85, 3.69) 0.129
Odds ratio	7.97	6.78	3.47	2.30 (0.91, 5.79) 0.077	1.95 (0.78, 4.92) 0.154
Subgroup of patients with HFEM ≥ 3 prior treatment failures (proposed PBS population)					
Risk difference	0.41	0.44	0.23	0.18 (-0.10, 0.46) 0.202	0.212 (-0.04, 0.47) 0.103
Risk ratio	13.20	14.17	2.51	5.25 (0.6, 46.12) 0.135	5.64 (0.65, 48.64) 0.116
Odds ratio	22.79	25.95	3.43	6.64 (0.59, 75.06) 0.126	7.56 (0.70, 82.08) 0.096

Source: Table ES.7 based on Tables 2-35 & 2-39, pp74, 77 of the submission.

FREM= fremanezumab; GALC= galcanezumab; PBO= placebo; EM= episodic migraine; HFEM= high frequency episodic migraine; CI= confidence interval; M= monthly; PBS=Pharmaceutical Benefits Scheme; Q= quarterly.

Note: For the sake of brevity, results for EM (≥ 3 prior therapies) were not presented in the table. The results showed non statistical significance ($p > 0.05$). Source: Table 14, pp 21 of Attachment 1- ITC of the submission

6.24 The key secondary outcome results also showed a trend favouring fremanezumab versus galcanezumab for all subgroups, however, there were no statistically significant differences for fremanezumab quarterly, or monthly dosing compared with galcanezumab (all $p > 0.05$).

Comparative harms

6.25 A summary of the key adverse events for fremanezumab and galcanezumab in the trials is presented in Table 7.

*Public Summary Document – November 2022 PBAC Meeting with Out of Session Addendum
August 2023*

Table 7: Summary of key adverse events in the trials (double-blind safety analysis set in full trial population including chronic and episodic migraine patients)

Trial ID	FOCUS				CONQUER	
	FREM Q 675mg/PBO/ PBO (N=276)	FREM M 225/225/225 mg (N=111)	FREM 675/225/225 mg ^a (N=174)	PBO (N=277)	GALC (N=232)	PBO (N=230)
Summary of adverse events						
Treatment emergent adverse events, n (%)	151 (55)	44 (40)	37 (21)	134 (48)	119 (51)	122 (53)
Treatment-related adverse events, n (%)	57 (21)	18 (16)	85 (49)	55 (20)	37 (16)	34 (15)
Serious adverse events, n (%)	2 (<1)	1 (<1)	3 (2)	4 (1)	2 (1)	2 (1)
Discontinuation related to adverse events, n (%)	1 (<1)	1 (<1)	3 (2)	3 (1)	1 (<1)	0
Most frequently reported treatment emergent adverse events						
Patients with ≥1 TEAE, n (%)	151 (55)	44 (40)	85 (49)	134 (48)	119 (51)	122 (53)
Nasopharyngitis	13 (5)	1 (<1)	6 (3)	11 (4)	16 (7)	21 (9)
Injection site erythema	19 (7)	4 (4)	12 (7)	15 (5)	8 (3)	6 (3)
Injection site pain	11 (4)	3 (3)	6 (3)	8 (3)	5 (2)	13 (6)
Upper respiratory tract infection	4 (1)	4 (4)	5 (3)	3 (1)	5 (2)	5 (2)
Nausea	6 (2)	2 (2)	0 (0)	6 (2)	4 (2)	5 (2)
Injection site reaction induration	12 (4)	3 (3)	10 (6)	12 (4)	0	6 (3)
Insomnia	6 (2)	4 (4)	3 (2)	2 (<1)	0	5 (2)

Source: Tables 50 and 51, pp167-169, Fremanezumab CSR; Table 8, Galcanezumab PSD, March 2022 PBAC meeting.

CI= confidence interval; FREM= fremanezumab; GALC= galcanezumab; PBO= placebo; ITT= intention-to-treat; M= monthly; n= number of participants reporting data; N= total participants in group; Q= quarterly; RD= risk difference; RR= relative risk.

^a FREM 675 mg initially in the first month followed by 225 mg in second and third months was an experimental dose to determine drug tolerance.

6.26 The overall incidence of adverse events was similar between treatment arms. There was a slightly greater incidence of treatment-emergent adverse events in the fremanezumab quarterly arm compared with the fremanezumab monthly arm and placebo in the FOCUS trial.

6.27 The most common treatment-emergent adverse events (TEAEs) (>2% of any group) were nasopharyngitis, injection site erythema, injection site pain, and injection site reaction.

- 6.28 The submission presented an indirect comparison of TEAEs for the HFEM subgroup with ≥ 3 prior treatment failures. No significant differences were observed between fremanezumab and galcanezumab in the incidence of TEAEs in the indirect comparisons (all $p > 0.05$).

Benefits/harms

- 6.29 A benefits and harms table was not presented as the submission made a claim of non-inferiority.

Clinical claim

- 6.30 The submission described fremanezumab as non-inferior in terms of effectiveness and safety compared with galcanezumab for treating patients with HFEM (8 to 14 monthly migraine days) who have an inadequate response, intolerance, or a contraindication to at least three prior prophylactic migraine medications.
- 6.31 The submission proposed an MCID of two days for the key primary outcome of change in monthly migraine days, and this was also nominated as the non-inferiority margin. This was considered reasonable based on previous PBAC considerations (para 7.6, Fremanezumab PSD, November 2019 PBAC meeting; para 6.16, Galcanezumab PSD, July 2019 PBAC meeting).
- 6.32 The ESC considered a claim of non-inferior efficacy and safety may be reasonable, albeit with the following concerns:
- The sample sizes for the HFEM population in the FOCUS (N=91) and CONQUER (N=80) trials were small.
 - The post-hoc analyses used for the HFEM population were at a high risk of bias as randomisation may no longer hold.
 - There is no long-term comparative effectiveness data. The double-blind duration of the two clinical trials, at 12 weeks, was short relative to the duration patients would receive the treatments in clinical practice.
- 6.33 The pre-PBAC response stated the treatments for prophylactic migraine were all recommended for PBS listing based on post-hoc sub-population analyses. In addition, the pre-PBAC response stated that only 12 weeks of comparative data has been available for other prophylactic migraine treatments listed on the PBS, and that the continuation of Australian patients on treatments for chronic migraine provides long-term evidence of their effectiveness (given that patients cannot continue accessing these treatments on the PBS if they are not responding). The pre-PBAC response stated that this Australian experience is supported by 24-week data from FOCUS, which shows that patients with chronic migraine and episodic migraine continue to achieve meaningful reduction in monthly migraine days, and that this could also be expected in the HFEM sub-population.

- 6.34 The PBAC recalled that at its meeting in March 2022, it accepted that galcanezumab resulted in a modest reduction in the number of migraine headache days per month compared to placebo based on results in the HFEM subgroup.
- 6.35 The PBAC noted that the upper limit of the 95% confidence interval for change from baseline in monthly migraine days was less than the proposed MCID for both fremanezumab and galcanezumab. The PBAC considered that the claim of non-inferior comparative effectiveness was reasonable.
- 6.36 The PBAC considered that the incidence of adverse events for fremanezumab and galcanezumab was similar, noting that there was a slightly higher incidence for quarterly administration of fremanezumab than monthly administration. The PBAC noted that there were no significant differences in adverse events for fremanezumab compared to galcanezumab. The PBAC considered that the claim of non-inferior comparative safety was reasonable.

Economic analysis

- 6.37 The submission presented a cost-minimisation approach. The key assumptions and components are summarised in Table 8. The cost-minimisation approach was consistent with the clinical claim of non-inferiority.

Table 8: Key components and assumptions of the cost-minimisation approach

Component	Claim or assumption
Therapeutic claim: effectiveness	Based on the evidence presented, the effectiveness of fremanezumab is assumed to be non-inferior to galcanezumab in patients with HFEM.
Therapeutic claim: safety	Based on the evidence presented, the safety of fremanezumab is assumed to be non-inferior to galcanezumab for the proposed population.
Evidence base	Indirect comparison of fremanezumab and galcanezumab.
Equi-effective doses	Fremanezumab 225 mg every month (or 675 mg quarterly) = Galcanezumab 240 mg initially followed by 120 mg every month.
Direct medicine costs	The proposed drug cost of fremanezumab (12 doses over one year) was estimated to be the same as the drug cost of galcanezumab based on its published price
Other costs or cost offsets	The submission assumed that there was no difference in administration costs or costs to treat adverse events between fremanezumab and galcanezumab.

Source: Compiled during the evaluation based on Section 3 of the submission.

HFEM= high frequency episodic migraine.

- 6.38 The submission proposed that fremanezumab 225 mg every month (or 675 mg quarterly) is equi-effective to galcanezumab 240 mg initially, followed by 120 mg every month. The PBAC has previously accepted these proposed equi-effective doses for patients with chronic migraine, advising that a CMA should be conducted over 2 years of treatment for both medicines (para 7.8, Fremanezumab PSD, November 2019 PBAC meeting).
- 6.39 The submission assumed that the price of fremanezumab for HFEM would remain unchanged from its current chronic migraine listing (effective AEMP of \$1 per syringe/pen at the time of submission). Previously, the PBAC considered galcanezumab would be cost-effective for the HFEM patient population at a price no

*Public Summary Document – November 2022 PBAC Meeting with Out of Session Addendum
August 2023*

higher than the current effective price for patients with chronic migraine (para 7.5, Galcanezumab PSD, March 2022 PBAC meeting).

6.40 Results of the cost-minimisation approach, using the effective price for galcanezumab assumed in the submission, are presented in Table 9.

Table 9: Results of the cost-minimisation approach (fremanezumab effective AEMP and galcanezumab assumed effective AEMP)

Row	Component	Fremanezumab	Galcanezumab	Source / calculation
A	Time horizon, years	2	2	Assumption
Drug costs				
B	Dosing details	225 mg every month or 675 mg every 3 months	120 mg per month with an initial 240 mg loading dose	Product information
C	Effective AEMP per unit	\$	\$	Reported by the submission
D	Unit volume	225 mg	120 mg	
E	Number of doses first year	12	13	Reported by the submission
F	Number of doses second year	12	12	Reported by the submission
G	Units utilised over two years	24	25	E+F
H	Total drug costs over two years	\$	\$	C*G
I	Difference in cost over two years [effective AEMP]	-\$		Fremanezumab Row H- Galcanezumab Row H

Source: Compiled during the evaluation based on effective AEMP fremanezumab reported in the fremanezumab financial base case Excel sheet (3c Impact-proposed eff). Effective AEMP of galcanezumab as reported in the fremanezumab financial base case Excel sheet (4c Impact-affected eff). Table 3-1, p102 of the submission.
AEMP= approved ex manufacturer price.

6.41 The submission assumed no additional costs or cost offsets. The evaluation considered this was reasonable.

Drug cost/patient/year

6.42 The estimated costs per patient for fremanezumab and galcanezumab are presented in Table 10. The calculations used the effective prices reported in the submission.

*Public Summary Document – November 2022 PBAC Meeting with Out of Session Addendum
August 2023*

Table 10: Drug cost per patient for fremanezumab and galcanezumab (assumed effective AEMP and DPMQ)

	Fremanezumab		Galcanezumab	
	Cost-minimisation approach (based on AEMP per dose)	Financial estimates (based on DPMQ per script)	Cost-minimisation approach (based on AEMP per dose)	Financial estimates (based on DPMQ per script)
Dose	625 mg (225 mg x 3) administered quarterly, or 225 mg administered monthly		240 mg (120 mg x 2) loading dose followed by 120 mg monthly	
Number of doses/scripts in Year 1	12 doses	3 initial and 3 continuing scripts	13 doses	2 initial and 9 continuing scripts
Number of doses/scripts in Year 2	12 doses	4 continuing scripts	12 doses	12 continuing scripts
Drug cost per injection	\$	\$ (initial) \$ (quarterly continuing)	\$	\$ (initial) \$ (monthly continuing)
Cost/patient Year 1	\$	\$	\$	\$
Cost/patient Year 2	\$	\$	\$	\$
Total cost/ patient	\$	\$	\$	\$

Source: Table compiled during the evaluation based on information provided in the submission and Table 3-1 p102 of the submission.
Note: Duration of treatment is based on the PBAC advice that the cost-minimisation approach should be conducted over 2 years of treatment for both medicines (para 7.8, fremanezumab PSD, November 2019 PBAC meeting).

Estimated PBS usage & financial implications

- 6.43 This submission was not considered by DUSC. The submission used an epidemiological approach to estimate the utilisation and financial impacts of listing fremanezumab for patients with HFEM (≥3 prior migraine therapies).
- 6.44 The submission assumed that fremanezumab would displace only galcanezumab. The submission also assumed no overall market expansion if fremanezumab were to be PBS-listed. The evaluation considered that these assumptions are reasonable only if galcanezumab is listed on the PBS for the HFEM population.
- 6.45 Table 11 shows the key inputs for the financial estimates.

Table 11: Key inputs for financial estimates

Parameter	Value applied and source	Comment
Migraine prevalence (Australian population 18 to 90 years of age)	14.5%.	The PBAC has previously accepted this value as appropriate (para 7.6, Galcanezumab PSD, March 2022 PBAC meeting).
Proportion of patients diagnosed by physician (Episodic migraine)	45.9%. Based on the galcanezumab for HFEM submission (Table 15, Galcanezumab PSD, November 2020 PBAC meeting).	Assuming less than half of episodic migraine patients were diagnosed by physicians reduces the eligible patient pool significantly. The percentage is based on a sample survey of a European study (Table 15, Galcanezumab PSD, November 2020 PBAC Meeting). Physicians in Australia may diagnose more episodic migraine patients.
Proportion of migraine that is episodic	90%.	The PBAC has previously accepted this value as appropriate (para 7.6, Galcanezumab PSD, March 2022 PBAC meeting).
Proportion of episodic migraine that is high frequency	19.5%. Based on the average of 13% reported by general practitioners and 26% reported by neurologists cited in	Consistent with galcanezumab financial estimates.

*Public Summary Document – November 2022 PBAC Meeting with Out of Session Addendum
August 2023*

Parameter	Value applied and source	Comment
	the galcanezumab for HFEM submission (Table 16, Galcanezumab PSD, March 2022 PBAC meeting).	
On ≥3 preventatives and intolerant, contraindicated, or have failed, ≥3 prior preventative treatments	12.0% based on galcanezumab for chronic migraine submission (Table 15, Galcanezumab PSD, November 2020 PBAC meeting).	The galcanezumab submission estimated this value based on Ford (2017), a small US study.
Uptake rate (Initiating treatment)	Yr 1: █%; Yr 2: █%; Yr 3: █%; Yr 4: █% Yr 5: █%; Yr 6: █%. Based on the submission's expectations	
Response rate for continuing patients	47% of patients are expected to achieve a 50% reduction in migraine frequency and therefore, continue treatment. 100% in subsequent years	The response rate for continuing patients was higher than the response rate applied in the galcanezumab financial estimates (40%) (Table 16, Galcanezumab PSD, March 2022 PBAC meeting). The PBAC considered it was unlikely the response rate for fremanezumab would be different in clinical practice given the non-inferiority claim. The submission stated a continuation rate of 95% was applied in subsequent years; however, the spreadsheet assumed 100%. The PSCR confirmed that the continuation rate applied in the financial estimates was 100%. The PBAC noted the galcanezumab financial estimates applied a continuation rate of 95% in subsequent years (Table 16, Galcanezumab PSD, March 2022 PBAC meeting).
Grandfathered patients	None	The submission indicated that no such provisions are required for the proposed listing as there is currently no product familiarisation program for HFEM.
Dose & duration	First Year: Fremanezumab: 225 mg once monthly or 675 mg every three months Galcanezumab: 120 mg injected subcutaneously once monthly, after a 240 mg initial loading dose. Subsequent year: Fremanezumab: 675 mg every three months. Galcanezumab: 120 mg once monthly.	These assumptions were consistent with the economic evaluation. The assumptions around scripts per initial patient, continuing patients were as follows: Fremanezumab proposed 3 scripts (pack size 1) (3 months) for each initial patient, 3 quarterly scripts (pack size 3) (9 months) for first continuing and 4 quarterly scripts (pack size 3) (12 months) for ongoing patients. Galcanezumab: 2 scripts (pack size 2) (3 months) for each initial patient, 9 scripts (pack size 1) (9 months) for first continuing and 12 scripts (pack size 1) (12 months) for ongoing patients.
Costs		
Fremanezumab	\$█ (Initiating: Requested effective DPMQ) (Maximum quantity 1) \$█ (Continuing: Requested effective DPMQ) (Maximum quantity=3)	The costs were consistent with those applied in the economic evaluation and based on the assumed effective DPMQ of galcanezumab.

*Public Summary Document – November 2022 PBAC Meeting with Out of Session Addendum
August 2023*

Parameter	Value applied and source	Comment
Galcanezumab	The submission assumed: \$█ (Initiating: Requested effective DPMQ) (Maximum quantity 1) \$█ (Continuing: Requested effective DPMQ) (Maximum quantity=2)	

Source: Compiled during evaluation from information provided in the submission. Also based on Table 1-3 (p4 of the submission), Table 1-4 (p5 of the submission), Table 3-1 (p102 of the submission).

AEMP= approved ex-manufacturer price; DPMQ= dispensed price for maximum quantity; PBAC= Pharmaceutical Benefits Advisory Committee; HFEM= high frequency episodic migraine; PSD= public summary document; PSCR = Pre-Sub-Committee Response.

^a The Stark et al. (2007) estimate of 14.5% was included in the 2020 galcanezumab episodic migraine submission. The PBAC agreed with the ESC that a migraine prevalence, as reported in the Stark publication, would be appropriate and consistent with previous considerations of migraine (para 6.64, Galcanezumab PSD, March 2022 PBAC Meeting).

6.46 Table 12 presents the estimated use and financial implications for listing fremanezumab based on the assumed effective DPMQ of galcanezumab.

Public Summary Document – November 2022 PBAC Meeting with Out of Session Addendum
August 2023

Table 12: Estimated use and financial implications (based on the assumed effective DPMQ)

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of patients with HFEM	¹	¹	¹	¹	¹	¹
Number of patients with HFEM eligible for treatment (12%)	²	²	³	³	³	³
Cumulative Uptake rate	⁰	⁰	⁰	⁰	⁰	⁰
Number of patients initiating treatment	⁴	⁴	⁵	⁵	⁵	⁵
Continuing patients	⁵	⁴	⁴	⁴	⁶	⁶
Initiating (Monthly scripts)	²	²	⁴	⁴	⁴	⁴
Continuing (Quarterly scripts)	⁶	²	³	³	⁷	⁷
Scripts dispensed ^a	³	⁷	⁷	⁷	⁸	⁸
Estimated financial implications of fremanezumab						
Cost to PBS/RPBS less copayments (\$)	⁹	¹⁰	¹⁰	¹⁰	¹¹	¹¹
MBS costs ^c (\$)	¹²	¹²	¹²	¹²	¹²	¹²
Estimated financial implications of galcanezumab						
Total net savings of replacing GALC (less copayments) (\$)	¹³	¹³	¹³	¹³	¹³	¹³
MBS cost savings ^c (\$)	¹³	¹³	¹³	¹³	¹³	¹³
Net financial implications						
Savings to PBS/RPBS (\$)	¹³	¹³	¹²	¹²	¹²	¹²
Net cost to MBS ^b (\$)	\$0	\$0	\$0	\$0	\$0	\$0
Net cost to Government (\$)	¹³	¹³	¹²	¹²	¹²	¹²
Estimated financial implications of fremanezumab (if galcanezumab is not listed)						
Net cost to Government^d (\$)	⁹	¹⁰	¹⁰	¹⁰	¹¹	¹¹

Source: Compiled during evaluation based on Tables 4-4 to 4-7, pp 109-113 of the submission; Tables 4-11, 4-12, pp 115-116 of the submission and excel worksheet 2b Patient -prevalent, Frem-Financial Base case-6 July 2022.

HFEM = high frequency episodic migraine; GALC = galcanezumab; PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme; MBS= Medicare benefits schedule.

^a Assuming 12 doses per year as estimated by the submission

^b Assuming no change in MBS and hospitalisation costs. This scenario assumes that galcanezumab is listed.

^c Assuming a first visit, the next visit is after three treatment cycles (two visits in 3 months, initial), then ongoing follow-up every 6 treatment cycles (continuing). Total three neurologist visits in 12 months (initial +continuing: MBS item no. 116 and scheduled fee \$81.05 per visit. Total volume of visits Year 1 is |⁵, Year 2 is |⁵, Year 3 is |⁵, Year 4 is |⁵, Year 5 is |⁵ and Year 6 is |⁵.

^d Cost to PBS/RPBS less copayments plus MBS cost. Moreover, there will be no savings from replacing galcanezumab scripts.

The redacted values correspond to the following ranges:

¹ 200,000 to < 300,000

² 20,000 to < 30,000

³ 30,000 to < 40,000

⁴ 5,000 to < 10,000

⁵ 500 to < 5,000

⁶ 10,000 to < 20,000

*Public Summary Document – November 2022 PBAC Meeting with Out of Session Addendum
August 2023*

⁷ 40,000 to < 50,000

⁸ 50,000 to < 60,000

⁹ \$10 million to < \$20 million

¹⁰ \$20 million to < \$30 million

¹¹ \$30 million to < \$40 million

¹² \$0 to < \$10 million

¹³ Net cost save

- 6.47 The cost of listing fremanezumab on the PBS/RPBS for treatment-resistant HFEM was estimated to be \$10 million to < \$20 million in Year 1, increasing to \$30 million to < \$40 million in Year 6 of listing, a total of \$100 million to < \$200 million over the first six years of listing.
- 6.48 Assuming that galcanezumab is already listed on the PBS when fremanezumab is listed, the submission estimated that the total net cost to the Government over 6 years is \$0 to < \$10 million, which assumed no additional cost to the MBS. This includes an expected net saving to the PBS/RPBS in year one and in year two of listing. The saving is driven by the avoidance of the additional loading dose required for galcanezumab. In year three, there is expected to be an additional cost of approximately \$0 to < \$10 million, which increases to \$0 to < \$10 million by year six. The net cost from year three to year six is driven by the increased number of scripts required for galcanezumab.
- 6.49 If galcanezumab is not listed prior to fremanezumab listing, the total net cost to the Government will be increased by \$100 million to < \$200 million over six years (Table 12). The additional cost is a result of additional MBS services required for patient management and no offset from the displacing medicine.
- 6.50 A comparison of the key inputs for the financial estimates for fremanezumab and galcanezumab is presented in Table 13. The submission assumed 1.07% of patients with HFEM would be eligible for treatment, compared to the galcanezumab submission that assumed 0.7%. The PBAC agreed with the evaluation that this difference may not be reasonable.

Table 13: Key inputs for financial estimates (current fremanezumab submission vs galcanezumab HFEM submission)

Parameter	Current fremanezumab submission	Galcanezumab for HFEM submission
Migraine prevalence (Australian population aged 18-90 years)	14.5%	22.80%
Proportion of migraine that is episodic	90%	92.39%
Overall % of patients with EM	13.05%	21.7%¹
Patient diagnosed	45.9%	-
Proportion of episodic migraine that is high frequency	19.5%	19.5%
On ≥3 preventatives and intolerant, contraindicated, or have failed, ≥3 prior preventative treatments	12%	NA
Proportion currently taking an oral preventative	NA	74.5%
Proportion currently taking ≥3 oral preventatives	NA	10%
Proportion currently taking ≥3 oral preventatives and are intolerant, contraindicated, or have failed ≥3 preventative treatments	NA	48%
Overall % of patients with HFEM that would be eligible	1.07%²	0.70%³
Proportion of patients continuing treatment (i.e., proportion achieve a 50% reduction in migraine days)	47%	40%
Continuation rate in subsequent years	100%	95%
Uptake rates	Yr 1: █%; Yr 2: █%; Yr 3: █%; Yr 4: █%; Yr 5: █%; Yr 6: █%.	Not reported in PSD

Source: Compiled during evaluation from information provided in the submission. Also based on Table 1-3 (p4 of the submission), Table 1-4 (p5 of the submission), Table 3-1 (p102 of the submission). Table 16, galcanezumab PSD, March 2022, PBAC meeting.

NA = not applicable; EM = episodic migraine; HFEM = high frequency episodic migraine; PSD = public summary document

1. PBAC considered it would be appropriate to assume migraine prevalence of 14.5% and 90% have EM

2. $45.9\% \times 19.5\% \times 12\% = 1.07\%$

3. $48\% \times 19.5\% \times 74.5\% \times 10\% = 0.70\%$

6.51 The submission claimed that the main sources of uncertainty for the financial estimates were the percentage of HFEM patients who will be initiated onto treatment within 6 years and percentage of patients who are expected to achieve a 50% reduction in migraine frequency and continue treatment.

6.52 The evaluation considered the submission’s estimate that 47% of patients will continue treatment after the initial dose to be uncertain, stating that some patients who have less than a 50% reduction in MMDs may remain on treatment. Reasons for this include the lack of available treatments for patients with HFEM who have an inadequate response, intolerance, or contraindication to ≥3 prior treatments, and difficulty in assessing response in clinical practice. The evaluation also questioned whether the treatment effect in responders would be maintained indefinitely.

Quality Use of Medicines

6.53 The submission indicated that the launch of fremanezumab has been underpinned by comprehensive training of healthcare practitioners and patients.

6.54 The submission offered two ‘Patient Support Programs’ through the company Medical Info Hotline and the services of a third-party patient support app provider (MedAdvisor).

Financial Management – Risk Sharing Arrangements

- 6.55 The submission proposed that fremanezumab for HFEM should be added to the current risk sharing arrangement (RSA) for the HFEM indication. However, if the risk share caps have not been adjusted for the HFEM indication, the submission proposed that the projected fremanezumab script volume be added to the Tier 1 cap and (by inference) to the Tier 2 cap.
- 6.56 The PBAC previously considered that the HFEM population should be included in the RSA in place for chronic migraine to manage the risk of use being substantially higher than expected, and that the financial estimates for this population should be added to the Tier 1 chronic migraine expenditure caps. The PBAC previously considered that it would be appropriate for the Tier 2 expenditure caps to be based on the assumption that a proportion of patients achieve a 30% reduction in migraine headache days at the response assessment time point (paragraph 7.7, Galcanezumab, PSD, March 2022 PBAC Meeting).

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

7 PBAC Outcome

- 7.1 The PBAC recommended amending the current listing of fremanezumab for chronic migraine to include the treatment of patients with treatment-resistant high frequency episodic migraine (HFEM). Consistent with its March 2022 recommendation for galcanezumab in this population, the PBAC considered fremanezumab would be cost-effective for the HFEM population at a price no higher than the effective price for fremanezumab for patients with chronic migraine. The PBAC considered that the treatment-resistant HFEM population should be included in the current RSA in place for chronic migraine. The PBAC noted that patients may move between these categories and considered that including the HFEM population in the RSA would help to manage the risk of use in a broader population where treatment may be less cost-effective.
- 7.2 The PBAC considered that galcanezumab was the appropriate comparator for treatment-resistant HFEM, although noted it was not currently PBS listed for this population.
- 7.3 The PBAC noted that the submission presented a cost minimisation approach between fremanezumab and galcanezumab. The PBAC considered the equi-effective doses proposed in the submission were reasonable:
- fremanezumab 225 mg every month (or 675 mg quarterly) is equi-effective to galcanezumab 240 mg initially, followed by 120 mg every month.
- 7.4 The PBAC considered that it would be appropriate for the requested restriction to use the phrase 'migraine headache days' (as proposed in the submission) rather than 'migraine days' (as proposed by the evaluation) in order to align the terminology with

- the restriction recommended for galcanezumab for patients with HFEM at the March 2022 PBAC meeting. The PBAC noted some minor editorial changes to the restriction criteria that should be flowed on to galcanezumab should it be PBS listed for this population.
- 7.5 The PBAC noted the submission provided clinical evidence for fremanezumab versus placebo from one randomised controlled trial (FOCUS) in patients with chronic and episodic migraine who did not respond to 2 to 4 prior prophylactic treatments (n=838). The PBAC considered the subgroup of patients in the FOCUS study with HFEM with ≥ 3 prior treatment failures (n=91) was the most applicable for the requested PBS listing. The PBAC considered that, in the treatment-resistant HFEM population, fremanezumab resulted in a clinically significant reduction in the number of monthly migraine days (MMDs) compared to placebo, with a reduction of 3.9 (95% CI: -6.10, -1.68) and 4.7 (95% CI: -6.76, -2.70) MMDs at 12 weeks for quarterly and monthly dosing, respectively.
- 7.6 The PBAC noted the submission provided an indirect treatment comparison (using placebo as the common comparator) to support the clinical claim that fremanezumab was non-inferior to galcanezumab in terms of effectiveness and safety. The PBAC noted there was no statistically significant difference in the reduction of MMDs from baseline between fremanezumab and galcanezumab for patients with HFEM who had ≥ 3 prior treatment failures, and that the upper limit of the 95% CI was less than the non-inferiority margin of 2 days per month. The PBAC considered the claim of non-inferior effectiveness of fremanezumab to galcanezumab was reasonable.
- 7.7 The PBAC considered the claim that fremanezumab is non-inferior to galcanezumab in terms of safety was reasonably supported by the data presented.
- 7.8 The PBAC noted the proposed price for fremanezumab in the treatment-resistant HFEM population was the same as the price in the chronic migraine population. Consistent with its recommendation for galcanezumab (March 2022), the PBAC advised that fremanezumab would be cost-effective for the treatment-resistant HFEM population at a price no higher than the current effective price of fremanezumab for the chronic migraine population. The PBAC considered for the purpose of Section 101(3B) of the *National Health Act 1953*, that galcanezumab was an alternative therapy to fremanezumab, and that fremanezumab does not provide a significant improvement in efficacy and/or reduction of toxicity over galcanezumab. The PBAC advised the price of fremanezumab should therefore be no higher than the price of galcanezumab should it be PBS listed for this population.
- 7.9 The PBAC considered that as the proposed population is not well defined, there is a risk of fremanezumab use outside the proposed restriction. The PBAC considered the treatment-resistant HFEM population should be included in the current RSA in place for chronic migraine to manage the risk of use in a broader population where treatment may be less cost-effective. The PBAC considered the financial estimates

*Public Summary Document – November 2022 PBAC Meeting with Out of Session Addendum
August 2023*

were overestimated and advised some amendments would be appropriate (as outlined in Table 11 and paragraph 6.50) for consistency with the financial estimates considered appropriate in recommending galcanezumab for this population.

- 7.10 The PBAC advised that if galcanezumab is not PBS listed for the treatment-resistant HFEM population, the expenditure caps could be increased as outlined in paragraph 6.56 using the revised financial estimates outlined in paragraph 7.9. The PBAC considered that if galcanezumab were to progress to PBS-listing, fremanezumab should be included within the same agreed expenditure caps.
- 7.11 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because fremanezumab is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over galcanezumab, 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.
- 7.12 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

8 Recommended listing

8.1 Amend existing listing as follows:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
FREMANEZUMAB					
fremanezumab 225 mg/1.5 mL injection, 1.5 mL pen device	13115G	1	1	2	'a' Ajovy
fremanezumab 225 mg/1.5 mL injection, 1.5 mL syringe	12611R	1	1	2	'a' Ajovy
Restriction Summary 12028 / ToC: New: Authority Required: Streamlined					
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)				
(for internal Dept. use)	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required (Streamlined) [amendment to existing code]				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				

Public Summary Document – November 2022 PBAC Meeting with Out of Session Addendum
August 2023

	Administrative Advice No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Administrative Advice: Pharmaceutical benefits that have the form fremanezumab 225 mg/1.5 mL syringes and pharmaceutical benefits that have the form fremanezumab 225 mg/1.5 mL pen devices are equivalent for the purposes of substitution.
	Indication: <i>Treatment-resistant chronic migraine</i>
	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 <i>migraine headache</i> days per month, over a period of at least 6 months, prior to commencement of treatment with this medicine for this condition
	AND
	Clinical criteria:
	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 <i>their</i> practitioner for medication overuse headache, prior to initiation of treatment with this drug
	AND
	Population criteria:
	Patient must be aged 18 years or older <i>at least 18 years of age</i> .
	AND
	Prescribing instructions:
	Prophylactic migraine medications are propranolol, amitriptyline, pizotifen, candesartan, verapamil, nortriptyline, sodium valproate or topiramate.
	AND
	Prescribing instructions:
	Patient must have the number of migraine <i>headache</i> days per month documented in their medical records.

Public Summary Document – November 2022 PBAC Meeting with Out of Session Addendum
August 2023

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
FREMANEZUMAB					
fremanezumab 225 mg/1.5 mL injection, 1.5 mL pen device	13129B	3	3	1	'a' Ajovy
fremanezumab 225 mg/1.5 mL injection, 1.5 mL syringe	12603H	3	3	1	'a' Ajovy
Restriction Summary 12029 / ToC: New: Authority Required: Streamlined					
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)				
(for internal Dept. use)	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required (Streamlined) [amendment to existing code]				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Administrative Advice: Special Pricing Arrangements apply.				
	Administrative Advice: Pharmaceutical benefits that have the form fremanezumab 225 mg/1.5 mL syringes and pharmaceutical benefits that have the form fremanezumab 225 mg/1.5 mL pen devices are equivalent for the purposes of substitution.				
	Indication: Treatment-resistant migraine				
	Treatment Phase: Continuing treatment				
	Treatment criteria:				
	<i>Must be treated by a neurologist OR</i>				
	<i>Must be treated by a general practitioner in consultation with a neurologist</i>				
	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 at least 50% 50% or greater reduction from baseline in the number of migraine headache days per month				
	AND				
	Clinical criteria:				
	Patient must continue to be appropriately managed for medication overuse headache				
	AND				
	Prescribing instructions:				

Patient must have the number of migraine <i>headache</i> 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.

9 Context for Decision

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

10 Sponsor's Comment

The sponsor had no comment.

Addendum to the November 2022 PBAC Public Summary Document:

11 Background

- 11.1 At its November 2022 meeting, the PBAC recommended amending the current listing of fremanezumab for chronic migraine to include the treatment of patients with treatment-resistant high frequency episodic migraine (HFEM).
- 11.2 The PBAC recommended a listing with a maximum quantity of one 225 mg pre-filled syringe (or autoinjector pen) with two repeats under the initial treatment restriction, providing up to 3 months of treatment for the monthly dosing regimen. For the continuing treatment restriction, the PBAC recommended a maximum quantity of three 225 mg pre-filled syringes (or autoinjector pens) with one repeat, as requested in the submission, providing up to 6 months of treatment for the quarterly dosing regimen. The initial criteria were consistent with the current fremanezumab listing for chronic migraine, and the continuing criteria were consistent with a recommendation made by the PBAC in March 2022 for fremanezumab for quarterly dosing.
- 11.3 Subsequent to the November 2022 meeting, the sponsor indicated that at this stage, they will not be progressing with the March 2022 quarterly dosing recommendation but wish to progress a listing for treatment-resistant migraine with the monthly dosing regimen for initial and continuing treatment.
- 11.4 The PBAC previously considered fremanezumab would be cost-effective for the HFEM population at a price no higher than the effective price for fremanezumab for patients with chronic migraine. The listing of a monthly dosing regimen under the continuing treatment criteria will have no impact on the effective price of fremanezumab but will increase the number of scripts required for patients in the continuing treatment phase hence would be expected to result in a small decrease in the cost to the government compared to quarterly dosing.

12 PBAC outcome

- 12.1 The PBAC advised fremanezumab could be listed in the continuing treatment phase for either the quarterly dispensing regimen, with maximum quantity units of three autoinjector pens/ syringes and one repeat, or for the monthly dispensing regimen, with maximum quantity units of one autoinjector pen/ syringe with five repeats.

Outcome:

Recommended

13 Recommended listing

- 13.1 Amend existing listing as follows:

*Public Summary Document – November 2022 PBAC Meeting with Out of Session Addendum
August 2023*

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	13115G	1	1	2	'a' Ajovy
fremanezumab 225 mg/1.5 mL injection, 1.5 mL syringe	12611R	1	1	2	'a' Ajovy
Restriction Summary New 1 / ToC: New 2: Authority Required: Streamlined					
Category / Program: GENERAL – General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required (Streamlined) [<i>amendment to existing code-New 2</i>]					
Administrative Advice: No increase in the maximum quantity or number of units may be authorised.					
Administrative Advice No increase in the maximum number of repeats may be authorised.					
Administrative Advice: Special Pricing Arrangements apply.					
Administrative Advice: Pharmaceutical benefits that have the form fremanezumab 225 mg/1.5 mL syringes and pharmaceutical benefits that have the form fremanezumab 225 mg/1.5 mL pen devices are equivalent for the purposes of substitution.					
Indication: <i>Treatment-resistant chronic migraine</i>					
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 headache days per month, over a period of at least 6 months, prior to commencement of treatment with this medicine for this condition					
AND					
Clinical criteria:					
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 <i>their</i> practitioner for medication overuse headache, prior to initiation of treatment with this drug					
AND					
Population criteria:					
Patient must be aged 18 years or older <i>at least 18 years of age</i> .					
AND					

*Public Summary Document – November 2022 PBAC Meeting with Out of Session Addendum
August 2023*

	Prescribing instructions:
	Prophylactic migraine medications are propranolol, amitriptyline, pizotifen, candesartan, verapamil, nortriptyline, sodium valproate or topiramate.
	AND
	Prescribing instructions:
	Patient must have the number of migraine <i>headache</i> days per month documented in their medical records.

**The difference of max quantity and number of repeats is in the continuing treatment phase:
Monthly dosing regimen**

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
FREMANEZUMAB					
fremanezumab 225 mg/1.5 mL injection, 1.5 mL pen device	13129B	1	1	5	'a' Ajovy
fremanezumab 225 mg/1.5 mL injection, 1.5 mL syringe	12603H	1	1	5	'a' Ajovy

Restriction Summary / ToC: Authority Required: Streamlined

	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required (Streamlined) [<i>amendment to existing code- New 4</i>]
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Administrative Advice: Pharmaceutical benefits that have the form fremanezumab 225 mg/1.5 mL syringes and pharmaceutical benefits that have the form fremanezumab 225 mg/1.5 mL pen devices are equivalent for the purposes of substitution.
	Indication: Treatment-resistant migraine
	Treatment Phase: Continuing treatment
	Treatment criteria: <i>Must be treated by a neurologist OR Must be treated by a general practitioner in consultation with a neurologist</i>
	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:

*Public Summary Document – November 2022 PBAC Meeting with Out of Session Addendum
August 2023*

	Patient must have achieved and maintained at least 50% 50% or greater reduction from baseline in the number of migraine headache days per month
	AND
	Clinical criteria:
	Patient must continue to be appropriately managed for medication overuse headache
	AND
	Prescribing instructions:
	Patient must have the number of migraine <i>headache</i> days per month documented in their medical records.

Quarterly dosing regimen

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	13129B	3	3	1	'a' Ajovy
fremanezumab 225 mg/1.5 mL injection, 1.5 mL syringe	12603H	3	3	1	'a' Ajovy
Restriction Summary / ToC: Authority Required: Streamlined					
	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required (Streamlined) [<i>amendment to existing code</i>]				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Administrative Advice: Special Pricing Arrangements apply.				
	Administrative Advice: Pharmaceutical benefits that have the form fremanezumab 225 mg/1.5 mL syringes and pharmaceutical benefits that have the form fremanezumab 225 mg/1.5 mL pen devices are equivalent for the purposes of substitution.				
	Indication: Treatment-resistant migraine				
	Treatment Phase: Continuing treatment				
	Treatment criteria: <i>Must be treated by a neurologist OR</i> <i>Must be treated by a general practitioner in consultation with a neurologist</i>				
	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:				

*Public Summary Document – November 2022 PBAC Meeting with Out of Session Addendum
August 2023*

	Patient must have achieved and maintained at least 50% 50% or greater reduction from baseline in the number of migraine headache days per month
	AND
	Clinical criteria:
	Patient must continue to be appropriately managed for medication overuse headache
	AND
	Prescribing instructions:
	Patient must have the number of migraine <i>headache</i> 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.

14 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.

15 Sponsor’s Comment

The sponsor had no comment.