

**5.02 AFLIBERCEPT,
Solution for intravitreal injection,
11.43 mg in 100 microlitres (114.3 mg per mL)
pre-filled syringe,
Eylea[®],
Bayer Australia Limited**

1 Purpose of submission

- 1.1 The Category 2 submission requested Section 85 Authority Required listing for aflibercept 8 mg pre-filled syringe (PFS) for the treatment of patients with visual impairment due to diabetic macular oedema (DMO).
- 1.2 Listing was requested on the basis of a cost-minimisation approach (CMA) versus aflibercept 2 mg.

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

Component	Description
Population	Patients with visual impairment due to diabetic macular oedema (DMO)
Intervention	Aflibercept 8.0 mg intravitreal injection (pre-filled syringe)
Comparator	Aflibercept 2.0 mg intravitreal injection
Outcomes	Best corrected visual acuity (BCVA), quality of life, safety
Clinical claim	In patients with DMO, aflibercept 8 mg is non-inferior in terms of efficacy and safety when compared to aflibercept 2 mg

Source: Table 1.2, p5 of the submission.

- 1.3 A submission for aflibercept 8 mg PFS for the treatment of neovascular age-related macular degeneration (nAMD) was also considered at the November 2024 Pharmaceutical Benefits Advisory Committee (PBAC) meeting.

2 Background

Registration status

- 2.1 The submission was made under the TGA/PBAC Parallel Process. At the time of PBAC consideration aflibercept 8 mg pre-filled syringe was registered on the Australian Register of Therapeutic Goods.
- 2.2 The submission stated that an application to update the Product Information (PI) to allow extension of dosing intervals for up to 20 weeks had also been submitted to the TGA, with approval expected.

Previous PBAC consideration

- 2.3 The PBAC recommended listing of aflibercept in an 8 mg vial presentation at the May 2024 intracycle meeting for both nAMD and DMO. Aflibercept 8 mg vial was listed on

the PBS in October 2024. The PFS was included in the submission but was not considered at the May 2024 meeting as it had not yet been submitted to the TGA for approval (Paragraph 3.2, Aflibercept DMO Public Summary Document (PSD), May 2024 PBAC meeting).

2.4 The PBAC previously noted that:

- the cost-effectiveness of aflibercept 8 mg would be acceptable if it were cost-minimised to the lowest cost PBS-listed anti-VEGF treatment for the same indication (Paragraph 7.8, Aflibercept DMO PSD, May 2024 PBAC Meeting);
- the nominated comparator of aflibercept 2 mg was appropriate, and aflibercept 2 mg, faricimab and ranibizumab were all alternative therapies as they could be replaced in clinical practice, and no evidence was provided to demonstrate aflibercept 8 mg provided a significant improvement in efficacy and/or reduction of toxicity over the alternative therapies (Paragraph 7.4, Aflibercept DMO PSD, May 2024 PBAC Meeting);
- the equi-effective doses proposed by the sponsor favoured aflibercept 8 mg, and the equi-effective doses used in the CMA should be those previously accepted for faricimab:
 - Year 1: 8.23 injections of aflibercept 8 mg/faricimab to 6.38 injections of aflibercept 2 mg/ranibizumab
 - Year 2: 4.68 injections of aflibercept 8 mg/faricimab to 5.27 injections of aflibercept 2 mg/ranibizumab (Paragraph 7.11, Aflibercept DMO PSD, May 2024 PBAC Meeting).

2.5 The current submission for the PFS provided the full Clinical Study Report (CSR) for the 96-week data set of the PHOTON trial that was considered in May 2024, whereas the previous submission provided some draft exposure data for patients treated up to 96 weeks only. The only other changes to the current submission involved updating the cost of the MBS item for intravitreal (IVT) injection and updating the proposed effective price for the aflibercept 8 mg PFS.

2.6 The current submission proposed a change to the equi-effective doses recommended by the PBAC for the aflibercept 8 mg vial in May 2024, stating that the sponsor has submitted an application to the TGA for the extended dosing interval based on 96-week treatment data from the PHOTON trial. The submission requested a change to the equi-effective doses previously recommended by the PBAC, assuming that the TGA will allow an extension to the maximum dosing interval out to 20 weeks and that this would affect the PBAC's decision. The Pre-Subcommittee Response proposed that any change to the equi-effective doses for the PFS should also be applicable to aflibercept 8 mg vial.

2.7 Information previously reviewed by the PBAC is presented in abbreviated form or shaded light blue.

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

3 Requested listing

MEDICINAL PRODUCT medicinal product pack	Dispensed Price for Max. Qty	Max. qty packs	Max. qty units	No.of Rpts	Available brands
Aflibercept					
Aflibercept solution for intravitreal injection ^a 8 mg pre-filled syringe: 11.43mg/0.1mL, 0.1 mL syringe	\$934.08 published price \$ [redacted] effective price	1	1	5 (initial) 5 (continuing)	Eylea

^a Each PFS delivers a single dose of 70 µL solution for intravitreal injection containing 8 mg aflibercept.

Initial treatment

Category / Program: General Schedule Section 85
Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/>
Restriction type: <input checked="" type="checkbox"/> Authority Required (in writing only via post/HPOS upload)
Indication: Diabetic macular oedema (DMO)
Treatment Phase: Initial treatment
Clinical criteria:
The patient must have visual impairment due to diabetic macular oedema
AND
Clinical criteria:
Patient must have documented visual impairment defined as a best corrected visual acuity score between 78 and 39 letters based on the Early Treatment Diabetic Retinopathy Study chart administered at a distance of 4 metres (approximate Snellen equivalent 20/32 to 20/160), in the eye proposed for treatment
AND
Clinical criteria
The condition must be diagnosed by optical coherence tomography; or The condition must be diagnosed by fluorescein angiography
AND
Clinical criteria
The treatment must be as monotherapy; or The treatment must be in combination with laser photocoagulation
AND
Clinical criteria
The treatment must be the sole PBS-subsidised therapy for this condition
Treatment criteria:
Must be treated by an ophthalmologist or by an accredited ophthalmology registrar in consultation with an ophthalmologist
Administrative Advice: Authority approval for initial treatment of each eye must be sought. The first authority application for each eye must be made via the Online PBS Authorities System (real time assessment) or in writing via HPOS form upload or mail and must include: (1) Details (date, unique identifying number/code or provider number) of the optical coherence tomography or fluorescein angiogram report. If the application is submitted through HPOS form upload or mail, it must include: (a) A completed authority prescription form; and (b) A completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice). All reports must be documented in the patient's medical records.

Continuing treatment

Category / Program: General Schedule Section 85
Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/>
Restriction type: <input checked="" type="checkbox"/> Authority Required (streamlined)
Indication: Diabetic macular oedema (DMO)
Treatment Phase: Continuing treatment
Clinical criteria:
Patient must have previously received PBS-subsidised treatment with this drug for this condition for the same eye
AND
Clinical criteria:
AND
Clinical criteria
The treatment must be as monotherapy; or The treatment must be in combination with laser photocoagulation
AND
Clinical criteria
The treatment must be the sole PBS-subsidised therapy for this condition
Treatment criteria:
Must be treated by an ophthalmologist or by an accredited ophthalmology registrar in consultation with an ophthalmologist

- 3.1 The submission proposed restrictions for initial and continuing treatment that align with the restrictions for the 8 mg vial. The submission requested an effective AEMP of \$ [REDACTED] per 8 mg PFS. The effective AEMP of aflibercept 8 mg vial is \$ [REDACTED].

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

4 Population and disease

- 4.1 Diabetic retinopathy describes microvascular abnormalities on the interior surface of the eye (fundus) that develop in persons with diabetes. DMO is characterised by retinal thickening due to accumulation of fluid within the retina. DMO affects approximately 5% of patients with diabetes mellitus, but the prevalence is higher when diabetic control is poor. Symptoms of macular oedema include blurring or distortion of central vision, and disturbance in the perception of colours. The burden of DMO on society may increase with the increasing prevalence of diabetes mellitus.
- 4.2 The current standard of care for patients with DMO is IVT administration of anti-VEGF therapy. Three anti-VEGF IVT therapies (aflibercept 2 mg, aflibercept 8 mg (vial form), ranibizumab and faricimab) are currently listed on the PBS for the treatment of DMO.
- 4.3 Aflibercept 2 mg is currently the most widely used IVT anti-VEGF therapy for DMO. The dosing regimen for aflibercept 2 mg is five initial monthly loading doses, followed by an 8-week dosing interval, with possible extension of that interval based on physician's assessment of visual and/or anatomic outcomes. This is the treatment practice known as 'treat-and-extend' (T&E) whereby the dosing interval for anti-VEGF therapies is increased after the initial stabilisation period; T&E is applied to all IVT anti-VEGF therapies and is commonly employed in Australian clinical practice. Following

initial loading doses, the treatment interval is extended by increasing injection intervals in 2- or 4-weekly increments while maintaining stable visual and/or anatomic outcomes.

- 4.4 The proposed dose for aflibercept in the 8 mg pre-filled syringe form is IVT injection monthly for the first 3 consecutive months (as loading doses). Thereafter, the treatment interval may be extended based on physician's assessment, with the proposed maximum treatment interval being 16 weeks.
- 4.5 There are limited data suggesting that a pre-filled syringe for IVT injections may be associated with fewer episodes of endophthalmitis than a vial, but most of the data concerns ranibizumab PFS, and there appears to have been a trend to fewer cases of endophthalmitis arising from IVT injections, which complicates assessment of results with recently introduced agents.
- 4.6 There are limited data suggesting that use of aflibercept PFS may be associated with a higher incidence of acute increases in intra-ocular pressure following IVT injections.

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

5 Comparator

- 5.1 The submission nominated aflibercept 2 mg as the main comparator. Aflibercept 2 mg was accepted by the PBAC as the appropriate comparator at the May 2024 PBAC meeting, with the PBAC noting that other relevant therapies were faricimab and ranibizumab (Paragraph 7.4, Aflibercept DMO Public PSD, May 2024 PBAC Meeting).
- 5.2 In the context of the cost-minimisation approach taken by the submission, a further consideration for PBAC is that, under Section 101(3B) of the *National Health Act 1953*, when the proposed medicine is substantially more costly than an alternative therapy, the committee cannot make a positive recommendation unless it is satisfied that, for some patients, the proposed medicine provides a significant improvement in efficacy and/or reduction of toxicity over the alternative therapy. If the committee is so satisfied, it must make a statement to this effect.
- 5.3 For the requested population, the following PBS-listed medicines may be considered alternative therapies because they could be replaced in practice: aflibercept 2 mg, faricimab and ranibizumab. Some of these alternative therapies may be less costly than aflibercept 8 mg PFS. The ESC noted that the aflibercept 8 mg vial is also an alternative therapy.

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.

Clinical trials

6.3 The submission was based on the same head-to-head trial (PHOTON) as in the submission for aflibercept 8 mg vial, comparing aflibercept 8 mg given 12- or 16-weekly to aflibercept 2 mg given 8-weekly. Details of the trial presented in the submission is provided in Table 2.

6.4 The submission did not provide any clinical evidence related to use of aflibercept 8 mg in the PFS form.

6.5 Details of the trials presented in the submission are provided in Table 2. The submission provided updated clinical data based on the 96-week CSR.

Table 2: Trial and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
PHOTON (NCT04429503)	A randomized, double-masked, active-controlled Phase 2/3 study of the efficacy and safety of high dose aflibercept in patients with diabetic macular edema. VGFTe-8-DME-1934. Amendment 4	Clinical Study Protocol, April 2022
	A randomized, double-masked, active-controlled Phase 2/3 study of the efficacy and safety of high dose aflibercept in patients with diabetic macular edema	Clinical Study Report, January 2023
	A randomized, double-masked, active-controlled Phase 2/3 study of the efficacy and safety of high dose aflibercept in patients with diabetic macular edema. Amendment Version 2.0 / 19	Statistical analysis plan, August 2022
	Brown DM. Baseline Disease Characteristics of Patients Who Maintained 12- and 16-Week Aflibercept 8 mg Dosing Versus Patients with Shortened Treatment Intervals Through Week 48 in the Phase 2/3 PHOTON Trial.	Investigative Ophthalmology and Visual Science. 2023;64(8):2813
	Do DV. Aflibercept 8 mg for Diabetic Macular Edema: 48-Week Results From the Phase 2/3 PHOTON Trial.	Investigative Ophthalmology and Visual Science. 2023;64(8):2814
	Ghorayeb G. Intravitreal Aflibercept 8 mg for Diabetic Macular Edema: Week 48 Efficacy Outcomes by Baseline Demographics in the Phase 2/3 PHOTON Trial.	Investigative Ophthalmology and Visual Science. 2023;64(8):2707
Schneider E. Pooled Safety Analysis of Aflibercept 8 mg in the CANDELA, PHOTON, and PULSAR Trials.	Investigative Ophthalmology and Visual Science. 2023;64(8):3724	

Source: Table 2-3 p25 of the submission

DME = diabetic macular oedema; VEGF = Vascular endothelial growth factor

Note: Shaded information is unchanged from the submission for aflibercept 8 mg vial.

6.6 The key features of the direct randomised trial PHOTON are summarised in Table 3. The only difference compared to the submission for the aflibercept 8 mg vial was the provision of the CSR for 96 weeks although some of the 96-week data were reviewed in May 2024.

Table 3: Key features of the included evidence

Trial	N	Design/duration	Risk of bias	Patient population	Outcomes
PHOTON	660	R, MC, DB, non-inferiority Ongoing (96 weeks)	Low	Adults with macular thickening secondary to DMO involving the centre of the fovea BCVA ETDRS letter score of 78 to 24 in the study eye with decreased vision primarily because of DMO Type 1 or 2 diabetes CRT $\geq 300 \mu\text{m}$ (or $\geq 320 \mu\text{m}$ on Spectralis) as determined by the reading centre at the screening visit.	Primary: Change in BCVA Key secondary: Change in BCVA ≥ 2 -step improvement on the ETDRS DRS Additional secondary: Proportion of patients gaining ≥ 15 letters in BCVA Proportion of patients with BCVA ≥ 69 letters; Change in CST Proportion of patients with leakage on fluorescein angiography Quality of life (NEI VFQ-25) Adverse events

Source: Table 3, Paragraph 6.6, Aflibercept DMO PSD, May 2024 PBAC Meeting.

Note: Shaded information is unchanged from the submission for aflibercept 8 mg vial.

BCVA = best corrected visual acuity; CST = central subfield thickness; CRT = Central retinal thickness; DB = double blind; DMO = diabetic macular oedema; DRS = diabetic retinopathy severity; ETDRS = Early Treatment Diabetic Retinopathy Study; MC = multi-centre; NEI VFQ-25 = National Eye Institute Visual Functioning Questionnaire-25; R = randomised.

- 6.7 The trial intervention was the 8 mg vial form of aflibercept, not the pre-filled syringe.
- 6.8 Disposition of patients in the trial, separating the period up to 60 weeks from 60 to 96 weeks, is shown in Table 4. Updated data for the extent of exposure is shown in Table 5. It should be noted that although treatment durations beyond 96 weeks were recorded, injections given after week 96 were not counted.

Table 4: Disposition of patients at 60 and 96 weeks in the PHOTON trial

	Aflibercept 2 mg		Aflibercept 8 mg			
	2q8 N = 167		8q12 N = 329		8q16 N = 164	
	60 weeks	96 weeks	60 weeks	96 weeks	60 weeks	96 weeks
Completed study treatment	155	139	289	256	153	139
Withdrawals	0-60 weeks	60-96 weeks	0-60 weeks	60-96 weeks	0-60 weeks	60-96 weeks
n (%)	12 (7.2%)	16 (9.6%)	40 (12.2%)	33 (10.0%)	12 (7.3%)	13 (7.9%)
Adverse event, n (%)	0	1 (0.6%)	4 (1.2%)	7 (2.1%)	1 (0.6%)	1 (0.6%)
Patient decision, n (%)	4 (2.4%)	5 (3.0%)	12 (3.6%)	5 (1.5%)	2 (1.2%)	6 (3.7%)
Death, n (%)	5 (3.0%)	3 (1.8%)	9 (2.7%)	9 (2.7%)	4 (2.4%)	1 (0.6%)
Annualised rate of death	4.4	4.3	7.8	13.0	3.5	1.44
Other, ¹ n (%)	3 (1.8%)	5 (1.8%)	15 (4.6%)	5 (1.5%)	4 (2.4%)	4 (1.2%)

Source: 60-week CSR, Table 4, pp41-42; 96-week CSR, Table 3, p36.

¹ Includes physician decision, protocol deviations, lost to follow-up, Covid-19 related, and no reason given.

2q8 = 2 mg aflibercept 8 weekly; 8q12 = 8 mg aflibercept 12 weekly; 8q16 = 8 mg aflibercept 16 weekly; NA = not applicable.

Table 5: Extent of exposure through week 96 in the PHOTON trial

	Aflibercept 2 mg		Aflibercept 8 mg	
	2q8 N = 167	8q12 N = 328	8q16 N = 163	
Number of active injections				
Mean (SD)	12.9 (2.5)	8.6 (2.2)	7.5 (1.6)	
Median (range)	14.0 (1-14)	9.0 (1-13)	9.0 (1-13)	
Number of sham injections				
Mean (SD)	NR	NR	NR	
Median (range)				
Duration of treatment, weeks				
Mean (SD)	89.5 (20.0)	86.6 (23.9)	90.9 (20.3)	
Median (range)	96.0 (4-117)	96.0 (4-113)	96.1 (4-114)	

Source: 96 weeks CSR, Table 10, p49. 2q8 = aflibercept 2 mg every 8 weeks; 8q12 = 8 mg of aflibercept every 12 weeks; 8q16 = 8 mg of aflibercept every 16 weeks; NR = not reported; SD = standard deviation.

- 6.9 Changes in administration frequency were allowed in patients randomised to aflibercept 8 mg every 12 weeks (8q12) or aflibercept 8 mg every 12 weeks (8q16) if pre-defined dose regimen modification (DRM) criteria were met. From week 16 to week 52 treatment intervals could only be shortened, in four weeks decrements to a minimum of 8 weeks. From week 52, dosing intervals could be shortened or lengthened by four weeks, with the change coming into effect at or after the week 60 visit.
- 6.10 The DRM criteria were related to efficacy, not tolerability (i.e., dose intervals could not be shortened for adverse events):

- for shortening, both > 10 letter loss in best corrected visual acuity from week 12 in association with persistent or worsening DMO and > 50 µm increase in central retinal thickness from week 12;
- for lengthening, both < 5 letter loss in best corrected visual acuity from week 12 and central retinal thickness < 300 µm.

6.11 Changes in administration frequency among patients completing 96 weeks of treatment are shown in Table 6.

6.12 The 96-week data provides limited information about treatment at 20-week intervals. Of patients randomised to 8 mg doses, 171 (43.3%) had the treatment interval lengthened to 20 weeks. Because lengthening of the treatment interval could be decided on no earlier than the week 52 visit, the maximum number of injections received up to the week 96 data cut-off at intervals of 20 weeks or longer was two, since patients in the aflibercept 8q16 group who met the DRM criteria for treatment interval lengthening to 20 weeks at 52 weeks would have had injections at 72 and 92 weeks. Patients whose interval was lengthened to 20 weeks at the week 56 visit but before week 76 would have received only one injection before the week 96 cut-off. Patients who met the criteria for lengthening to 20 weeks after 76 weeks could not receive an injection at the longer interval before the data cut-off. The numbers whose dose intervals were lengthened to 20 weeks after 56 and 76 weeks were not provided.

Table 6: Changes in administration frequency among patients completing 96 weeks in the PHOTON trial.

	Aflibercept 8 mg	
	8q12 N = 256	8q16 N = 139
Treatment interval was shortened at any time, n (%)	36 (14.1%)	24 (17.3%)
Treatment interval was shortened to 8 weeks at any time, n (%)	32 (12.5%)	10 (7.2%)
Treatment interval was lengthened at any time, n (%)	NR	NR
Treatment interval was lengthened to 20 weeks, n (%)	108 (42.2%)	63 (45.3%)
Treatment interval was lengthened to 20 weeks and maintained at 20 weeks, n (%)	47 (18.4%)	18 (12.9%)
Treatment interval was lengthened to 20 weeks and lengthened again to 24 weeks, n (%)	61 (23.8%)	45 (32.4%)
Treatment interval was lengthened to 20 weeks at last visit, n (%)	NR	NR

Source: 96-week CSR, Table 11, p50. 8q12 = 8 mg aflibercept 12-weekly; 8q16 = 8 mg 16-weekly; NR = not reported.

Comparative effectiveness

6.13 The updated data in this submission were the results of the 96-week follow-up of the PHOTON trial, presented in Table 7 and Figure 1.

Table 7: Change from baseline in BCVA in PHOTON, (FAS; MMRM)

	Aflibercept 8 mg		Aflibercept 2 mg	Estimate for contrast (95% CI) ^a One-sided non-inferiority p-value ^b	
	8q12 (N=328)	8q16 (N=163)	2q8 (N=167)	8q12 vs 2q8	8q16 vs 2q8
Baseline BCVA (ETDRS letters score)	63.63	61.44	61.47	-	-
Week 48					
Patients n (%)	277 (84.5%)	149 (91.4%)	150 (89.8%)	-0.57 (-2.26, 1.13) <0.0001 ^b	-1.44 (-3.27, 0.39) 0.0031
Mean change from baseline in BCVA (SD)	8.77 (8.95)	7.86 (8.38)	9.21 (8.99)		
LS mean change from baseline in BCVA (SE)	8.10 (0.61)	7.23 (0.71)	8.67 (0.73)		
Week 60					
Patients n (%)	252 (76.8%)	138 (84.7%)	133 (79.6%)	-0.88 (-2.67, 0.91) 0.0003 ^b	-1.76 (-3.71, 0.19) 0.0122 ^b
Mean change from baseline in BCVA (SD)	9.05 (9.27)	7.96 (9.14)	9.62 (9.58)		
LS mean change from baseline in BCVA (SE)	8.52 (0.63)	7.64 (0.75)	9.40 (0.77)		
Week 96					
Patients with data (%)	222	127	124	0.45 (-1.55, 2.45) <0.0001	-1.11 (-3.27, 1.05) 0.0044
Mean change from baseline in BCVA (SD)	8.82 (9.93)	7.50 (9.86)	8.41 (11.10)		
LS mean change from baseline in BCVA (SE)	8.15 (0.63)	6.59 (0.77)	7.70 (0.89)		

Source: Table 2-16 p57, Table 2-17 p59 of the submission.

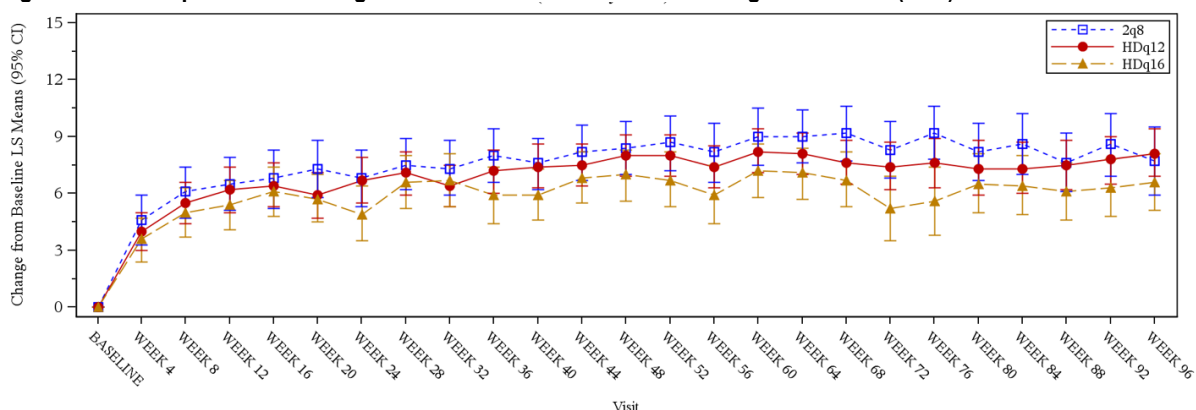
Note: Shaded information is unchanged from the submission for aflibercept 8 mg vial.

BCVA = best corrected visual acuity; CI = confidence interval; ETDRS = Early Treatment Diabetic Retinopathy Study; n = number of patients with event; FAS = full analysis set; MMRM = mixed model for repeated measurements; N = total patients in group; SE = standard error; SD = standard deviation; 2q8 = aflibercept 2 mg administered every 8 weeks; 8q12 = aflibercept 8 mg administered every 12 weeks; 8q16 = aflibercept 8 mg administered every 16 weeks.

a. Estimate for contrast was based on the MMRM model with baseline BCVA measurement as a covariate, treatment group and the stratification variables (geographic region [Japan vs Rest of World]; baseline CRT from reading centre [<400µm vs ≥400µm], prior treatment for DMO per EDC; [yes vs no]) as fixed factors, and terms for the interaction between baseline and visit and the interaction between treatment and visit, computed for the differences of aflibercept 8q12 minus 2q8 and 8q16 minus 2q8, respectively with 2-sided 95% CIs

b. p-value for the 1-sided non-inferiority test at a margin of 4 letters

Figure 1: Least square mean change from baseline in BCVA score through to week 96 (FAS)



Source: Figure 2.8, p60 of the submission. Abbreviations: 2q8, aflibercept 2 mg administered every 8 weeks; BCVA, best corrected visual acuity; CI, confidence intervals; FAS, full analysis set; HDq12, aflibercept 8 mg administered every 12 weeks; HDq16, aflibercept 8 mg administered every 16 weeks; LS, least squares.

Comparative harms

- 6.14 The submission did not present any safety data from the use of the pre-filled syringe product.
- 6.15 The submission did not present the 96-week safety data for the PHOTON trial. Table 8 presents the results extracted from the 96-week CSR for the outcomes that were presented in the previous submission.
- 6.16 The number of adverse events related to IVT injection procedures was similar in all groups. However, the CSR did not present results separately for active and sham injections, which may favour trial arms with fewer active injections. Sham and active injections were given by unblinded staff, and the sham injections were mock injections, using a syringe with no needle, so blinding of patients may not have been complete and not all adverse events were equally likely with active and sham injections.
- 6.17 Adverse events reported for the 96-week data set but not for the 60-week data set are shown in Table 9. Because a study treatment was given at week 60, and treatment emergent adverse events included events up to 30 days after the last treatment, it is not clear what time periods are covered by the two data sets. However, an exploratory calculation (done during the evaluation) of an annualised rate for some adverse events is given based on the assumption of 60 weeks and 96 weeks exposure and is shown in Table 9.
- 6.18 Adverse event rates in PHOTON were generally lower than in PULSAR, the trial of aflibercept for age-related macular degeneration, and there was no indication that the rates were higher in the second year of treatment.

Table 8: Summary of adverse events in the PHOTON trial

	96 weeks			60 weeks		
	Aflibercept 8 mg		Aflibercept 2 mg	Aflibercept 8 mg		Aflibercept 2 mg
	8q12 N = 328 n (%)	8q16 N = 163 n (%)	2q8 N = 167 n (%)	8q12 N = 328 n (%)	8q16 N = 163 n (%)	2q8 N = 167 n (%)
Any AE	279 (85.1%)	145 (89.0%)	136 (81.4%)	247 (75.3%)	128 (78.5%)	124 (74.3%)
Any study drug-related TEAE	8 (2.4%)	3 (1.8%)	3 (1.8%)	6 (1.8%)	1 (0.6%)	3 (1.8%)
Any study drug-related ocular TEAE	8 (2.4%)	1 (0.6%)	3 (1.8%)	6 (1.8%)	0	3 (1.8%)
Any TEAE related to intravitreal injection procedure	50 (15.2%)	21 (12.9%)	24 (14.4%)	45 (13.7%)	13 (8.0%)	19 (11.4%)
Any TEAE leading to discontinuation	14 (4.3%)	2 (1.2%)	4 (2.4%)	9 (2.7%)	2 (1.2%)	3 (1.8%)
Any ocular TEAE leading to discontinuation	3 (0.9%)	0	0	2 (0.6%)	0	0
Any SAE	88 (26.8%)	49 (30.1%)	48 (28.7%)	65 (19.8%)	29 (17.8%)	36 (21.6%)
Any ocular serious TEAE	9 (2.7%)	5 (3.1%)	6 (3.6%)	6 (1.8%)	2 (1.2%)	5 (3.0%)
Any serious TEAE in the study eye	3 (0.9%)	3 (1.8%)	2 (1.2%)	2 (0.6%)	1 (0.6%)	1 (0.6%)
Any TEAE	277 (84.5%)	143 (87.7%)	134 (80.2%)	245 (74.7%)	126 (77.3%)	123 (73.7%)
Any serious TEAE related to intravitreal injection procedure	1 (0.3%)	0	0	1 (0.3%)	0	0
Any AE with outcome death	18 (5.5%)	5 (3.1%)	9 (5.4%)	9 (2.7%)	4 (2.5%)	5 (3.0%)
Any TEAE of intraocular inflammation in study eye	5 (1.5%)	1 (0.6%)	1 (1.2%)	4 (1.2%)	1 (0.6%)	1 (0.6%)
Any treatment-emergent APTC	22 (6.7%)	11 (6.7%)	12 (7.2%)	13 (4.0%)	9 (5.5%)	6 (3.6%)
Cardiovascular death	7 (2.1%)	2 (1.2%)	5 (3.0%)	3 (0.9%)	2 (1.2%)	3 (1.8%)
Non-fatal myocardial infarction	10 (3.0%)	3 (1.8%)	5 (3.0%)	7 (2.1%)	3 (1.8%)	3 (1.8%)
Non-fatal stroke	5 (1.5%)	6 (3.7%)	2 (1.2%)	3 (0.9%)	4 (2.5%)	0
Any TEAE of hypertension	51 (15.5%)	34 (20.9%)	27 (16.2%)	42 (12.8%)	28 (17.2%)	23 (13.8%)

Source: 96-week CSR, Table 23, pp67-70; Table 34, pp88-89; 60-week CSR, Table 38, pp95-98; Table 45, p112. Note: Shaded information is unchanged from the submission for aflibercept 8 mg vial.

Abbreviations: 2q8 = aflibercept 2 mg administered every 8 weeks, 8q12 = aflibercept 8 mg administered every 12 weeks, 8q16 = aflibercept 8 mg administered every 16 weeks, AE = adverse event, APTC = Anti-Platelet Trialists Collaboration; CI = confidence interval, IVT = intravitreal, n = number of participants with event, N = total number of participants in treatment arm, OR = odds ratio, RD = risk difference, SAE = serious adverse event, SAF = safety analysis set, TEAE = treatment-emergent adverse events.

TEAEs are defined as AEs that started in the time from first injection to the last injection (active or sham) in the study plus 30 days. Post-treatment AEs are defined as AEs that started more than 30 days after the last injection (active or sham) in the study.

Table 9: Selected additional adverse events reported in the 96-week CSR compared to the 60-week CSR

	Aflibercept 8 mg				Aflibercept 2 mg	
	8q12 N = 328		8q16 N = 163		2q8 N = 167	
	60 weeks	60-96 weeks	60 weeks	60-96 weeks	60 weeks	60-96 weeks
Any TEAE related to intravitreal injection procedure, n (rate per year per 100 patients)	45 (11.9)	5 (2.2)	13 (6.9)	8 (7.1)	19 (9.9)	5 (4.3)
Any TEAE leading to discontinuation, n (rate per year per 100 patients)	9 (2.4)	5 (2.2)	2 (1.1)	0	3 (1.6)	1 (0.9)
Any serious TEAE in the study eye, n (rate per year per 100 patients)	2 (0.5)	1 (0.4)	1 (0.5)	2 (1.8)	1 (0.5)	1 (0.9)
Any AE with outcome death, n (rate per year per 100 patients)	9 (2.4)	9 (4.0)	4 (2.1)	1 (0.9)	5 (2.6)	4 (3.6)
Any treatment emergent adjudicated APTC, n (rate per year per 100 patients)	13 (3.4)	9 (4.0)	9 (4.8)	2 (1.8)	6 (3.2)	6 (5.2)
Adjudicated cardiovascular death, n (rate per year per 100 patients)	3 (0.8)	4 (1.8)	2 (1.1)	0	3 (1.6)	2 (1.7)
Any TEAE of hypertension, n (rate per year per 100 patients)	42 (11.1)	9 (3.95)	28 (14.9)	6 (5.3)	23 (12.0)	4 (3.4)

Source: Data from Table 9 and calculated from data in the CSR during the evaluation

Note: Shaded information is unchanged from the submission for aflibercept 8 mg vial.

Abbreviations: 2q8 = 2mg aflibercept 8-weekly; 8q12 = 8mg aflibercept 12-weekly; 8q16 = 8mg aflibercept 16-weekly; AE = adverse event; TEAE = treatment emergent adverse event; APTC = Anti-Platelet Trialists Collaboration.

6.19 The submission provided data in support of the claim that use of a PFS is associated with lower rates of endophthalmitis. Taken as a whole, the data are consistent with an association of lower rates of endophthalmitis with use of PFS, but causation has not been established. Some data suggest that endophthalmitis may be less frequent with ranibizumab PFS than with aflibercept PFS.

6.20 There may be an increased risk of acute rises in intra-ocular pressure with use aflibercept PFS. This risk was not discussed in the submission.

Benefits/harms

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

Clinical claim

6.22 The submission described aflibercept 8 mg PFS (administered 12-weekly or 16-weekly) as non-inferior in terms of effectiveness and safety in patients with visual impairment due to DMO compared to aflibercept 2 mg (administered 8-weekly).

6.23 This claim has previously been accepted by the PBAC, but as noted above, no clinical data were submitted using the PFS product.

- 6.24 There were no data in the submission from which comparative effectiveness and safety of the 8 mg vial preparation versus the pre-filled syringe could be assessed. As the pre-filled syringe has been approved by the TGA, effectiveness and safety would be expected to be the same. The injection burden would be the same for these two presentations.
- 6.25 The PBAC considered that the claim of non-inferior comparative effectiveness was reasonable.
- 6.26 The PBAC considered that the claim of non-inferior comparative safety was reasonable.

Economic analysis

- 6.27 The submission presented a CMA comparing aflibercept 8 mg PFS to aflibercept 2 mg, as presented in the submission for the 8 mg vial. The key assumptions and components of the analysis are presented in Table 10 and were unchanged from the initial CMA proposed in May 2024 other than updating the MBS scheduled fee for the IVT injection.

Table 10: Key assumptions and components of the cost-minimisation approach.

Component	Claim or assumption
Therapeutic claim: effectiveness	Based on evidence presented in Section 2, aflibercept 8 mg PFS is non-inferior in effectiveness to aflibercept 2 mg
Therapeutic claim: safety	Based on evidence presented in Section 2, aflibercept 8 mg PFS is non-inferior in safety to aflibercept 2 mg
Evidence base	Direct randomised trial - PHOTON
Equi-effective doses	Year 1: 6.20 doses of aflibercept 8 mg PFS annually to 6.68 doses of aflibercept 2 mg annually Year 2: 3.67 doses of aflibercept 8 mg PFS annually to 5.28 doses of aflibercept 2 mg annually
Direct medicine costs	Calculated from equi-effective doses accounting for drug (effective AEMP) and administration costs (MBS fees)
Other costs or cost offsets	Administration costs: MBS item 42738 – Fee = \$342.65

Source: Table 3.2, p 104 of the submission. Abbreviations: PFS = pre-filled syringe; AEMP =ex-manufacturer price; MBS=Medicare Benefits Schedule

- 6.28 In this submission, the equi-effective doses were estimated as the same as those originally proposed in May 2024:
- Year 1: 6.20 doses of aflibercept 8 mg PFS annually to 6.68 doses of aflibercept 2 mg annually
 - Year 2: 3.67 doses of aflibercept 8 mg PFS annually to 5.28 doses of aflibercept 2 mg annually
- 6.29 The equi-effective doses were not as recommended by the PBAC in May 2024, which were, over 2 years, 12.91 doses of aflibercept 8mg/ faricimab and 11.65 doses of aflibercept 2 mg/ ranibizumab, as follows:
- Year 1: 8.23 injections of aflibercept 8 mg/ faricimab to 6.38 injections of aflibercept 2 mg/ ranibizumab

- Year 2: 4.68 injections of aflibercept 8 mg/ faricimab to 5.27 injections of aflibercept 2 mg/ ranibizumab.

6.30 The reversion to the originally proposed equi-effective doses was explained in the submission as being based on the 96-week data from PHOTON. The sponsor claimed that dosing in clinical practice is expected to be extended up to 20 weeks based on these results. The ESC noted the change to the PI to allow extension to 20 weeks is not expected until [REDACTED].

6.31 The results of the CMA in the current submission are shown in Table 11.

Table 11: Results of cost-minimisation approach – November 2024 submission

Row	Parameter	Aflibercept 2 mg	Aflibercept 8 mg PFS	Reference /Calculation
A	Drug costs per administration (AEMP)	\$ [REDACTED]	\$ [REDACTED]	Aflibercept 2 mg: known to sponsor Aflibercept 8 mg: Calculated ((F – E) / B)
B	Administration frequency - two-year analysis period	11.96	9.87	Aflibercept 2 mg: DUSC analysis (Primary analysis, Table 3-6). Aflibercept 8 mg: PHOTON RCT
C	Total drug costs (AEMP)	\$ [REDACTED]	\$ [REDACTED]	A x B
D	Administration (unit cost)	\$342.65		MBS item: 42738
E	Total administration costs	\$4,098.09	\$3,380.76	D x B
F	Total drug and administration costs	\$ [REDACTED]	\$ [REDACTED]	C + E

Source: Table 3.7, p111 of the submission. Abbreviations: PFS = pre-filled syringe; AEMP= ex-manufacturer's price; DUSC= Drug Utilisation Sub Committee; MBS= Medicare Benefits Schedule; RCT= randomised controlled trial

6.32 No evidence was provided that aflibercept 8 mg PFS provides a significant improvement in efficacy and/or reduction in safety over aflibercept 2 mg or aflibercept 8 mg vial, faricimab or ranibizumab.

Drug cost/patient/year

6.33 The drug cost per patient per year is shown in Table 12.

Table 12: Drug cost per patient for proposed and comparator drugs

	Aflibercept 8 mg trial dose and duration	Aflibercept 8 mg CMA	Aflibercept 8 mg financial estimates	Aflibercept 2 mg trial dose and duration	Aflibercept 2 mg CMA	Aflibercept 2 mg financial estimates
Mean dose/scripts	4.875 ^a	5.075 ^b	5.075 ^b	7.485 ^c	5.98 ^d	5.98 ^d
DPMQ per script		\$ [REDACTED]			\$ [REDACTED]	
Cost/patient/year	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]

Source: Updated from Table 12, PSD May 2024 PBAC Meeting.

Note: Shaded information is unchanged from the submission for aflibercept 8 mg vial.

Abbreviations: CMA= cost-minimisation approach; mg = milligrams.

^a Averaged over 2-years treatment including 24-week interval doses (6.20 doses in Year 1 and 4.94 doses in Year 2).

^b Averaged over 2-years treatment, assuming a maximum treatment interval of 16 weeks as proposed in the TGA Delegate's Overview (6.20 doses in Year 1 and 3.95 doses in Year 2).

^c Average of the total number of doses (14.97 doses) estimated per patient at the week 96 data cut, adjusted for treatment duration and apportioned to two years (104 weeks).

^d Averaged over 2-years treatment (6.68 doses in Year 1 and 5.28 doses in Year 2).

Estimated PBS usage & financial implications

- 6.34 This submission was not considered by DUSC.
- 6.35 The submission presented the same market share approach and financial estimates model as that used in the May 2024 submission for the aflibercept 8 mg vial. The financial estimates workbook used an updated price for aflibercept 8 mg as well as the updated MBS fee.
- 6.36 The estimates of use did not differentiate between the 8 mg vial and the 8 mg pre-filled syringe. The submission assumed all patients would receive the PFS.
- 6.37 The updated estimates of the financial impact of listing, using the proposed effective price of the aflibercept 8 mg PFS are shown in Table 13.

Table 13: Net financial implications to the PBS/RPBS of the proposed listing of aflibercept 8 mg for DMO, effective pricing

Year	2025	2026	2027	2028	2029	2030
Total aflibercept 8 mg scripts						
PBS/RPBS total	1	1	2	3	4	5
Total financial impact (less co-pay)						
PBS/RPBS total	6	6	7	7	8	8
Changes in financial impact of other medicines (less co-pay)						
PBS/RPBS total	9	9	9	9	9	9
Net financial impact (less co-pay)						
PBS/RPBS total	6	6	5	6	6	6
Net cost to MBS - 85% benefit	9	9	9	9	9	9
Net cost to Government	6	6	6	9	9	9

Source: Table 4.23, p128; Table 4.26, p130, Table 4.28, p 131 of the submission; Table 14 PSD May 2024 PBAC Meeting.

Abbreviations: PBS, Pharmaceutical Benefits Scheme; RPBS, Repatriation Pharmaceutical Benefits Scheme; MBS = Medicare Benefits Schedule.

The redacted values correspond to the following ranges:

1 10,000 to < 20,000

2 20,000 to < 30,000

3 30,000 to < 40,000

4 40,000 to < 50,000

5 50,000 to < 60,000

6 \$0 to < \$10 million

7 \$10 million to < \$20 million

8 \$20 million to < \$30 million

9 net cost saving

- 6.38 The total cost to the PBS/RPBS of listing aflibercept 8 mg PFS was estimated to be \$0 to < \$10 million in Year 1, and a total of \$100 million to < \$200 million in the first 6 years of listing. The net impact to the PBS/RPBS was estimated as \$0 to < \$10 million in Year 1 and a total of \$10 million to < \$20 million in the first 6 years of listing. The ESC noted the financials included a net cost to the Government in the first few years,

likely driven by initiating patients requiring loading doses, and a net save in later years due to the dosing interval extension.

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

7 PBAC Outcome

- 7.1 The PBAC recommended the Authority Required listing of aflibercept 8 mg pre-filled syringe (PFS) for the treatment of patients with visual impairment due to diabetic macular oedema. The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of aflibercept 8 mg PFS would be acceptable if it were cost-minimised to the lowest cost PBS-listed anti-VEGF treatment for the same indication.
- 7.2 The PBAC noted that the submission did not provide any clinical data that specifically related to the PFS, and that the submission used the same data package (with updated trial data) that was used when the Committee considered aflibercept 8 mg vial in May 2024.
- 7.3 The PBAC recalled it had previously accepted the claim that aflibercept 8 mg was non-inferior in terms of comparative efficacy and safety versus aflibercept 2 mg.
- 7.4 The PBAC considered that the equi-effective doses for the aflibercept 8 mg vial recommended at the May 2024 PBAC meeting remain appropriate for the 8 mg PFS, noting that over 2 years these are 12.91 doses of aflibercept 8mg/ faricimab and 11.65 doses of aflibercept 2 mg/ ranibizumab, as follows:
- Year 1: 8.23 injections of aflibercept 8 mg/ faricimab to 6.38 injections of aflibercept 2 mg/ ranibizumab
 - Year 2: 4.68 injections of aflibercept 8 mg/ faricimab to 5.27 injections of aflibercept 2 mg/ ranibizumab
- 7.5 The PBAC noted it would be unable to consider amending the equi-effective doses until the change to the Product Information to include a 20-week dosing interval had been approved by the TGA.
- 7.6 The PBAC considered that the listing would be cost-neutral to the PBS/RPBS.
- 7.7 The PBAC considered that a grandfather restriction was appropriate and that it should be in operation for a maximum of 12 months from listing.
- 7.8 The PBAC advised, under Section 101 (4AACD) of the *National Health Act*, that aflibercept 8 mg vial and aflibercept 8 mg pre-filled syringe should be considered equivalent for the purposes of substitution (i.e., 'a' flagged in the Schedule with a NOTE stating PBS of one form and PBS of another form are equivalent for the purposes of substitution).
- 7.9 The PBAC advised that aflibercept 8 mg PFS is not suitable for prescribing by nurse practitioners.

- 7.10 The PBAC recommended that the Early Supply Rule should not apply.
- 7.11 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because aflibercept 8 mg PFS is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over aflibercept 2 mg, 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 Add new item:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
AFLIBERCEPT					
Initial treatment					
aflibercept 8 mg/0.07 mL injection, 0.07 mL syringe	NEW	1	1	5	Eylea
Continuing treatment					
aflibercept 8 mg/0.07 mL injection, 0.07 mL syringe	NEW	1	1	5	Eylea
Restriction Summary edit / Treatment of Concept: edit					
Category / Program: GENERAL – General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required (in writing - legacy) – Postal/HPOS upload or Online PBS Authorities immediate assessment					
	Administrative Advice: Special Pricing Arrangements apply.				
	Administrative Advice: No increase in the maximum number of repeats may be authorised				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised for applications for treatment of one eye.				
	Administrative Advice: Where both eyes are affected by the condition, a quantity of 2 units may be requested through the same authority application.				
	Administrative Advice: Pharmaceutical benefits that have the form aflibercept 0.07mL injection syringe and pharmaceutical benefits that have the form aflibercept 0.07mL injection vial are equivalent for the purposes of substitution.				
Indication: Diabetic macular oedema (DMO)					
Treatment Phase: Initial treatment					

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	Treatment criteria:
	Must be treated by an ophthalmologist or by an accredited ophthalmology registrar in consultation with an ophthalmologist
	Clinical criteria:
	Patient must have visual impairment due to diabetic macular oedema
	AND
	Clinical criteria:
	Patient must have documented visual impairment defined as a best corrected visual acuity score between 78 and 39 letters based on the early treatment diabetic retinopathy study chart administered at a distance of 4 metres (approximate Snellen equivalent 20/32 to 20/160), in the eye proposed for treatment
	AND
	Clinical criteria:
	The condition must be diagnosed by optical coherence tomography; or
	The condition must be diagnosed by fluorescein angiography
	AND
	Clinical criteria:
	The treatment must be as monotherapy; or
	The treatment must be in combination with laser photocoagulation
	AND
	Clinical criteria:
	The treatment must be the sole PBS-subsidised therapy for this condition
	Prescribing Instructions: Authority approval for initial treatment of each eye must be sought.
	Prescribing Instructions: The first authority application for each eye must be made via the Online PBS Authorities System (real time assessment) or in writing via HPOS form upload or mail and must include: (1) Details (date, unique identifying number/code or provider number) of the optical coherence tomography or fluorescein angiogram report. If the application is submitted through HPOS form upload or mail, it must include: (a) details of the proposed prescription; and (b) A completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice). All reports must be documented in the patient's medical records.
	Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authorisation under this restriction should be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/hpos) Alternatively, applications for authority to prescribe can be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001
Restriction Summary / Treatment of Concept:	
	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners

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	Restriction type: <input checked="" type="checkbox"/> Authority Required (STREAMLINED) [new code]
	Indication: Diabetic macular oedema (DMO)
	Treatment Phase: Continuing treatment
	Treatment criteria:
	Must be treated by an ophthalmologist or by an accredited ophthalmology registrar in consultation with an ophthalmologist
	Clinical criteria:
	Patient must have previously received PBS-subsided treatment with this drug for this condition for the same eye
	AND
	Clinical criteria:
	The treatment must be as monotherapy; or
	The treatment must be in combination with laser photocoagulation
	AND
	Clinical criteria:
	The treatment must be the sole PBS-subsidised therapy for this condition
	Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).
Restriction Summary edit / Treatment of Concept: edit	
	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required (in writing – legacy) – Postal/HPOS upload or Online PBS Authorities immediate assessment
	Indication: Diabetic macular oedema (DMO)
	Treatment Phase: Transitioning from non-PBS to PBS-subsidised treatment - Grandfather arrangements
	Treatment criteria:
	Must be treated by an ophthalmologist or by an accredited ophthalmology registrar in consultation with an ophthalmologist
	Clinical criteria:
	Patient must have received non-PBS-subsidised treatment with this drug for this PBS indication for the same eye prior to [PBS listing date],
	AND
	Clinical criteria:
	Patient must have visual impairment due to diabetic macular oedema
	AND
	Clinical criteria:
	Patient must have documented visual impairment defined as a best corrected visual acuity score between 78 and 39 letters based on the early treatment diabetic retinopathy study chart administered at a distance of 4 metres (approximate Snellen equivalent 20/32 to 20/160), in the eye proposed for treatment
	AND
	Clinical criteria:
	The condition must be diagnosed by optical coherence tomography; or
	The condition must be diagnosed by fluorescein angiography
	AND
	Clinical criteria:

	The treatment must be as monotherapy; or
	The treatment must be in combination with laser photocoagulation
	AND
	Clinical criteria:
	The treatment must be the sole PBS-subsidised therapy for this condition
	<p>Prescribing Instructions: The first authority application for each eye must be made via the Online PBS Authorities System (real time assessment) or in writing via HPOS form upload or mail and must include: (1) Details (date, unique identifying number/code or provider number) of the optical coherence tomography or fluorescein angiogram report. If the application is submitted through HPOS form upload or mail, it must include: (a) details of the proposed prescription; and (b) A completed authority application form relevant to the indication and treatment phase (the latest version is located on the website specified in the Administrative Advice). All reports must be documented in the patient's medical records.</p>
	<p>Administrative advice: This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.</p>
	<p>Administrative advice: Patients may qualify for PBS-subsidised treatment under this restriction once only per eye. For continuing PBS-subsidised treatment, a 'Grandfather' patient must qualify under the 'Continuing treatment' criteria.</p>
	<p>Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authorisation under this restriction should be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/hpos) Alternatively, applications for authority to prescribe can be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>

8.2 Flow-on changes to the Administrative Advice for aflibercept 8 mg vial [14627W, 14635G] will be required to allow for interchangeability with aflibercept 8 mg pre-filled syringe.

These restrictions 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.