Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1695 – Implantation and refill-exchange of the Port Delivery System with ranibizumab to treat neovascular age-related macular degeneration in patients who have previously responded to prior anti-VEGF treatment

Applicant: **Roche Products Pty Limited**

Date of MSAC consideration: **31 March 2022 – 1 April 2022**

1. Purpose of application

The application requested new Medicare Benefits Schedule (MBS) listings for the implantation, initial fill, refill-exchange and explantation (if required) procedures for the Port Delivery System (PDS) ocular implant to deliver ranibizumab 100 mg/mL (Susvimo®) for the treatment of neovascular (wet) age-related macular degeneration (nAMD) in patients who have previously responded to prior anti-vascular endothelial growth factor (anti-VEGF) treatment.

2. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness and cost-effectiveness, MSAC deferred its decision regarding the creation of Medicare Benefits Schedule (MBS) items for the implant, refill-exchange and explant of the Port Delivery System (PDS) to deliver ranibizumab 100 mg/mL to treat neovascular age-related macular degeneration (nAMD). MSAC advised that the proposed cost-minimisation approach also needs to include the hospital costs of the implant procedure beyond those of the device and the specialist implanting the device. MSAC foreshadowed that it would expeditiously reconsider these items if the Pharmaceutical Benefits Advisory Committee (PBAC) recommends the ranibizumab 100 mg/mL formulation.

Consumer summary
MSAC noted that this application was from Roche Products Pty Ltd requesting Medicare Benefits Schedule (MBS) listing of procedures for implanting, refilling and removing a Port Delivery System to deliver a medicine called ranibizumab to treat neovascular age-related macular degeneration (nAMD). nAMD is a chronic disease of the eye. It affects the retina – the part of the eye that receives light and sends nerve signals to the brain for visual recognition. nAMD causes vision loss over time. The most common treatment for nAMD involves injecting medicines (such as

Consumer summary

ranibizumab) into the eye that can help maintain eyesight. These are called intravitreal injections and usually need to be given every 1 to 2 months.

The Port Delivery System is a tiny device that is surgically implanted into the eye. It is filled with a special formulation of ranibizumab that is gradually released into the eye over time. Patients who have this device implanted need to have it refilled every 6 months, instead of having intravitreal injections every 1 to 2 months.

MSAC noted that this was a codependent application. This means that the applicant is seeking to list the procedures on the MBS at the same time as listing the medicine on the Pharmaceutical Benefits Scheme (PBS) and the implantable device on the Prostheses List. The Pharmaceutical Benefits Advisory Committee was of a mind to recommend the listing of the medicine but deferred this until it could review data on comparative safety from the Therapeutic Goods Administration and receive advice from MSAC.

MSAC advised that changes be made to the economic and financial estimates to ensure that all relevant costs are included.

MSAC supported the proposal of the MBS Review Taskforce Review of Ophthalmology Items to reduce the MBS fees for intravitreal injections, but noted that this proposal had not been implemented.

MSAC's advice to the Commonwealth Minister for Health

MSAC deferred its advice on procedures related to the Port Delivery System for nAMD because the Pharmaceutical Benefits Advisory Committee had deferred its decision about the medicine. MSAC will reconsider the application in a short timeframe if the Pharmaceutical Benefits Advisory Committee recommends to list the medicine on the PBS.

3. Summary of consideration and rationale for MSAC's advice

MSAC noted the purpose of the application was to request new MBS listings for the implantation, initial fill, refill-exchange and explantation (if required) procedures for the PDS ocular implant to deliver ranibizumab 100 mg/mL for the treatment of nAMD in patients who have previously responded to prior anti-VEGF treatment. MSAC noted that this was a codependent application requesting listing on the Pharmaceutical Benefits Scheme (PBS) of the customised formulation of ranibizumab and listing on the Prostheses List (PL) for the PDS ocular implant. MSAC also noted that, although the medicine and the implant were not yet included on the Australian Register of Therapeutic Goods (ARTG), the Therapeutic Goods Administration (TGA) is currently considering the relevant applications.

MSAC noted that the PBAC had deferred its recommendation on listing of the medicine pending advice from the TGA delegate on the comparative safety of the two approaches to delivering the medicine, and advice from MSAC on the procedures associated with the implant. The PBAC was of a mind to recommend the PBS listing.

MSAC noted that the proposed intervention involves a surgically implanted device delivering a long-acting treatment that continuously suppresses VEGF in the eye. The PDS is a permanent, refillable, intraocular drug delivery system designed for continuous delivery of a customised formulation of ranibizumab 100 mg/mL (Susvimo®), resulting in delivery of a

2 mg (0.02 mL of solution) ranibizumab formulation, refilled every 24 weeks (approximately every 6 months).

MSAC noted the consultation feedback from the Macular Disease Foundation Australia and the Royal Australian and New Zealand College of Ophthalmologists (RANZCO), which was supportive. Both organisations identified patient groups who would be most likely to benefit from the PDS. RANZCO also noted the differences in comparative safety between intravitreal (IVT) injections and the PDS.

MSAC noted the Department's suggested amendments to the proposed MBS item descriptors and the applicant's agreement with these in its pre-MSAC response. MSAC advised against a generic reference to "ocular implant" in the item descriptor, given that the implant device is new and not comparable to existing devices, and the method of implantation is also new. MSAC considered that limiting the number of implants or explants a patient can receive during their lifetime is unnecessary, because explantation of the device would only be because of serious complications, and any reimplantation would require serious consideration by the patient and the surgeon (as noted in the pre-MSAC response). MSAC advised that, to avoid double claiming, the MBS item descriptor for the implantation and initial fill procedure should specify that the procedure includes conjunctival peritomy, pars planar sclerotomy and ciliary body endolaser, or should state that the item cannot be co-claimed with items 42725 or 42809.

MSAC considered that the proposed MBS fees for the implantation and initial fill procedure and for the explantation procedure were reasonably justified with reference to relevant existing MBS benchmarks.

MSAC supported a separate MBS item for the refill-exchange procedure. MSAC noted that the proposed MBS fee for the refill-exchange procedure was based on similar time and complexity of ocular procedures covered under existing MBS items for IVT injections. MSAC had no objections to this proposal. However, MSAC supported a fee reduction of IVT injections, noting that listings of the various anti-VEGF medicines on the PBS had been associated with large increases in MBS billing for the associated regular IVT injections. In this context, MSAC noted that the MBS Review Taskforce Review of Ophthalmology Items had proposed reducing the fee for these items from $312.95 to $97.40, to align with other items of similar complexity. MSAC noted the substantial volume of feedback received by the Taskforce from clinicians, private health peak bodies and public hospitals that opposed the fee reduction. This suggested that if ophthalmologists did not similarly reduce the fees they charged, this would increase out-of-pocket costs for consumers. MSAC advised that, if the current fee for IVT injections is reduced, then the fee for the PDS refill-exchange procedure should also be reduced to match this reduced fee due to their similar time requirements and complexity.

MSAC noted that the PDS would not change the current treatment management pathway, but it is intended to provide an alternative method of treatment delivery to the regular IVT injections that are the current standard of treatment delivery for nAMD and are given at intervals of 4 weeks or longer. MSAC considered that IVT injection of an anti-VEGF treatment was the appropriate comparator.

MSAC did not agree with the applicant that the majority of procedures would be conducted in private settings (hospital or clinic), and considered that the procedure would also be performed in public hospital settings. MSAC also noted that the procedure would likely be limited to retinal specialists at first, with eventual expansion to general ophthalmologists.

MSAC considered that the clinical need addressed by this application was limited because patients must demonstrate responsiveness to previous IVT injected treatment before they are eligible for the PDS. MSAC therefore considered that the application did not address unmet needs of patients who are not currently accessing treatment, but provided an alternative option for those who would prefer less frequent doses of therapy. Results of the PDS patient preference questionnaire in the key Phase III trial (ARCHWAY) reported that 93.2% (218/234) of patients randomised to the PDS preferred the PDS over IVT injections. Common reasons for this preference were fewer treatments and less discomfort associated with the treatment.

MSAC noted data on safety and efficacy from the ARCHWAY trial and the extended safety assessment up to 96 weeks. The studies indicated that the ocular implant procedure and refill-exchange procedures were generally well tolerated, but the adverse effect profile of PDS treatment was less favourable than monthly IVT ranibizumab treatment. MSAC noted that the initial trial period included only a single refill-exchange of the PDS, and considered that some adverse events were attributed to the PDS being a new device that involves a learning curve for clinicians, suggesting that procedure complications may be more common in practice than in the trial setting. MSAC considered that the follow-up period of 96 weeks was not sufficiently long for a lifetime device. Overall, MSAC considered that the PDS did not have non-inferior safety compared with IVT injections, but that the adverse events were manageable.

MSAC considered that, overall, the PDS and IVT injections were equi-effective during the trial period and follow-up period. MSAC noted that IVT injection intervals were fixed at 4 weeks during the trial with an intensive monitoring protocol, which does not reflect clinical practice in Australia, where "treat and extend" (T&E) regimens are used, monitoring is not standardised and difficult to predict in the context of the proposed PDS option. A total of 5.2% of patients in the PDS arm (13/241) required supplemental IVT injections during the 40 weeks of the trial. MSAC considered that it was uncertain whether this rate would be maintained over a longer time.

MSAC noted that the economic evaluation was a cost-minimisation analysis based on the claim of non-inferior efficacy and inferior but manageable safety. The economic evaluation was assessed by the PBAC and was revised to incorporate the effective price of ranibizumab, which is committee-in-confidence with the PBAC. MSAC noted the proposed price of the proposed ranibizumab formulation was based on equi-effective doses of 2.17 PDS administrations per patient per year and 7.09 IVT injections per patient per year (with the latter estimate based on an analysis from the Drug Utilisation Sub-Committee [DUSC] in 2018). However, an updated analysis by the DUSC secretariat found that the equi-effective doses per patient per year were 2.17 PDS administrations and 6.31 IVT injections, and the applicant accepted this more recent basis for the cost-minimisation calculations. MSAC also advised that the cost-minimisation calculations should also include hospital costs beyond those of the device and the specialist implanting the device.

MSAC also noted that the requested benefit for listing the PDS implant on the PL was $400, and that this had been incorporated in the cost-minimisation calculations. MSAC had no objections to the size of this requested benefit.

MSAC considered that there was a need to update the financial analysis to reflect the updated estimate of 6.31 IVT injections per patient per year. MSAC also noted that the MBS costs associated with adverse events were not included in the financial estimates. MSAC

considered that these costs would not greatly affect the overall estimates, but should be included for completeness.

MSAC advised that, if listed, the listing should be reviewed after 1–2 years, with an emphasis on monitoring patient out-of-pocket costs over time given their unpredictability. If the PDS implant is listed on the PL, access to private health insurance may affect uptake. If it is not listed on the PL, cost barriers for all patients may further reduce uptake. Optical coherence tomography (OCT) is covered under MBS item 11219 for diagnosis. However, MSAC noted that this item is not claimable for monitoring treatment and therefore could not be used for regular monitoring after PDS implantation.

4. Background

MSAC has not previously considered Application 1695. Roche Products has lodged a codependent application for Pharmaceutical Benefits Advisory Committee (PBAC) consideration, requesting Pharmaceutical Benefits Scheme (PBS) listing of a customised formulation of ranibizumab for the treatment of nAMD in patients who have responded to prior anti-VEGF treatment. B Braun has lodged a codependent application requesting a Prostheses List listing for the PDS ocular implant.

Intravitreal (IVT) injections with anti-VEGF drugs are the current standard of care for nAMD, administered by an ophthalmologist as an injection into the eye/s under a local anaesthetic. The PBS-listed medicines for nAMD, diabetic macular oedema (DMO), branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO) are shown in Table 1.1. Bevacizumab is another monoclonal anti-VEGF therapy, like ranibizumab. However, it is neither TGA registered nor PBS listed for ophthalmic indications.

These PBS listings were associated with large increases in MBS billing for the associated procedures for these regular injections with a current fee of $312.95 per injection.

Table 1.1: Anti-vascular endothelial growth factor listings on the Pharmaceutical Benefits Scheme (PBS)

	Abridged restriction	Date listed
Ranibizumab	Subfoveal choroidal neovascularisation (CNV) due to age-related macular degeneration (AMD).	1 August 2007
Aflibercept	CNV due to AMD.	1 December 2012
Ranibizumab	Visual impairment due to macular oedema (MO) secondary to branch retinal vein occlusion (BVRO) and central retinal vein occlusion (CRVO).	1 July 2015
Ranibizumab	Visual impairment due to diabetic macular oedema (DMO).	1 July 2015
Aflibercept	Visual impairment due to DMO.	1 October 2015
Aflibercept	Visual impairment due to macular oedema secondary to CRVO.	1 October 2015
Aflibercept	Visual impairment due to macular oedema secondary to BRVO.	1 December 2016
Brolucizumab	CNV due to AMD for patients unsuitable for, contraindicated to, or who have failed aflibercept or ranibizumab.	1 October 2021

5. Prerequisites to implementation of any funding advice

The ranibizumab 100 mg/mL (Susvimo®) formulation was not registered on the Australian Register of Therapeutic Goods (ARTG) when the application was lodged. A submission for Susvimo® (ranibizumab) was lodged with the TGA in May 2021 for the following indication:

> Susvimo is indicated for the treatment of adult patients with neovascular (wet) age-related macular degeneration (AMD).

The dosing and administration for ranibizumab (Susvimo®) was proposed to be:

> Susvimo has been specially developed for use with the implant.

The recommended dose of Susvimo is 2 mg in 0.02 mL continuously delivered via the Susvimo implant with refills administered every 24 weeks (approximately 6 months).

Susvimo® was approved for use by the Food and Drug Administration (FDA) on 22 October 2021.

A submission for the PDS ocular implant was lodged with the TGA on 1 June 2021.

6. Proposal for public funding

Proposed MBS fees and MBS item descriptors
The MSAC application requested public funding for the procedures for the implantation, refill-exchange and explantation of the PDS ocular implant to deliver a new formulation of ranibizumab in the treatment of nAMD. The proposed MBS fees were based on similar complexity and time to ocular procedures covered under existing MBS item numbers as shown in Tables 1.2 and 1.3 below.

Table 1.2: Proposed MBS fees

Procedure	Proposed MBS fee	Reason for the proposed fee
Initial fill and implantation	$1193.18	Intermediate in complexity and time between MBS items 42752 and 42746 (i.e., $1392.65 + $993.70 divided by 2)
Refill-exchange	$312.95	Similar in terms of complexity and time to MBS item numbers 42738, 42739 and 42740 (which all currently have a schedule fee of $312.95)
Explantation (if needed)	$400.00	More complex and time consuming than MBS item 42505 ($312.95)

Table 1.3: Current MBS items utilised for the basis of the proposed MBS fees

MBS item	MBS descriptors and fees
42752	Category 3 - THERAPEUTIC PROCEDURES Group T8 - Surgical Operations Subgroup 9 - Ophthalmology GLAUCOMA, insertion of drainage device incorporating an extraocular reservoir for, such as a Molteno device Fee: $1,392.65 Benefit: 75% = $1,044.50
42746	Category 3 - THERAPEUTIC PROCEDURES Group T8 - Surgical Operations Subgroup 9 - Ophthalmology GLAUCOMA, filtering operation for, where conservative therapies have failed, are likely to fail, or are contraindicated Fee: $993.70 Benefit: 75% = $745.30
42738	Category 3 - THERAPEUTIC PROCEDURES Group T8 - Surgical Operations Subgroup 9 - Ophthalmology PARACENTESIS OF ANTERIOR CHAMBER OR VITREOUS CAVITY, or both, for the injection of therapeutic substances, or the removal of aqueous or vitreous humours for diagnostic or therapeutic purposes, 1 or more of, as an independent procedure. Fee: $312.95 Benefit: 75% = $234.75 85% = $266.05
42739	Category 3 - THERAPEUTIC PROCEDURES Group T8 - Surgical Operations Subgroup 9 - Ophthalmology PARACENTESIS OF ANTERIOR CHAMBER OR VITREOUS CAVITY, or both, for the injection of therapeutic substances, or the removal of aqueous or vitreous humours for diagnostic or therapeutic purposes, one or more of, as an independent procedure, for a patient requiring the administration of anaesthetic by an anaesthetist. Fee: $312.95 Benefit: 75% = $234.75 85% = $266.05

42740	Category 3 - THERAPEUTIC PROCEDURES Group T8 - Surgical Operations Subgroup 9 - Ophthalmology INTRAVITREAL INJECTION OF THERAPEUTIC SUBSTANCES, or the removal of vitreous humour for diagnostic purposes, 1 or more of, as a procedure associated with other intraocular surgery. Fee: $312.95 Benefit: 75% = $234.75 85% = $266.05	
42505	Category 3 - THERAPEUTIC PROCEDURES Group T8 - Surgical Operations Subgroup 9 - Ophthalmology Complete removal from the eye of a trans-trabecular drainage device or devices, with or without replacement, following device related medical complications necessitating complete removal. Fee: $312.95 Benefit: 75% = $234.75 85% = $266.05	

The requested MBS items are presented in Tables 1.4 to 1.6 below, based on the format of MBS items 42752 and 42755.

Table 1.4: MBS descriptor for initial fill and implantation

Category 3 - THERAPEUTIC PROCEDURES
Group T8 - Surgical Operations Subgroup 9 - Ophthalmology Neovascular age-related macular degeneration, initial fill and implantation of an ocular implant for Susvimo® (ranibizumab) Fee: $1193.18

Table 1.5: MBS descriptor for refill-exchange

Category 3 - THERAPEUTIC PROCEDURES
Group T8 - Surgical Operations Subgroup 9 - Ophthalmology Neovascular age-related macular degeneration, refill-exchange of an ocular implant for Susvimo® (ranibizumab) Fee: $312.95

Table 1.6: MBS descriptor for explantation

Category 3 - THERAPEUTIC PROCEDURES
Group T8 - Surgical Operations Subgroup 9 - Ophthalmology Neovascular age-related macular degeneration, explantation of an ocular implant for Susvimo® (ranibizumab) Fee: $400.00

Table 1.7 outlines the components, purpose, procedures, source of funding associated with the PDS, together with the applicant's expectations regarding out of pocket costs.

Table 1.7: Components, purpose and sources of funding associated with the requested procedures

Procedure	Component	Purpose	Foreshadowed funding scheme	Foreshadowed out of pocket costs
Initial fill and implantation	PDS ocular implant	Continuous release of ranibizumab 100 mg/mL in the eye	Prostheses List	None, if the patient has *the appropriate* private health insurance
	Insertion tool assembly	Hold the implant and to place the implant in the eye during the implant procedure	*Prostheses List* (when co-packaged in the same carton as the PDS ocular implant)	None*, if the patient has the appropriate private health insurance*
	Initial fill needle	Fill the PDS ocular implant with ranibizumab 100 mg/mL prior to implantation	None	None
	Susvimo® vial	Ranibizumab 100 mg/mL	Pharmaceutical Benefits Scheme	PBS co-payment
Refill-exchange	Refill needle	Refill the implant with ranibizumab 100 mg/mL *in situ*	None	None
	Susvimo® vial	Ranibizumab 100 mg/mL	Pharmaceutical Benefits Scheme	PBS co-payment
Explantation	Explant tool	Remove the implant, if needed	None	None

The application stated that all components are single use consumables and anticipated that there would be no out-of-pocket costs to patients for components/consumables not funded through the Prostheses List or the PBS. As the insertion tool assembly is co-packaged with the PDS ocular implant, it would be considered for funding through the Prostheses List. The application anticipated that the initial fill needle, refill needle and explant tool would be provided to clinics and hospitals at no cost, either through existing distribution channels (i.e., standard wholesalers) or directly from Roche Products.

7. Summary of public consultation feedback/consumer Issues

Targeted consultation feedback was received from two (2) organisations, the Macular Disease Foundation Australia (MDFA) and the Royal Australian and New Zealand College of Ophthalmologists (RANZCO). Both organisations were supportive of the application.

RANZCO considered that ranibizumab PDS should only be for patients that are unable to obtain disease quiescence with 8 weeks or more intervals with traditional intra-vitreal therapy. RANZCO noted that there is an increased risk of complication and infection with this system and considered that this needs to be balanced against the current standard of care.

MDFA noted that without timely access to treatment patients with nAMD progressively develop irreversible severe loss and blindness, which also has consequences for the patient's family and carer(s). MDFA noted that the biggest challenges for patients with existing treatments is the frequency of injections and associated financial burdens, along with access issues to effective treatment in regional, rural and remote areas.

MDFA considered that for patients who have responded well to prior anti-VEGF therapy, ranibizumab PDS appears to offer the advantage of substantially fewer visits to the ophthalmologists for treatment and disease monitoring, which would assist with reducing the

overall treatment burden, compared with intravitreal ranibizumab injections. Further benefits may be reduced out-of-pocket costs (after Medicare rebates) for the treatment procedure and reduced travel related costs.

MDFA anticipates ranibizumab PDS will be of interest to patients requiring frequent injections and unable to extend treatment intervals, those facing geographical or personal circumstances that would limit their ability to access to sight-saving treatment, as well as patients who require bilateral treatment but for whom same-day intravitreal injections are either not advised or are impractical, and patients who have successfully responded to treatment over several years but are at risk of delaying or stopping therapy due to treatment cost, treatment fatigue or other factors.

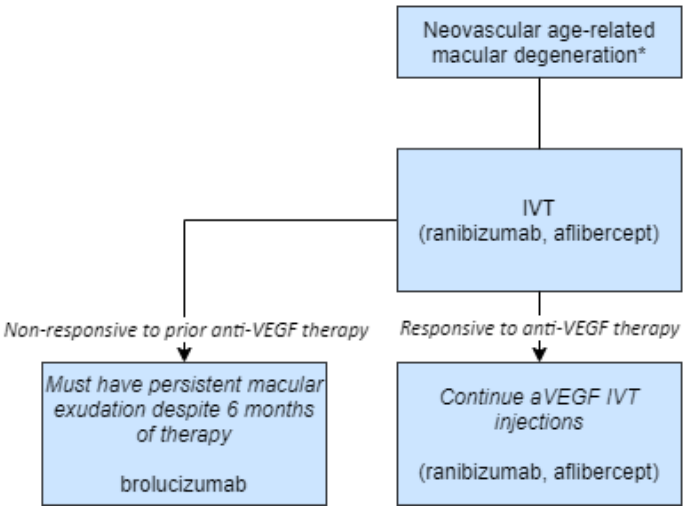
8. Proposed intervention's place in clinical management

Description of proposed intervention
The PDS with ranibizumab 100 mg/mL (via ocular implant) was the first and only surgically implanted long-acting treatment solution that continuously suppresses VEGF in the eye. The PDS is a permanent, refillable, intraocular drug delivery system designed for continuous delivery of a customised formulation of ranibizumab 100 mg/mL (Susvimo®), resulting in delivery of a 2 mg (0.02 mL of solution) ranibizumab formulation, refilled every 24 weeks (approximately every 6 months).

Description of medical condition
Age-related macular degeneration is a chronic eye disease characterised by progressive degenerative abnormalities in the central retina (macula) and is the leading cause of severe vision loss and legal blindness in people over the age of 65 years. There are two types of AMD: the non-neovascular (atrophic) or dry form, and the neovascular (exudative) or wet form (nAMD) which occurs in around 10-15% of overall AMD cases. IVT injections with anti-VEGF drugs are the current standard of care for nAMD.

Current clinical management pathway
As outlined in Figure 1.1 below, the current management of nAMD required formal diagnosis with optical coherence tomography (MBS item 11219) or fluorescein angiography (MBS 11215) by an ophthalmologist prior to patients receiving treatment with IVT injections (ranibizumab or aflibercept). Patients would then continue to receive an anti-VEGF therapy provided that a response has been demonstrated. For patients unresponsive to a minimum of 6 months' treatment with at least one prior anti-VEGF therapy, brolucizumab may be trialled.

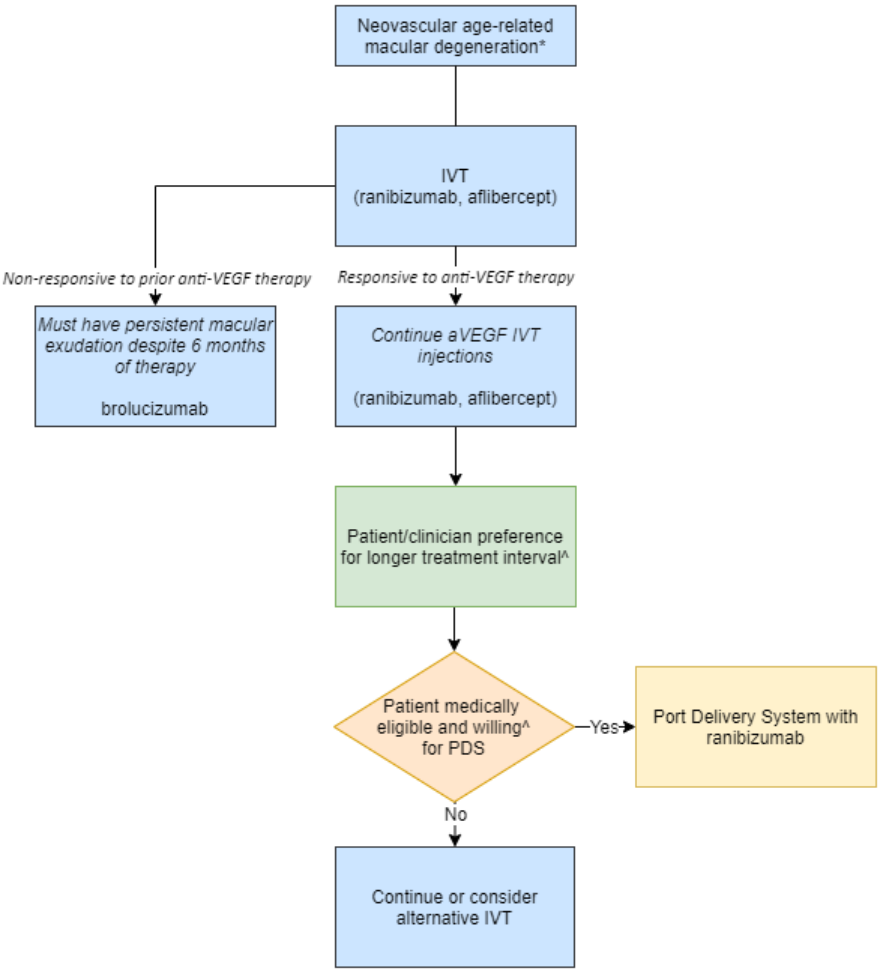
Figure 1.1: Current clinical management pathway



Proposed clinical management pathway

The proposed clinical management did not change the current treatment management pathway, rather, it provided an alternative method of delivery/treatment option to patients who have previously responded to standard of care IVT injections as depicted below in Figure 1.2.

Figure 1.2: Proposed clinical management pathway



9. Comparator

The nominated comparator for the application was continuing ranibizumab 10 mg/mL (via IVT injection) as a proxy for standard of care. Currently, anti-VEGF ranibizumab (Lucentis®) and aflibercept (Eylea®) are available through the PBS for the treatment of nAMD. These anti-VEGFs are administered at a minimum of 4 weekly intervals by an ophthalmologist or retinal specialist in a clinic. The PDS proposed by the applicant offered an alternative to the current subsidised anti-VEGF treatments, aiming to reduce the administration intervals, patient treatment burden and the associated MBS costs with frequent eye injections.

10. Comparative safety

Data from the pivotal phase III study ARCHWAY indicated that the ocular implant procedure and refill-exchange procedures were generally well tolerated, but the systemic adverse effects profile of PDS treatment was less favourable than monthly IVT ranibizumab treatment. Results of the PDS patient preference questionnaire in ARCHWAY reported that 93.2% (218/234) of patients preferred the continuous delivery of ranibizumab using the PDS over ranibizumab IVT injections. Common reasons for this preference among the patients who preferred the PDS option were fewer treatments and less discomfort.

11. Comparative effectiveness

Data from the pivotal phase III study ARCHWAY showed that more than 90% of patients treated with the PDS did not receive supplemental treatment before each refill-exchange procedure, meaning that PDS patients were able to go six months without needing additional treatment while achieving visual and anatomical outcomes overall non-inferior to patients receiving IVT ranibizumab 0.5 mg every 4 weeks (Q4W).

Clinical claim
In patients with nAMD, ranibizumab 100 mg/mL via ocular implant is as effective as ranibizumab 10 mg/mL via intravitreal injection at maintaining best corrected visual acuity (with a reduction in frequency visits for treatment administration).

12. Economic evaluation

The economic evaluation will be assessed by the March 2022 PBAC meeting. MSAC will be advised of the outcomes prior to its consideration at the March/April 2022 MSAC meeting.

13. Financial/budgetary impacts

Utilisation estimates
Given the anticipated treated population is a subset of a relatively mature PBS eligible population, a market-based approach was utilised to estimate the size of the proposed population. Table 2.1 presents the number of services for MBS items 42738, 42739 and 42740 in the preceding five years. This represents utilisation in addition to nAMD (including, but not limited to, the administration of IVT injections in diabetic macular oedema and retinal vein occlusion) and thus is limited in estimating the relative size of the proposed population.

Table 2.1: Utilisation of MBS services for MBS items 42738, 42739 and 42740

MBS item	2016	2017	2018	2019	2020
42738	384,124	429,405	475,786	515,448	554,891
42739	9,245	9,036	9,141	9,600	9,044
42740	15,074	15,846	13,606	14,223	13,743
Total	**408,443**	**454,287**	**498,533**	**539,271**	**577,678**

Table 2.2 presents market utilisation of anti-VEGF therapy specific to nAMD.

Table 2.2: nAMD PBS-listed therapy utilisation

Product	2016	2017	2018	2019	2020
Lucentis® (ranibizumab)	134,197	133,145	132,253	141,566	152,673
Eylea® (aflibercept)	140,125	169,630	189,955	216,170	244,301
Total utilisation	**274,322**	**302,775**	**322,207**	**357,736**	**396,974**

Source: MBS+PHI budget impact.xlsx, spreadsheet 'Projected growth'.

Table 2.3 provides a forward estimate of market utilisation of anti-VEGF therapy specific to nAMD; a linear extrapolation of the preceding 5 years informed this estimate.

Table 2.3: Forecasted nAMD PBS-listed therapy utilisation

	2022	2023	2024	2025	2026	2027
Total utilisation	[redacted] 1	[redacted] 1	[redacted] 2	[redacted] 2	[redacted] 2	[redacted] 2

Source: MBS+PHI budget impact.xlsx, spreadsheet 'Projected growth'.
The redacted values correspond to the following ranges:
[1] 400,000 to <500,000
[2] 500,000 to <600,000

Table 2.4 estimates the number of patients on nAMD therapy; this was estimated by dividing the projected market utilisation by the average number of injections per patient per year (i.e., 7.09). This was informed by an average number of IVT injections per year estimate reported in the Drug Utilisation Sub-Committee Report (DUSC, 2018). This utilisation analysis was updated for consideration by PBAC, with the average number of IVT injections per patient per year reduced to 6.31. Given the acceptance of this updated estimate by the applicant and PBAC, the following calculations are indicative only and would need to be updated.

Table 2.4: Forecasted patients with nAMD

	2022	2023	2024	2025	2026	2027
Prevalent patient pool	[redacted] 1	[redacted] 1	[redacted] 2	[redacted] 2	[redacted] 2	[redacted] 3

Source: MBS+PHI budget impact.xlsx, spreadsheet 'MBS+PL Utilisation+Cost'.
The redacted values correspond to the following ranges:
[1] 60,000 to <70,000
[2] 70,000 to <80,000
[3] 80,000 to <90,000

Table 2.5 presents the number of patients forecasted to be treated with the PDS. These uptake rates were not clearly justified and are likely to be influenced by many factors.

Table 2.5: Patients forecasted to be treated with the PDS

Patients	2022	2023	2024	2025	2026	2027
Treated prevalent patient pool	[redacted] 1	[redacted] 1	[redacted] 2	[redacted] 2	[redacted] 2	[redacted] 3
Uptake	5%	10%	15%	15%	15%	15%
PDS prevalent treated patients	[redacted] 4	[redacted] 5	[redacted] 6	[redacted] 6	[redacted] 6	[redacted] 6
Of which, are incident	[redacted] 4	[redacted] 4	[redacted] 4	[redacted] 4	[redacted] 4	[redacted] 4
Of which, are continuing	[redacted] 7	[redacted] 4	[redacted] 5	[redacted] 6	[redacted] 6	[redacted] 6

Source: MBS+PHI budget impact.xlsx, spreadsheet 'MBS+PL Utilisation+Cost'.
The redacted values correspond to the following ranges:
[1] 60,000 to <70,000
[2] 70,000 to <80,000
[3] 80,000 to <90,000
[4] 500 to <5,000
[5] 5,000 to <10,000
[6] 10,000 to <20,000
[7] <500

Table 2.6 presents the estimated number of services for the patients forecasted to be treated with the PDS.

Table 2.6: Estimated number of services for the PDS patients

Patients	Service	2022	2023	2024	2025	2026	2027
Incident	Initial fill and implantation	[redacted]1	[redacted]1	[redacted]1	[redacted]1	[redacted]1	[redacted]1
	Refill-exchange	[redacted]1	[redacted]1	[redacted]1	[redacted]1	[redacted]1	[redacted]1
Continuing	Refill-exchange	[redacted]5	[redacted]2	[redacted]3	[redacted]4	[redacted]4	[redacted]4
Total	**Initial fill and implantation**	[redacted]1	[redacted]1	[redacted]1	[redacted]1	[redacted]1	[redacted]1
	Refill-exchange	[redacted]1	[redacted]3	[redacted]3	[redacted]4	[redacted]4	[redacted]4

Source: MBS+PHI budget impact.xlsx, spreadsheet 'MBS+PL Utilisation+Cost'.
The redacted values correspond to the following ranges:
[1] 500 to <5,000
[2] 5,000 to <10,000
[3] 10,000 to <20,000
[4] 20,000 to <30,000
[5] <500

Table 2.7 presents the estimated number of monitoring services for the patients forecasted to be treated with the PDS.

Table 2.7: Estimated number of monitoring services for PDS patients

Patients	Service	2022	2023	2024	2025	2026	2027
Incident	Monitoring	[redacted]1	[redacted]1	[redacted]2	[redacted]3	[redacted]3	[redacted]3
Continuing	Monitoring	[redacted]4	[redacted]5	[redacted]1	[redacted]2	[redacted]2	[redacted]2
Total	**Monitoring**	[redacted]1	[redacted]2	[redacted]6	[redacted]2	[redacted]2	[redacted]2

Source: MBS+PHI budget impact.xlsx, spreadsheet 'MBS+PL Utilisation+Cost'.
The redacted values correspond to the following ranges:
[1] 10,000 to <20,000
[2] 20,000 to <30,000
[3] 500 to <5,000
[4] <500
[5] 5,000 to <10,000
[6] 30,000 to <40,000

Table 2.8 presents the estimated number of potential explantation services for the patients forecasted to be treated with the PDS.

Table 2.8: Estimated number of explantation services for PDS patients

Patients	Service	2022	2023	2024	2025	2026	2027
Patients	Explantation	[redacted]1	[redacted]1	[redacted]1	[redacted]1	[redacted]1	[redacted]1

Source: MBS+PHI budget impact.xlsx, spreadsheet 'MBS+PL Utilisation+Cost'.
The redacted values correspond to the following ranges:
[1] <500

Replaced utilisation

Two patient populations were identified (and presented in the PBAC submission) from the prevalent treated population which are relevant to the calculation of replaced utilisation:

- Patients who have the highest treatment burden; comprising patients who are responsive to treatment but are unable to treat and extend treatment beyond Q4W (the Q4W population).
- Patients where the treatment burden has the greatest impact on their personal lives, that is, people who are working, or the time taken out of the day to receive treatment is significant (the patient preference population).

For the patients "replaced" in clinical practice with the PDS, that 50% would come from the Q4W population and the Patient Preference population respectively.

Table 2.9 presents the number of patients forecasted to be in these two groups.

Table 2.9: Replaced prevalent treated population

Patients	Proportion	2022	2023	2024	2025	2026	2027
Replaced prevalent treated population		[redacted] 1	[redacted] 2	[redacted] 3	[redacted] 3	[redacted] 3	[redacted] 3
Q4W population	50%	[redacted] 1	[redacted] 1	[redacted] 2	[redacted] 2	[redacted] 2	[redacted] 2
patient preference population	50%	[redacted] 1	[redacted] 1	[redacted] 2	[redacted] 2	[redacted] 2	[redacted] 2

Source: MBS+PHI budget impact.xlsx, spreadsheet 'MBS+PL Utilisation+Cost'.
The redacted values correspond to the following ranges:
1 500 to <5,000
2 5,000 to <10,000
3 10,000 to <20,000

Table 2.10 presents the estimated number of paracentesis services for the replaced prevalent treated population.

Table 2.10: Estimated number of paracentesis services for the replaced prevalent treated population

Patients	Service	2022	2023	2024	2025	2026	2027
Q4W population	Paracentesis	[redacted] 1	[redacted] 4	[redacted] 6	[redacted] 6	[redacted] 6	[redacted] 7
Patient preference population	Paracentesis	[redacted] 2	[redacted] 1	[redacted] 3	[redacted] 4	[redacted] 4	[redacted] 4
Total	**Paracentesis**	[redacted] 3	[redacted] 5	[redacted] 8	[redacted] 8	[redacted] 8	[redacted] 8

Source: MBS+PHI budget impact.xlsx, spreadsheet 'MBS+PL Utilisation+Cost'.
The redacted values correspond to the following ranges:
1 20,000 to <30,000
2 10,000 to <20,000
3 30,000 to <40,000
4 40,000 to <50,000
5 60,000 to <70,000
6 70,000 to <80,000
7 80,000 to <90,000
8 100,000 to <200,000

Net financial implications to the MBS

A summary of the net impact to the MBS is shown in Table 2.11. The analysis provided showed that savings to the MBS would be expected ranging from approximately $10 million to <$20 million in 2022 to $20 million to <$30 million in 2027 (at 100% MBS fee). However, given the acceptance by the applicant and PBAC of the updated estimate of the average number of IVT injections per patient per year being reduced to 6.31, the estimated financial implications to the MBS require re-calculation.

Table 2.11: Net impact to the MBS

MBS service	2022	2023	2024	2025	2026	2027
Proposed costs						
Initial fill and implantation	$[redacted] 1	$[redacted] 1	$[redacted] 1	$[redacted] 1	$[redacted] 1	$[redacted] 1
Refill-exchange	$[redacted] 1	$[redacted] 1	$[redacted] 1	$[redacted] 1	$[redacted] 1	$[redacted] 1
Monitoring	$[redacted] 1	$[redacted] 1	$[redacted] 1	$[redacted] 1	$[redacted] 1	$[redacted] 1
Explantation	$[redacted] 1	$[redacted] 1	$[redacted] 1	$[redacted] 1	$[redacted] 1	$[redacted] 1
Total	**$**[redacted] 1	**$**[redacted] 1	**$**[redacted] 1	**$**[redacted] 1	**$**[redacted] 1	**$**[redacted] 2
Replaced costs						
Paracentesis	$[redacted] 1	$[redacted] 3	$[redacted] 4	$[redacted] 4	$[redacted] 4	$[redacted] 4
Total	**$**[redacted] 1	**$**[redacted] 3	**$**[redacted] 4	**$**[redacted] 4	**$**[redacted] 4	**$**[redacted] 4
Overall net cost to the MBS (proposed cost – replaced cost)						
Net cost to MBS	**$**[redacted] 5	**$**[redacted] 5	**$**[redacted] 5	**$**[redacted] 5	**$**[redacted] 5	**$**[redacted] 5

Source: MBS+PHI budget impact.xlsx, spreadsheet 'MBS+PL Utilisation+Cost'.
The redacted values correspond to the following ranges:
1 $0 to <$10 million
2 $10 million to <$20 million
3 $20 million to <$30 million
4 $30 million to <$40 million
5 Net cost saving

Net change to private health insurance via the Prostheses List
The requested benefit for the PDS ocular implant on the Prostheses List was $400. The annual expenditure by private health insurers cost for the ocular implant was estimated to range from approximately $0 to <$10 million to $0 to <$10 million million per year (Table 2.12). However, given the acceptance by the applicant and PBAC of the updated estimate of the average number of IVT injections per patient per year being reduced to 6.31, these estimates also require re-calculation.

Table 2.12: Net impact to private health insurance via the Prostheses List due to the cost of the PDS ocular implant

	2022	2023	2024	2025	2026	2027
Estimated incident patients	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][2]
Proposed cost of the PDS ocular implant	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]
Total cost for listing on the Prostheses List	**$**[redacted][3]	**$**[redacted][3]	**$**[redacted][3]	**$**[redacted][3]	**$**[redacted][3]	**$**[redacted][3]

Source: MBS+PHI budget impact.xlsx, spreadsheet 'MBS+PL Utilisation+Cost'.
The redacted values correspond to the following ranges:
[1] 5,000 to < 10,000
[2] 500 to < 5,000
[3] $0 to < $10 million

These costs to private health insurers were understated as they only included the cost of the PDS ocular implant. There would be other payments made by insurers for the in-hospital services including the contracted payment for the admission and the gap payment to the surgeon.

The overall impact on health care expenditure of a patient switching to the proposed ranibizumab delivery system would affect the MBS, the PBS, private health insurance and patient out-of-pocket payments. It would reduce the frequency of procedures by ophthalmologists and retinal specialists, which is a significant MBS contribution to the costs of patient management. However, it would also represent a cost shift from the MBS to private health insurance which has been underestimated.

14. Summary of application – key issues for MSAC consideration

MBS item descriptors
The Department noted that the MBS item descriptors initially proposed by the applicant contained specification of registered trademark components. However, the applicant indicated that it is open to amendments to the MBS item descriptors without specification of registered trademark components. The Department also noted that the wording of the proposed MBS descriptors should restrict access to PBS eligible patients, including any continuation criteria, and thus not allow broader access than the population proposed for the corresponding PBS listing. Suggested amendments to the proposed MBS item descriptors by the Department are shown in 'strikethrough' and bold italics below (refer to Tables 3.1-3.3).

The Department queried whether there was a need for an MBS item for the purpose of refilling the PDS ocular implant (see Table 3.2). The Department considered that, if the refilling process of the implant is a relatively straightforward non-invasive procedure compared to an eye injection, the proposed MBS schedule fee should be less compared to MBS item 42738, or alternately be absorbed into a standard specialist/consultation physician item. However, the Department also noted this approach may reduce the incentive for the ophthalmologist (through reduced income) to offer this novel ranibizumab delivery option. As a result, the Department is requesting public consultation and policy advice on whether there is a need for an MBS item for the purpose of refilling the implant.

The application did not state whether there would be a maximum number of implantation and explantation services that a patient should undergo within their lifetime, nor whether there would be an appropriate timeframe for any reimplantation following an explantation. MBS items often have restrictions on the number of times a procedure can be undertaken within a given timeframe, especially if there is a safety concern. If MSAC considers that there is such a safety concern, the Department notes it may be appropriate for the item descriptors to contain such restrictions.

Table 3.1: MBS descriptor for initial fill and implantation

Category 3 - THERAPEUTIC PROCEDURES		
	Group	T8 - Surgical Operations
	Subgroup	9 - Ophthalmology
~~Neovascular age-related macular degeneration,~~***Implantation and*** initial fill ~~and implantation~~ of an ocular implant for ~~Susvimo®~~ ~~(~~***PBS-subsidised*** ranibizumab ***100 mg/mL for the treatment of neovascular age-related macular degeneration***~~)~~ Fee: $1193.18		

Table 3.2: MBS descriptor for refill-exchange

Category 3 - THERAPEUTIC PROCEDURES		
	Group	T8 - Surgical Operations
	Subgroup	9 - Ophthalmology
~~Neovascular age-related macular degeneration, r~~***R***efill-exchange of an ocular implant for ~~Susvimo®~~ ~~(~~***PBS-subsidised*** ranibizumab ***100 mg/mL for the treatment of neovascular age-related macular degeneration***~~)~~ Fee: $312.95		

Table 3.3: MBS descriptor for explantation

Category 3 - THERAPEUTIC PROCEDURES		
	Group	T8 - Surgical Operations
	Subgroup	9 - Ophthalmology
~~Neovascular age-related macular degeneration, e~~***E***xplant~~ation~~ of an ocular implant ~~for Susvimo® (ranibizumab)~~ ***used for PBS-subsidised ranibizumab 100 mg/mL for the treatment of neovascular age-related macular degeneration*** Fee: $400.00		

Reduced equity of access to Australians who do not have private health insurance

The Department has advised the applicant that its streamlined codependent submission made to PBAC and MSAC should provide a rationale for the reduced equity of access to the prerequisite implant for Australians who do not have private health insurance. However, this does not appear to be addressed in the application to MSAC submitted by the applicant.

Questions have been raised whether this type of drug delivery implant will continue be eligible for listing on the Prostheses List when the definitions and criteria for listing are clarified as one of the Prostheses List Reforms measures. According to the proposed changes[1], it is expected that this type of implant will continue to be eligible for listing on the Prostheses List.

Access to the MBS insertion service would be limited to patients with the appropriate private health insurance unless the MBS item includes an 85% benefit. If surgeons would be prepared to insert the device in a licensed day surgery, an 85% benefit would enable them to

[1] Prostheses List Reforms Consultation Paper 1: Prostheses List Purpose, Definitions and Scope

bill the MBS (plus any additional charges to the patient). The Department seeks MSAC's advice on the reasonableness of this option in terms of patient safety and would also seek the views of the Royal Australian and New Zealand College of Ophthalmologists (RANZCO) about this option. In this way, insured and uninsured patients could get the same procedural service. However, private health insurers would not be required to cover the cost of the PDS ocular implant for appropriately insured patients not having the procedure as an inpatient.

Public hospitals may also choose to provide the insertion procedure service if they perceive a benefit for them due to a reduction in the frequency of subsequent injections in the context of these eye injections taking up a substantial proportion of public ophthalmology waiting lists.

Coordination of PLAC-PBAC-MSAC codependent consideration
Application 1695 is being managed as a streamlined codependent submission, for MSAC purposes being coordinated with:

- a PBAC consideration of the new formulation of ranibizumab in March 2022
- a consideration of the implant sponsored by B Braun for the next Prostheses List update in November 2022.

15. Other policy and implementation issues

Uncertainties about estimated patient uptake of services
Some patient populations have difficulty accessing the current treatments available for nAMD. This occurs for various reasons including ophthalmology workforce availability and distribution, availability of treatments within the public hospital system, and costs associated with treatment. Due to the need for patients to demonstrate responsiveness to previous intravitreal injection treatment, the proposed services would have limited ability to address the unmet needs of those patients who are not currently receiving treatment for macular disease. This also creates uncertainty about the overall uptake of this service.

There may also be uncertainties relating to the definition of the requirement that the condition must have previously responded to anti-VEGF treatment. This may have implications for the MBS item criteria.

There are existing uncertainties around patient out-of-pocket costs, primarily around the cost of the PDS ocular implant. If this is listed on the Prostheses List, it is unknown whether a patient's access to private health insurance may affect the uptake of the codependent procedures. If it is not listed on the Prostheses List, cost barriers for all patients may further reduce the anticipated patient uptake of these services.

Overall, the application claimed a large cost save to the MBS, with the magnitude of the save driven by the uptake of the PDS. Rural patients who currently find it difficult to access services that require monthly visits to urban-based specialists might particularly seek this treatment option, despite the possible need for supplemental ranibizumab.

Percentage of patients requiring additional treatment
The application estimated that 5.2% of patients would require intravitreal injections (or possibly additional refill exchange procedures beyond the standard 2 per year) as a "top up" treatment in addition to the regular delivery of the drug provided by the implanted device. Any variation from the estimates regarding these additional treatments would have implications for overall MBS expenditure.

Additionally, if patients require additional attendances with treating clinicians to monitor the patient's tolerance of the implant (including any aftercare and follow up visits), this would

have implications for overall MBS expenditure. The number of follow up visits required may need to be reflected in the MBS item and reflect evidence provided in trials. Higher rates of adverse events and ocular adverse events in patients with the implanted device may add further uncertainty to estimations of overall MBS expenditure.

Unclear number of patients who may require explantation and their continued treatment
Given the challenges mentioned above in accessing current intravitreal injection services, there is uncertainty about the number of patients in an Australian health care setting who may require explantation of their device and return to subsequent intravitreal injections versus completely disengaging from treatment. This will have impacts upon the overall MBS costs. The economic modelling includes an estimate of the proportion of patients requiring an explant procedure, but this estimate would likely increase over time.

Change in patient out-of-pocket costs for monitoring
A key concern for patients undergoing treatment for nAMD is high out-of-pocket costs. Several factors contribute to patient out-of-pocket costs. The application noted that response to treatment is detected using optical coherence tomography (OCT); and that current dosing intervals are determined using OCT. There is a current MBS item (11219) for the diagnosis of an ocular condition, claimable once in a 12-month period. However, this item cannot be used for post-diagnosis monitoring as outlined in the application. The application does not address the impact for patients of the use of OCT to monitor effectiveness and progress of treatment. Patients are therefore likely to face out-of-pocket costs during their treatment.

Private health insurance
As the items relate to amendments to Schedules 1 and 3 of the Benefit Requirement Rules, MSAC advice is sought on the types of procedure the services should be categorized under:

- Type A procedures are overnight procedures.
- Type B procedures are same-day hospital procedures where the patient leaves the hospital on the same day they have surgery.
- Type C procedures are often out-of-hospital procedures which do not normally require hospital accommodation/admission.

Current intravitreal injection services are classified as Type B procedures. There has been an ongoing discussion around the reclassification of intravitreal injections as Type C procedures. There is some opposition from the profession regarding the classification of intravitreal injections as Type C procedures. Similar discussions may apply to the proposed refill-exchange service. However, it appears appropriate that the implantation and explantation procedures are likely to be Type B procedures.

16. Applicant comments on MSAC's Public Summary Document

The applicant had no comment.

17. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website: visit the MSAC website