Australian Government

Department of Health

MSAC Application 1695

Procedures for the implantation and refill-exchange of the Port Delivery System with ranibizumab to treat neovascular age-related macular degeneration

This application form is to be completed for new and amended requests for public funding (including but not limited to the Medicare Benefits Schedule (MBS)). It describes the detailed information that the Australian Government Department of Health requires to determine whether a proposed medical service is suitable.

Please use this template, along with the associated Application Form Guidelines to prepare your application. Please complete all questions that are applicable to the proposed service, providing relevant information only. Applications not completed in full will not be accepted.

Should you require any further assistance, departmental staff are available through the Health Technology Assessment Team (HTA Team) on the contact numbers and email below to discuss the application form, or any other component of the Medical Services Advisory Committee process.

Email: hta@health.gov.au
Website: www.msac.gov.au

PART 1 – APPLICANT DETAILS

1. Applicant details (primary and alternative contacts)

Corporation / partnership details (where relevant): Roche Products Pty Ltd
Corporation name: Roche Products Pty Ltd
ABN: 70 000 132 865
Business trading name: Roche Products Pty Ltd

Primary contact name: REDACTED

Primary contact numbers
Business: **REDACTED**
Mobile: **REDACTED**
Email: **REDACTED**

Alternative contact name: REDACTED

Alternative contact numbers
Business: **REDACTED**
Mobile: **REDACTED**
Email: **REDACTED**

2. (a) Are you a lobbyist acting on behalf of an Applicant?

☐ Yes
☒ No

(b) If yes, are you listed on the Register of Lobbyists?

☐ Yes
☐ No

PART 2 – INFORMATION ABOUT THE PROPOSED MEDICAL SERVICE

3. Application title

Procedures for the implantation and refill-exchange of the Port Delivery System with ranibizumab to treat neovascular age-related macular degeneration

4. Provide a succinct description of the medical condition relevant to the proposed service (no more than 150 words – further information will be requested at Part F of the Application Form)

Age related macular degeneration (AMD) 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. Neovascular (wet) AMD (nAMD) occurs in around 10-15% of overall AMD cases and is characterised by choroidal neovascularisation (CNV), a process in which new blood vessels grow beneath the retina and macula. In wet AMD, the protein vascular endothelial growth factor (VEGF) is predominantly responsible for the abnormal growth of blood vessels and fluid leakage under the retina. Anti-VEGF medication can block the activity of this VEGF protein, thereby stopping the growth of abnormal blood vessels and fluid leakage.

The current standard of care are the Pharmaceutical Benefits Scheme (PBS) listed anti-VEGF intravitreal injections, Lucentis® (ranibizumab) and Eylea® (aflibercept).

Real-world data suggest that this burden of frequent intravitreal injections and office visits (and associated out of pocket costs) with current standard of care contributes to many patients not achieving or maintaining vision outcomes comparable with those observed in controlled clinical trials. Further, access to ophthalmological care in rural and remote areas is disparate to metropolitan areas in Australia.

Therefore, there is a need for novel interventions that reduce treatment burden, subsequently reducing patient clinic visits for treatment administration, an expense to the MBS. The Port Delivery System with ranibizumab (PDS) is a permanent refillable ocular implant that continuously delivers a customised formulation of ranibizumab over a period of months, reducing the treatment burden and associated MBS costs with frequent eye injections.

5. Provide a succinct description of the proposed medical service (no more than 150 words – further information will be requested at Part 6 of the Application Form)

The proposed services seek appropriate Medical Benefits Scheme (MBS) reimbursement to allow the initial fill and implantation and refill-exchange of the Port Delivery System's ocular implant with ranibizumab for the treatment of neovascular age-related macular degeneration. The proposed services represent new (or change to existing) co-dependent MBS items to cover the administration of a drug, ranibizumab. Proposed fees are informed by ocular procedures reimbursed on the MBS that are similar in terms of complexity and time, as suggested by consulted medical experts.

MBS reimbursement is also sought for the explantation of the ocular implant, if required.

The applicant notes than an expedited MSAC pathway is appropriate given a clear PICO for the technology. Furthermore, MSAC Process frameworks acknowledge that professional services for the administration of the drug do not require a separate HTA to be conducted by MSAC to inform the MBS listing when the HTA is being conducted by the PBAC for the drug (p.30, MSAC Final Process Framework).

6. (a) Is this a request for MBS funding?

☒ Yes
☐ No

(b) If yes, is the medical service(s) proposed to be covered under an existing MBS item number(s) or is a new MBS item(s) being sought altogether?

☐ Amendment to existing MBS item(s)
☒ New MBS item(s)

(c) If an amendment to an existing item(s) is being sought, please list the relevant MBS item number(s) that are to be amended to include the proposed medical service:

N/A

(d) If an amendment to an existing item(s) is being sought, what is the nature of the amendment(s)?

N/A

(e) If a new item(s) is being requested, what is the nature of the change to the MBS being sought?

i. ☒ A new item which also seeks to allow access to the MBS for a specific health practitioner group
ii. ☒ A new item that is proposing a way of clinically delivering a service that is new to the MBS (in terms of new technology and / or population)
iii. ☐ A new item for a specific single consultation item
iv. ☐ A new item for a global consultation item(s)

(f) Is the proposed service seeking public funding other than the MBS?

☐ Yes
☒ No

No other source of funding for the procedures other than the MBS is sought.
It is foreshadowed that public funding will be sought for Susvimo®, a customised version of ranibizumab for use in the ocular implant on the PBS.

(g) If yes, please advise:

N/A

7. What is the type of service:

☐ Therapeutic medical service
☐ Investigative medical service
☐ Single consultation medical service
☐ Global consultation medical service
☐ Allied health service
☒ Co-dependent technology
☐ Hybrid health technology

8. For investigative services, advise the specific purpose of performing the service *(which could be one or more of the following)*:

i. ☐ To be used as a screening tool in asymptomatic populations
ii. ☐ Assists in establishing a diagnosis in symptomatic patients
iii. ☐ Provides information about prognosis
iv. ☐ Identifies a patient as suitable for therapy by predicting a variation in the effect of the therapy
v. ☐ Monitors a patient over time to assess treatment response and guide subsequent treatment decisions

9. Does your service rely on another medical product to achieve or to enhance its intended effect?

☒ Pharmaceutical / Biological
☒ Prosthesis or device
☐ No

It is foreshadowed that funding will be sought for Susvimo®, a customised concentrated version of ranibizumab, for use in the ocular implant on the PBS.

It is foreshadowed that funding will be sought for the ocular implant on the Prostheses List.

10. (a) If the proposed service has a pharmaceutical component to it, is it already covered under an existing Pharmaceutical Benefits Scheme (PBS) listing?

☐ Yes
☒ No

(b) If yes, please list the relevant PBS item code(s):

It should be noted that, whilst Susvimo® (ranibizumab) contains the same active ingredient as PBS-listed Lucentis® (ranibizumab), it is a customised concentrated formulation and is not interchangeable with Lucentis® (ranibizumab). Similarly, the refill-exchange procedure must be performed with Susvimo® and the provided, proprietary refill needle; this needle allows the content of the implant to be extracted simultaneously as the implant is filled with replacement ranibizumab.

(c) If no, is an application (submission) in the process of being considered by the Pharmaceutical Benefits Advisory Committee (PBAC)?

☐ Yes (please provide PBAC submission item number below)
☒ No

An application seeking PBS listing for a customised formulation of ranibizumab for the treatment of patients with nAMD is foreshadowed to be lodged for PBAC's consideration. It is anticipated that that PBS funding criteria sought would be consistent with current PBS listed treatments Lucentis® (ranibizumab) and Eylea® (aflibercept).

(d) If you are seeking both MBS and PBS listing, what is the trade name and generic name of the pharmaceutical?

Trade name: Susvimo®
Generic name: ranibizumab

11. (a) If the proposed service is dependent on the use of a prosthesis, is it already included on the Prostheses List?

☐ Yes
☒ No

(b) If yes, please provide the following information (where relevant):

N/A

(c) If no, is an application in the process of being considered by a Clinical Advisory Group or the Prostheses List Advisory Committee (PLAC)?

☐ Yes
☒ No

An application seeking a Prostheses List billing code for the ocular implant (for the treatment of patients with nAMD) is foreshadowed to be lodged for PLAC's consideration.

(d) Are there any other sponsor(s) and / or manufacturer(s) that have a similar prosthesis or device component in the Australian market place which this application is relevant to?

☐ Yes
☒ No

(e) If yes, please provide the name(s) of the sponsor(s) and / or manufacturer(s):

N/A

12. Please identify any single and / or multi-use consumables delivered as part of the service?

Single use consumables: A tabulation of the ancillary devices (as well as the implant) used to support the procedures and the drug component used within each procedure is noted below.

Procedure	Component	Purpose
Initial fill and implantation	Ocular implant	Continuous release of ranibizumab 100 mg/mL in the eye
	Initial Fill Needle	Fill the ocular implant with ranibizumab 100 mg/mL prior to implantation
	Susvimo® vial	ranibizumab 100 mg/mL
	Insertion Tool Assembly	Hold the implant and to place the implant in the eye during the implant procedure
Refill-exchange	Refill Needle	Refill the implant with ranibizumab 100 mg/mL in-situ
	Susvimo® vial	ranibizumab 100 mg/mL
Explantation	Explant Tool	Remove the implant, if needed.

Multi-use consumables: No multi-use consumables expected to be delivered as part of the service.

PART 3 – INFORMATION ABOUT REGULATORY REQUIREMENTS

13. (a) If the proposed medical service involves the use of a medical device, in-vitro diagnostic test, pharmaceutical product, radioactive tracer or any other type of therapeutic good, please provide the following details:

Initial fill and implantation
Type of therapeutic good: Medical device, Ocular implant
Manufacturer's name: B. Braun Pty Ltd
Sponsor's name: B. Braun Pty Ltd

Type of therapeutic good: Drug, ranibizumab, Susvimo®
Manufacturer's name: Roche Products Pty Ltd
Sponsor's name: Roche Products Pty Ltd

Refill-exchange
Type of therapeutic good: Drug, ranibizumab, Susvimo®
Manufacturer's name: Roche Products Pty Ltd
Sponsor's name: Roche Products Pty Ltd

Explantation (if needed)
Type of therapeutic good: Explant tool
Manufacturer's name: B. Braun Pty Ltd
Sponsor's name: B. Braun Pty Ltd

(b) Is the medical device classified by the TGA as either a Class III or Active Implantable Medical Device (AIMD) against the TGA regulatory scheme for devices?

☒ Class III – Ocular implant
☐ AIMD
☐ N/A

14. (a) Is the therapeutic good to be used in the service exempt from the regulatory requirements of the *Therapeutic Goods Act 1989*?

☐ Yes (If yes, please provide supporting documentation as an attachment to this application form)
☒ No

(b) If no, has it been listed or registered or included in the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TGA)?

☐ Yes (if yes, please provide details below)
☒ No

15. If the therapeutic good has not been listed, registered or included in the ARTG, is the therapeutic good in the process of being considered for inclusion by the TGA?

Therapeutic good: Drug, ranibizumab, Susvimo®

☒ Yes (please provide details below)
☐ No

Date of submission to TGA: 30th May 2021
Estimated date by which TGA approval can be expected: July 2022
TGA Application ID: PM-2021-02235-1

TGA approved indication(s), if applicable: Treatment of adult patients with neovascular (wet) age-related macular degeneration

16. If the therapeutic good is not in the process of being considered for listing, registration or inclusion by the TGA, is an application to the TGA being prepared?

Therapeutic good: Medical device, Ocular implant (and associated insertion tool assembly)

☒ Yes (please provide details below)
☐ No

Estimated date of submission to TGA: Q3 2021
Proposed indication(s), if applicable: For use with Susvimo® (ranibizumab 100 mg/mL) only for treatment of adult patients with neovascular (wet) age-related macular degeneration (nAMD)

Therapeutic good: Medical device, Explant tool for ocular implant

☒ Yes (please provide details below)
☐ No

Estimated date of submission to TGA: Q3 2021
Proposed indication(s), if applicable: For use for the removal of the implant for Susvimo®

PART 4 – SUMMARY OF EVIDENCE

17. **Provide an overview of all key journal articles or research published in the public domain related to the proposed service that is for your application (limiting these to the English language only).** ***Please do not attach full text articles, this is just intended to be a summary.***

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
Primary evidence^					
1.	Phase 3, randomised, multicentre, open-label (visual assessor [VA]-masked), active-comparator study	Archway Primary Analysis Results of the Phase 3 Archway Trial of the Port Delivery System With Ranibizumab for Patients With Neovascular AMD^ NCT03677934	Assess the efficacy, safety, and pharmacokinetics of 100mg/ml delivered via the PDS compared with ranibizumab intravitreal injections at 0.5 mg (10 mg/mL) in participants with nAMD The primary efficacy objective was to evaluate non-inferiority and equivalence of ranibizumab delivered via the PDS every 24 weeks compared with that of intravitreal ranibizumab injections delivered every 4 weeks.	Media release Retina Society 2020 Presentation	22 July 2020
Additional evidence					
2.	Phase 2, randomised, multicentre, active treatment–controlled clinical trial.	Ladder The Port Delivery System with Ranibizumab for Neovascular Age-Related Macular Degeneration NCT02510794	Evaluate the safety and efficacy of the Port Delivery System with ranibizumab (PDS) for nAMD treatment	Publication (Primary Analysis) Publication (End of Study Results)	1 April 2019
3.	Prospective, open-label, Phase 1 single centre study	Phase 1 Clinical Study of the Port Delivery System with ranibizumab for continuous treatment of neovascular age-related macular degeneration	Evaluate the safety, clinical benefit, pharmacokinetics (PK), and integrity of the PDS in treatment-naïve patients with nAMD	Abstract	June 2020

** Categorise study design, for example meta-analysis, randomised trials, non-randomised trial or observational study, study of diagnostic accuracy, etc.*
***Provide high level information including population numbers and whether patients are being recruited or in post-recruitment, including providing the trial registration number to allow for tracking purposes.*
**** If the publication is a follow-up to an initial publication, please advise.*
^NB: Key registration trial; Product Information dosing and administration is consistent with the Phase 3 trial

18. Identify yet to be published research that may have results available in the near future that could be relevant in the consideration of your application by MSAC (limiting these to the English language only). *Please do not attach full text articles, this is just intended to be a summary.*

	Type of study design*	Title of research (including any trial identifier if relevant)	Short description of research (max 50 words)**	Website link to research (if available)	Date***
1.	Phase IIIb, global, multicentre, randomised, visual assessor-masked study^	A Study of the Efficacy, Safety, and Pharmacokinetics of A 36-Week Refill Regimen for the Port Delivery System With Ranibizumab in Patients With Neovascular Age-Related Macular Degeneration (Velodrome)	Assess the efficacy, safety, and pharmacokinetics of the PDS 100 mg/mL delivered every 36 weeks (Q36W) compared with every 24 weeks (Q24W) in patients with nAMD	NCT04657289	Estimated Study Start Date: 7 Jul 2021 Estimated Primary Completion Date: 21 Sep 2023

** Categorise study design, for example meta-analysis, randomised trials, non-randomised trial or observational study, study of diagnostic accuracy, etc.*
***Provide high level information including population numbers and whether patients are being recruited or in post-recruitment.*
****Date of when results will be made available (to the best of your knowledge).*
^NB: Future trial; not anticipated to be the basis for future submission claims

PART 5 – CLINICAL ENDORSEMENT AND CONSUMER INFORMATION

19. List all appropriate professional bodies / organisations representing the group(s) of health professionals who provide the service (please attach a statement of clinical relevance from each group nominated):

Australian Society of Ophthalmologists (ASO)

Royal Australian and New Zealand College of Ophthalmologists (RANZCO)

The applicant recommends that the Department of Health approach the professional bodies directly.

20. List any professional bodies / organisations that may be impacted by this medical service (i.e. those who provide the comparator service):

As above.

21. List the consumer organisations relevant to the proposed medical service (please attach a letter of support for each consumer organisation nominated):

Macular Disease Foundation Australia

A letter of support has been provided with the application.

22. List the relevant sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed medical service:

There are no comparable devices on the Prostheses List. There are no MBS items where the MBS item descriptor reasonably describes the implantation or explantation of the proposed ocular implant.

Pharmaceutical companies that have a pharmacological comparator include Novartis Pharmaceuticals Australia (Lucentis®, ranibizumab), Bayer Australia Limited (Eylea®, aflibercept).

23. Nominate two experts who could be approached about the proposed medical service and the current clinical management of the service(s):

Name of expert 1: **REDACTED**

Telephone number(s): **REDACTED**

Email address: **REDACTED**

Justification of expertise: Vitreoretinal surgeon

Name of expert 2: **REDACTED**

Telephone number(s): **REDACTED**

Email address: **REDACTED**

Justification of expertise: Vitreoretinal surgeon

PART 6 – POPULATION (AND PRIOR TESTS), INTERVENTION, COMPARATOR, OUTCOME (PICO)

PART 6a – INFORMATION ABOUT THE PROPOSED POPULATION

24. Define the medical condition, including providing information on the natural history of the condition and a high level summary of associated burden of disease in terms of both morbidity and mortality:

Disease overview

Age related macular degeneration (AMD) 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.

Neovascular (wet) AMD occurs in around 10-15% of overall AMD cases. Neovascular AMD (nAMD) is characterised by choroidal neovascularisation (CNV), a process in which new blood vessels grow beneath the retina and macula. VEGF is widely considered the main growth factor responsible for this neovascularisation. These blood vessels leak, causing separation of Bruch's membrane, the retinal pigment epithelium (RPE) and the retina from each other, with accumulation of sub-RPE, sub-retinal or intra-retinal fluid.

CNV lesions are classified according to the location of the lesion relative to the fovea (the central area of the macula and provides the sharpest vision): subfoveal (located directly below the fovea), juxtafoveal (located adjacent to fovea) and extrafoveal (located away from the fovea).

Intravitreal injections with anti-VEGF drugs are the current standard of care for nAMD. In Australia, Lucentis® (ranibizumab) and Eylea® (aflibercept) are PBS-listed for this indication.

Treatment burden

Real-world data suggest that the burden of frequent intravitreal injections and office visits contributes to many patients not achieving or maintaining vision outcomes comparable with those observed in controlled clinical trials (Cohen SY, 2013) (Finger RP, 2013) (Holz FG, 2015). The use of "treat and extend" (T&E) administration strategies, in which the intervals between treatments are extended as long as the macula remains dry, were introduced to lower the frequency of injections and is a commonplace treatment strategy in Australian clinical practice. Studies have demonstrated that treat and extend regimens with are no worse than fixed monthly intervals in achieving visual acuity outcomes with reduced injections; in a clinical trial, visual acuity outcomes were similar with 17.6 injections of ranibizumab in the treat-and-extend group compared with 23.5 in the monthly group (Kertes PJ, 2020).

However, this only partly resolves the treatment burden; recent Australian studies show that injections are still frequent. Australian Phase IV studies have shown that the average number of injections received per year with ranibizumab was 9.6 (95% CI, 9.2-10.0) and 9.5 (95% CI, 9.1-9.9) with aflibercept using a treat and extend regimen in the first 12 months (Gillies MC H. A., 2019a). The distribution of injection intervals at month 12 found that almost half of participants were still on 4 weekly intervals in both arms (Gillies MC H. A., 2019a). The number of injections administered between months 12 and 24 were similarly frequent with 8.9 injections in the ranibizumab group and 8.3 injections in the aflibercept group (Gillies MC H. A., 2020b). Data from a 2018 DUSC utilisation report of ranibizumab and aflibercept noted the mean number of injections in Year 1 is 8.52 in nAMD, where fixed monthly/Q4W treatment would require 12-13 injections per year (DUSC, 2018).

Management of nAMD is recognised for its substantial burden on patients and caregivers. Australian studies have noted that attendance of appointments to administer intravitreal injections results in lost productivity of 4.4±1.7 hours per month, with additional time lost by caregivers. Financial strain was incurred by direct medical costs associated with intravitreal assessment and injections at an average of AU$199.2 per month. Indirect costs incurred averaged $64.8 per month. Qualitative indirect costs due to

loss of productivity for the patient, unpaid caregivers, and loss of productivity due to premature mortality were additionally noted to represent a considerable burden (Spooner KL, 2018).

The Department of Health's Medical Cost Finder notes that, 30% of patients pay nothing for the administration of intravitreal injections; however, for patients that do, the typical amount paid after Government Medicare payment was $224 (DoH, 2021).

Geographical challenges

Further, whilst anti-VEGF therapies are generally available, access varies due to workforce limitations and geography. Clinician groups have acknowledged misdistribution of the ophthalmology workforce across metropolitan and regional/remote areas (RANZCO, 2020); in rural areas, community members may often have to wait until an ophthalmologist visits the area or they may need to travel to a regional or metropolitan hospital for more complex diagnosis and treatment.

Clinician groups, patient organisations and peak bodies have stated that addressing geographic care inequities represents a priority in ophthalmology (DoH, 2019) (DoH, 2018) (RANZCO, 2021). The PBAC and the Department of Health have noted these barriers in prior considerations and public documents (Ozurdex PSD, March 2016) (DUSC, 2018).

Unmet need and the Port Delivery System

A need exists for novel interventions that reduce treatment burden, subsequently reducing patient clinic visits for treatment administration. The Port Delivery System (PDS) is a permanent refillable ocular implant that continuously delivers a customised formulation of ranibizumab over a period of months, reducing the treatment burden associated with frequent eye injections.

The PBAC and the Department of Health have previously noted consumer comments for treatment options that require less frequent administrations; consumer input noting interventions being particularly beneficial for patients in rural and remote areas. Consumer input has highlighted the benefits of less frequent injections positively impacting patient acceptability, the reduced financial burden on patients, their carers and the healthcare system (Beovu PSD, 2019).

As noted earlier, the proposed services seek appropriate Medical Benefits Scheme reimbursement to enable the appropriate implantation, refill-exchange and explantation (if required) of the Port Delivery System's ocular implant. The proposed services represent new co-dependent MBS items to cover the administration of a therapeutic.

25. Specify any characteristics of patients with the medical condition, or suspected of, who are proposed to be eligible for the proposed medical service, including any details of how a patient would be investigated, managed and referred within the Australian health care system in the lead up to being considered eligible for the service:

Based on foreshadowed PBS funding criteria, patients with nAMD would be eligible for the proposed "Initial fill and implantation" medical service. This is consistent with the proposed TGA indication. It is noted that, in clinical practice, patients with nAMD who have previously been treated with and have responded to anti-VEGF therapy would be treatment candidates. This would be consistent with the primary trial evidence referred to in Q17.

Clinician feedback to date suggests that patients are more likely to elect treatment with the PDS when

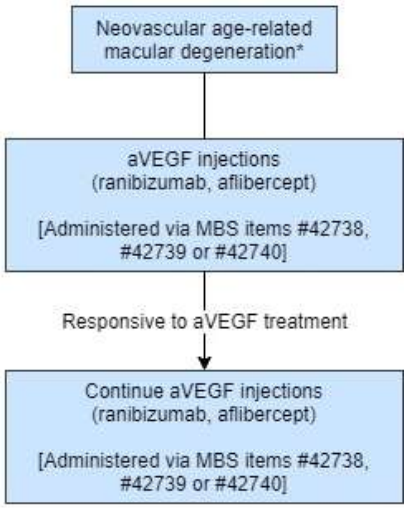
- Frequent injections are required (ie. unable to treat and extend beyond monthly treatment)
- Geographical or personal circumstances (ie. living remotely, low workforce access, or medical problems limiting frequent visits) limiting access to clinical care consistent with their injection frequency needs

26. Define and summarise the current clinical management pathway *before* patients would be eligible for the proposed medical service (supplement this summary with an easy to follow flowchart [as an attachment to the Application Form] depicting the current clinical management pathway up to this point):

Clinical management pathways preceding patients being eligible for the proposed medical services would be unchanged.

Current management of nAMD requires formal diagnosis by an ophthalmologist. Consistent with current PBS criteria, optical coherence tomography or fluorescein angiography is used for diagnosis (MBS item numbers #11219, #11215, respectively). Treatment with intravitreal injections are also provided by ophthalmologists; MBS item number #42738, #42739 and #42740 are commonly used for the injection of therapeutic substances into the eye. It is noted that, patients continue on therapy when they respond to treatment. This is depicted in Figure 1.

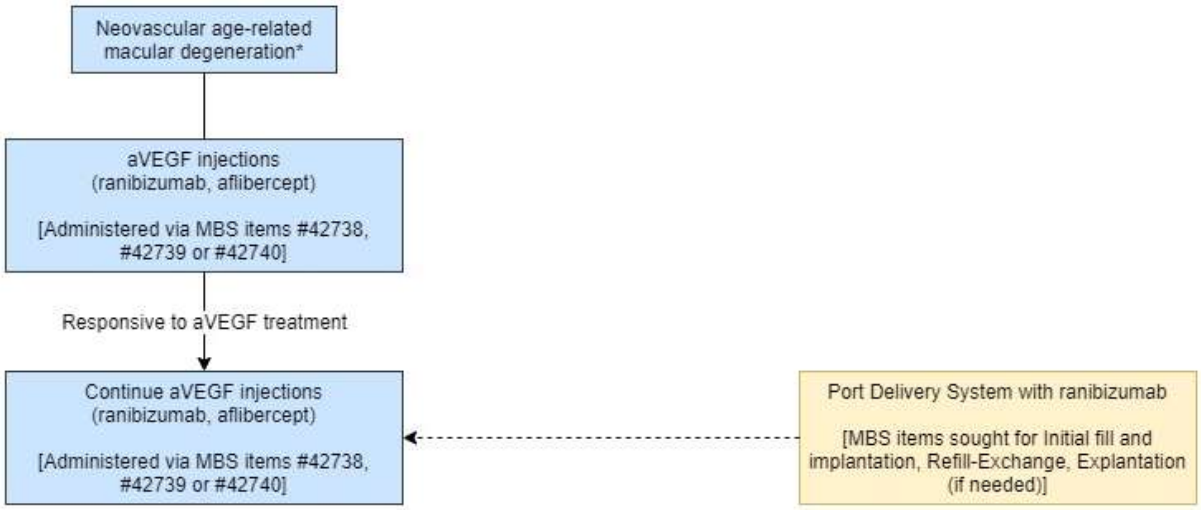
Figure 1: Current clinical management pathway



*Diagnosed by optical coherence tomography or fluorescein angiography (as per PBS criteria)

The proposed clinical management flowchart notes that the PDS, comprising ranibizumab delivered via the ocular implant, would be an alternative treatment option for patients who respond to standard of care intravitreal injections, as depicted by a dotted line (Figure 2).

Figure 2: Proposed clinical management pathway



*Diagnosed by optical coherence tomography or fluorescein angiography (as per PBS criteria)

PART 6b – INFORMATION ABOUT THE INTERVENTION

27. Describe the key components and clinical steps involved in delivering the proposed medical service:

Initial fill and implantation –The ocular implant, the size of a grain of rice, is surgically implanted at the pars plana. Prior to implantation, the ocular implant is filled with Susvimo®, a customised form of ranibizumab. Once filled and implanted, the implant is designed to be permanent (ie. lifelong) and provide continuous release of ranibizumab over an extended period of time.

Overall, the procedure will take approximately an hour. This will be conducted by a vitreoretinal surgeon (ie. A retina specialist who has specialised in ophthalmology and subspecialised in diseases and surgery of the vitreous body of the eye and the retina).

There are no similar procedures on the existing Medicare Benefits Schedule. Steps in the procedure are:

- Filling of the PDS device with Susvimo®
- Conjunctival peritomy (similar to that in glaucoma filtering procedure, MBS item #42746) and external diathermy
- Creation of pars plana sclerotomy (as performed in pars plana vitrectomy, MBS item #42725, but a single/larger sclerotomy)
- Endolaser to ciliary body (MBS item #42809)
- External vitrectomy of any prolapsed vitreous
- Insertion of the PDS device through the pars plana sclerotomy
- Suture closure of conjunctiva and Tenon's capsule

In the absence of a directly comparable procedure, consulted vitreoretinal surgeons have noted that the implantation procedure represents is intermediate in complexity and time between the MBS item numbers #42752 and #42746. This is further discussed, related to the proposed fee in Q51.

Further details on the initial fill of the implant and the implantation procedure is provided in the "Instructions for Use" attachment (p. 16-41).

Refill-exchange – Consistent with the proposed dosing and administration of Susvimo® (ranibizumab), a patient will attend a consultation and have their ocular implant refilled every six months. This refill-exchange procedure is performed using the provided, proprietary refill needle; it allows implant contents to be extracted simultaneously as the implant is filled with replacement ranibizumab. Ranibizumab passively diffuses into the vitreous following the refill-exchange procedure.

A retinal specialist (an ophthalmologist with a subspecialty in the retina) will perform this. After more experience with PDS in Australia, training in the refill-exchange procedure may be broadened to general ophthalmologists who are experienced in conducting intravitreal injections.

Consulted retinal specialists have noted that the refill-exchange procedure is similar in terms of complexity and time to MBS item numbers #42738, #42739 and #42740. Clinicians have noted that the current MBS item descriptor for these item numbers sufficiently capture the refill-exchange procedure and that a separate MBS item number for refill-exchange may not be required.

Further details on the refill-exchange procedure is provided in the "Instructions for Use" attachment (p. 54-62).

Explantation (if needed) – In the uncommon clinical circumstance that the ocular implant needs to be removed, this will be conducted by a vitreoretinal surgeon. The explant tool is a pair of forceps used to grasp and engage the implant during removal.

Steps in the procedure are

- Conjunctival peritomy
- Remove any fibrous capsule covering the implant
- Stabilise the globe and align the explant tool
- Grasp and remove the implant
- Suture the sclera
- Close Tenon's capsule and conjunctiva completely

In the absence of a directly comparable procedure, consulted vitreoretinal surgeons have noted that the explantation procedure is somewhat more complex and time consuming than current MBS item number #42505. Clinician advice is that the explantation of the PDS involves more steps including scleral suturing and may also require potential vitrectomy of prolapsed vitreous, than #42505.

Further details on the ocular implant removal procedure is provided in the "Instructions for Use" attachment (p. 78-91).

28. Does the proposed medical service include a registered trademark component with characteristics that distinguishes it from other similar health components?

The proposed medical service for "Initial fill and implantation" is likely to acknowledge "*the initial fill and implantation of an ocular implant for Susvimo®"*. This is not unprecedented; MBS item numbers #42752 (insertion) reference to ocular implantable devices with trademark components.

The applicant is amenable to a more generic item descriptor, but recognises that the clear specification ensures clear and unequivocal intent of the service.

29. If the proposed medical service has a prosthesis or device component to it, does it involve a new approach towards managing a particular sub-group of the population with the specific medical condition?

As previously noted, no change is proposed to the management pathway in patients with nAMD, rather, this represents a new method of delivering (via an ocular implant) into the eye a well-established active ingredient with the same pharmacological effect as products currently listed on the PBS.

As noted before, the proposed intervention (inclusive of the proposed medical services), describes an intervention which represents an alternative option to current PBS listed therapies (delivered via intravitreal injection).

30. If applicable, are there any limitations on the provision of the proposed medical service delivered to the patient (i.e. accessibility, dosage, quantity, duration or frequency):

None foreshadowed.

31. If applicable, identify any healthcare resources or other medical services that would need to be delivered at the same time as the proposed medical service:

None foreshadowed.

32. If applicable, advise which health professionals will primarily deliver the proposed service:

As noted in Q27.

Initial fill and implantation – Vitreoretinal surgeons

Refill-exchange – Vitreoretinal surgeons, retinal specialists (ophthalmology subspecialty), general ophthalmologists (after more experience with PDS in Australia, and for ophthalmologists trained and experienced in administering intravitreal injections)

Explantation (if needed) – Vitreoretinal surgeons

33. If applicable, advise whether the proposed medical service could be delegated or referred to another professional for delivery:

It is not anticipated that any other professional, other than those listed in Q32, would be able to conduct these procedures.

34. If applicable, specify any proposed limitations on who might deliver the proposed medical service, or who might provide a referral for it:

Not applicable; proposed TGA indications limit the use of the device and drugs to patients with nAMD.

35. If applicable, advise what type of training or qualifications would be required to perform the proposed service, as well as any accreditation requirements to support service delivery:

Vitreoretinal surgeons would be Fellows of the Royal Australian and New Zealand College of Ophthalmology (RANZCO).

The applicant foreshadows additional risk minimisation activities as part of regulatory approval; the PDS Surgical Training Program is a training curriculum aimed to establish consistency in following the "*Instructions For Use*" (provided by the device Sponsor) and confidence in surgical procedures by developing surgical competence through pre-case training. In addition, ongoing surgical support tailored to physicians performing the PDS procedures will be made available by the sponsor.

36. (a) Indicate the proposed setting(s) in which the proposed medical service will be delivered (select ALL relevant settings):

- ☐ Inpatient private hospital (admitted patient)
- ☐ Inpatient public hospital (admitted patient)
- ☐ Private outpatient clinic
- ☐ Public outpatient clinic
- ☐ Emergency Department
- ☐ Private consulting rooms - GP
- ☐ Private consulting rooms – specialist
- ☐ Private consulting rooms – other health practitioner (nurse or allied health)
- ☐ Private day surgery clinic (admitted patient)
- ☐ Private day surgery clinic (non-admitted patient)
- ☐ Public day surgery clinic (admitted patient)
- ☐ Public day surgery clinic (non-admitted patient)
- ☐ Residential aged care facility
- ☐ Patient's home
- ☐ Laboratory
- ☒ Other – please specify below

(b) Where the proposed medical service is provided in more than one setting, please describe the rationale related to each:

Given the three distinct procedures, the settings where the proposed medical services could be delivered are noted below.

Initial fill and implantation, explantation

Consulted clinicians note that these procedures need to be conducted in an operating room. As such the appropriate settings where the proposed medical services will be delivered are:

- Inpatient private hospital (admitted patient),
- Inpatient public hospital (admitted patient),
- Private day surgery clinic (admitted patient),
- Private day surgery clinic (non-admitted patient),
- Public day surgery clinic (admitted patient),
- Public day surgery clinic (non-admitted patient)

Due to resource limitations on operating theatre access, capacity constraints and waiting lists (for other ophthalmological procedures) in the public hospital system, private settings (hospital or clinic) would be anticipated to conduct the majority of the implantation procedure services.

Refill-exchange

Consulted clinicians note that the refill-exchange procedure can be conducted in an outpatient setting. As such the appropriate settings where the proposed medical service will be delivered are:

- Private outpatient clinic
- Public outpatient clinic
- Private consulting rooms – specialist

These settings are consistent with where intravitreal injections are currently performed. This would be consistent with RANZCO's "Choosing Wisely" Committee's advice that "*intravitreal injections may be safely performed on an outpatient basis. Don't perform routine intravitreal injections in a hospital or day surgery setting unless there is a valid clinical indication.*"

It is anticipated that these procedures are "Type C" procedures, given they can be conducted out-of-hospital and do not normally require admission.

37. Is the proposed medical service intended to be entirely rendered in Australia?

- ☒ Yes
- ☐ No – please specify below

PART 6c – INFORMATION ABOUT THE COMPARATOR(S)

38. Nominate the appropriate comparator(s) for the proposed medical service, i.e. how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian health care system (including identifying health care resources that are needed to be delivered at the same time as the comparator service):

The appropriate comparator is current standard of care, represented by regular intravitreal injections of ranibizumab or aflibercept.

39. Does the medical service (that has been nominated as the comparator) have an existing MBS item number(s)?

☒ Yes (please list all relevant MBS item numbers below)
☐ No

Intravitreal injections are administered via MBS items #42738, #42739 or #42740.

40. Define and summarise the current clinical management pathway/s that patients may follow *after* they receive the medical service that has been nominated as the comparator (supplement this summary with an easy to follow flowchart [as an attachment to the Application Form] depicting the current clinical management pathway that patients may follow from the point of receiving the comparator onwards, including health care resources):

Please refer to Q26.

41. (a) Will the proposed medical service be used in addition to, or instead of, the nominated comparator(s)?

☐ In addition to (i.e. it is an add-on service)
☒ Instead of (i.e. it is a replacement or alternative)

(b) If instead of (i.e. alternative service), please outline the extent to which the current service/comparator is expected to be substituted:

Clinician guidance suggests that approximately 20% of patients on current standards of care may be appropriate for therapy, of which 75% may elect therapy. Therefore, it is foreshadowed that the services currently delivered would be substituted in approximately 15% of patients in the initial years of introduction.

42. Define and summarise how current clinical management pathways (from the point of service delivery onwards) are expected to change as a consequence of introducing the proposed medical service, including variation in health care resources (Refer to Question 39 as baseline):

The expected change to the current clinical management pathway as a consequence of introducing the proposed medical service has been represented by a dotted line in the clinical management pathway (Figure 2). As previously noted, new MBS item numbers are required to enable appropriate remuneration for the procedures of the ocular implant to enable the delivery of Susvimo® (ranibizumab).

PART 6d – INFORMATION ABOUT THE CLINICAL OUTCOME

43. Summarise the clinical claims for the proposed medical service against the appropriate comparator(s), in terms of consequences for health outcomes (comparative benefits and harms):

It is foreshadowed that the PDS is non-inferior to current standard of care intravitreal injections. This claim will be informed by the Archway trial.

In Archway, PDS with ranibizumab 100mg/mL administered every 24 weeks (Q24W) demonstrated non-inferior and equivalent visual acuity outcomes compared with intravitreal ranibizumab 0.5mg every 4 weeks (Q4W). The ocular implant procedure and refill-exchange procedures were generally well tolerated; in general, the systemic safety profile of PDS treatment was comparable with monthly intravitreal ranibizumab treatment. Overall, the PDS device, procedure, drug combination was well tolerated with a favourable benefit-risk profile.

Results of the PDS patient preference questionnaire reported that 93.2% (218/234) preferred the continuous delivery of ranibizumab using PDS to ranibizumab intravitreal injections. Common reasons for preference reasons among patients who preferred PDS include fewer treatments and less discomfort. No preference was stated for 13/234 patients; three patients preferred intravitreal injections (One cited "Requires less time for treatment", two did not specify a reason).

The applicant notes that the ranibizumab intravitreal injections are a reasonable proxy for standard of care ranibizumab or aflibercept, given PBAC's prior conclusion that aflibercept is non-inferior to ranibizumab and that these medicines should be priced on an injection: injection basis (ie. one injection of ranibizumab is equivalent to one injection of aflibercept) (DoH, 2019).

44. Please advise if the overall clinical claim is for:

☐ Superiority
☒ Non-inferiority

45. Below, list the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be specifically measured in assessing the clinical claim of the proposed medical service versus the comparator:

Safety Outcomes: Adverse events (both ocular and non-ocular)
Clinical Effectiveness Outcomes: Primary: Change in best corrected visual acuity (BCVA), Change in central point thickness, change in central subfield thickness

Overall, the applicant notes that an Expedited MSAC pathway is appropriate; whilst the PDS has a level of clinical novelty due to the method of drug delivery, fundamentally, the technology has a clear intention for a well-defined population, replacing well-established standards of care with respect to PBS funded therapies, and MBS funded procedural costs (ie. the PICO is clear). The basis for the clinical claim is informed by a well-designed Phase III study, with trial endpoints (BCVA) consistent with trials informing clinical claims for past PBAC decision-making. Furthermore, given the claim of non-inferiority, it is anticipated to have neutral or cost-saving budgetary implications; in the specific context of the MBS, MBS savings are foreshadowed. Similarly, it is anticipated to result in cost savings for patients with respect to out of pocket costs related to treatment administration.

Further, this request represents a "*new co-dependent MBS item to cover the complex administration of a drug*" (p.30, MSAC Final Process Framework). The MSAC Process Framework states "*a HTA paradigm may be unnecessary for co-dependent applications between MSAC and PBAC, where PBAC is assessing the merits of a drug (via a HTA) and MSAC considers the professional service for the administration of the drug".* The MSAC Process Framework further notes that, "*the vast majority of applications to PBAC do not require a separate listing on the MBS for the delivery of the drug, but occasionally there is a drug where the time and complexity of administering that drug warrants the creation of an accompanying MBS item. In this situation, the accompanying professional service for the administration of the drug does not require a separate HTA to be conducted by MSAC to inform the MBS listing, alongside the HTA conducted by PBAC for the drug*".

It is further noted that "*applications may progress, after endorsement of the MSAC Exec, straight to an internal utilisation and financial analysis conducted by the Department with the intention of representing this analysis to the MSAC Exec for consideration and approval at a later date (MSAC Exec meet ten times per year)*". Conversely, whilst the Framework states, "*alternatively the MSAC Exec may recommend that this analysis be scrutinised by ESC and the full committee of MSAC if the application is associated with potentially large net changes in MBS expenditure if it were granted approval*"; this is not necessary, given the aforementioned foreshadowed MBS savings (and illustrated on a per patient level in Q53).

As such, whilst noting that the Port Delivery System (device, procedure and drug) represents the intervention in totality, it is foreshadowed that the comparative efficacy and cost effectiveness will be primarily conducted via the PBAC. The clinical evaluation will be primarily informed by the Archway trial, of which the Clinical Study Report presents trial data from the PDS collectively as the intervention (ie. does not separate outcomes by device, procedure, drug). The relevant and appropriate economic analysis in the PBAC submission will draw on the relevant price and cost information referred to within submissions to PLAC and MSAC committees, representing the proposed costs for the device and

procedures, respectively. It is foreshadowed that an application to MSAC is likely to represent information similar to that presented within and accompanying this MSAC Application Form.

An overall summary of the PICO foreshadowed to be addressed are noted in Table 1.

Table 1 Key components of the clinical issue to be addressed in the PBAC submission

Component	Description
Population	Patients with nAMD
Intervention	ranibizumab (via ocular implant)
Comparator	ranibizumab (via intravitreal injection), as a proxy for standard of care
Outcomes	Primary efficacy outcome: Best corrected visual acuity (BCVA) Adverse events (ocular and non-ocular)
Clinical claim	In patients with nAMD, ranibizumab via ocular implant is as effective as ranibizumab via intravitreal injection at maintaining BCVA (with a reduction in frequency of treatment administration)

PART 7 – INFORMATION ABOUT ESTIMATED UTILISATION

46. Estimate the prevalence and/or incidence of the proposed population:

In 2015, the Drug Utilisation Subcommittee noted as "*age-related macular degeneration is strongly related to advancing age, and as Australia has an ageing population, it is expected that the prevalent treated group of patients will continue to grow."* It notes "*Published data from the Blue Mountains Eye Study (BMES) has been used to estimate the incidence and prevalence of patients with AMD in Australia. The BMES estimated the overall 5-year incidence of advanced age-related macular degeneration to be 1.1%; increasing from 0% in individuals under 60 years of age to 5.4% in those aged 80 years or older. Wang et al. (2007) assessed the 10-year incidence of age-related maculopathy (ARM) in an older cohort from the BMES. Comparing across age groups, which were categorised based on the age at base-line, they reported a higher incidence of AMD than from the previously published data. The incidence of AMD rose from 0.17% in the less than 60 years group to 24.3% for the 80 years and older group. Overall, 3.7% of participants (aged ≥49 years) developed late ARM over the ten year period."* (DUSC, 2015)

Given the anticipated treated population is a subset of a relatively mature PBS eligible population, a market based approach was considered appropriate to estimate the size of the proposed population.

Table 2 presents the number of services for MBS items #42738, #42739 and #42740 in the preceding 5 years. It should be noted that this represents utilisation in addition to the nAMD, including, but not limited to, the administration of intravitreal injections in diabetic macular oedema and retinal vein occlusion, and thus, is limited in estimating the relative size of the proposed population.

Table 2 MBS services for #42738, #42739 and #42740

MBS item number	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

Source: Medicare Item Reports Statistics, July 2021

Consequently, a market-based patient number approach was used to estimate the prevalence and incidence of the proposed population.

Estimations of the current treated prevalent pool

Table 3 presents the number of patients with nAMD on PBS-listed therapy; this was informed by a recent PBS 10% sample commissioned by the applicant.

Table 3 REDACTED

Table 4 (overleaf) presents a forward estimate of the patients with nAMD on PBS-listed therapy; a linear extrapolation of the preceding 5 years informed this estimate.

Table 4 REDACTED

47. a patient per year:

Initial fill and implantation – On commencement of therapy, as a "once-off" service.

Refill-exchange – Every 24 weeks, approximately twice per year, as chronic therapy

Explantation (if needed) – As required; guidance from the Susvimo® (ranibizumab) Product Information states explantation is only to be performed in the circumstance that the benefit of removal outweighs the risk of the procedure. For context, in Archway, four patients (out of the 248 patients, 1.6% treated with PDS) had their implants removed (Archway, Primary Analysis).

48. How many years would the proposed medical service(s) be required for the patient?

See Q47.

49. Estimate the projected number of patients who will utilise the proposed medical service(s) for the first full year:

A simplified prevalence approach was used to estimate the proposed medical services utilisation across the forward estimates.

For the purposes of the analysis, 20% of patients on current standard of care are assumed to be appropriate and therapy is recommended; of which, 75% will elect therapy (Q41b) estimating a peak uptake of 15% of patients. To estimate the PDS prevalent treated population, this uptake rate was assumed to be reached within a 3-year period; this was applied to the projected treated prevalent pool.

Two patient populations were subsequently estimated,

- An incident treated patient population; this was estimated by determining the difference in patients on treatment between the current and preceding year
- A continuing treated patient population; this was estimated by determining the difference between the prevalent treated population and incident population

Table 5 presents the number of patients forecasted to be treated with PDS.

Table 5 REDACTED

Table 6 (overleaf) presents the estimated number of services for the patients forecasted to be treated with PDS.

Table 6 REDACTED

50. Estimate the anticipated uptake of the proposed medical service over the next three years factoring in any constraints in the health system in meeting the needs of the proposed population (such as supply and demand factors) as well as provide commentary on risk of 'leakage' to populations not targeted by the service:

See Question 49.

Given the nature of the proposed medical services (ie. procedures), 'leakage' to populations not targeted by the service is unlikely.

PART 8 – COST INFORMATION

51. Indicate the likely cost of providing the proposed medical service. Where possible, please provide overall cost and breakdown:

For the proposed services, the likely MBS service fee has been estimated based on similar complexity and time to ocular procedures covered under existing MBS item numbers. This was previously noted in Q27.

Initial fill and implantation – Consulted vitreoretinal surgeons note that the initial fill and implantation procedure is intermediate in complexity and time between MBS item numbers #42752 (*Fee: $1392.65*) and #42746 (*Fee: $993.70*).

The implantation procedure (after the initial fill of the implant with Susvimo), requires insertion through the pars plana after scleral incision. MBS item #42746, (glaucoma filtration surgery), has similarities in terms of complexity (an invasive procedure which requires conjunctival peritomy, scleral dissection, incision and suturing) and time (1 hour), but does not capture the additional complexity of device insertion and laser photocoagulation to the base of the scleral incision. On the other hand, MBS item #42752 (insertion of a drainage device for glaucoma), involves device insertion, but has additional steps which make the overall procedure more complex than the PDS insertion procedure.

As such, a proposed fee of *$1193.18* is proposed for the initial fill and implantation procedure, which is intermediate between items #42752 and #42746 (ie. $1392.65 + $993.70 divided by 2)

It was further noted that the implantation procedure, while containing some elements in common, is not considered as complex as a vitrectomy (#42725) (which has the same MBS service fee as #42752).

Refill-exchange – Consulted retinal specialists have noted that the refill-exchange procedure is similar in terms of complexity and time to MBS item numbers #42738, #42739 and #42740. It was noted that both procedures would be anticipated to take approximately 15 minutes overall.

As such, a proposed fee of *$312.95* is proposed for the refill-exchange procedure.

Clinicians have noted that the current MBS item descriptor for these item numbers sufficiently capture the refill-exchange procedure and that a separate MBS item number for refill-exchange may not be required. A separate item number has been suggested in this Application Form as an option should this be desired to track utilisation separate to standard of care intravitreal injections.

Explantation (if needed) – Consulted vitreoretinal surgeons note that the explantation procedure is somewhat more complex and time consuming than current MBS item number #42505. This is due to having more steps than #42505, including scleral suturing and the potential vitrectomy of prolapsed vitreous. As such, a proposed fee of *$400.00* is proposed for the explantation procedure.

52. Specify how long the proposed medical service typically takes to perform:

Initial fill and implantation: Approximately 1 hour
Refill-exchange: Approximately 15 minutes
Explantation: Approximately 30 minutes

53. If public funding is sought through the MBS, please draft a proposed MBS item descriptor to define the population and medical service usage characteristics that would define eligibility for MBS funding.

Proposed MBS item descriptors have followed a similar format to that for MBS item numbers #42752 and #42755, that is, specifying the population's indication, intent of procedure and associated components.

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		

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		

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		

For the purposes of the MSAC Application Form, an illustrative net per patient MBS cost analysis shows the anticipated per patient savings to MBS budgets, in the circumstance that the Port Delivery System replaces intravitreal injections administered every four weeks.

Analysis inputs

MBS Administration costs	**Scheduled FEE (85%)**	**Frequency**	**Proxy cost**
Standard of care injections	$266.01	per injection	#42738
PDS – Initial fill and implantation	$1,014.20	once-off; implantation	#42752 / #42746
PDS – Refill-Exchange	$266.01	per refill-exchange	#42738

Illustrative MBS cost analysis

	Standard of care	**Port Delivery System**	**Difference**
Year 1			
Initial fill and implantation			
Cost per initial fill and implantation	$1,014.20		
Frequency	0	1	1.00
Administering injections / refill-exchange			
Cost per injection / refill-exchange	$266.01		
Frequency	13	1.17	-11.83
Total administration cost			
Year 1 administration cost	$3,427.45	$1,480.80	-$2,133.56
Subsequent years			
Administering injections / refill-exchange			
Cost per injection / refill-exchange	$266.01		
Frequency	13	2.17	-10.83
Total administration cost			
Subsequent year administration cost	$3,427.45	$571.24	-$2,881.75

Source: MSAC Application Form calculations.xls

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