Medical Services Advisory Committee (MSAC) Public Summary Document

Application No. 1734 resubmission – Intravascular lithotripsy for the treatment of moderately or severely calcified peripheral artery disease

Applicant:	Shockwave Medical Inc (Manufacturer) and
	Diverse Devices Pty Ltd (Distributor)

Date of MSAC consideration: 29 November 2024

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, <u>visit the</u> <u>MSAC website</u>

1. Purpose of application

An application requesting Medicare Benefits Schedule (MBS) listing for providing intravascular lithotripsy (IVL) in patients with moderately or severely calcified peripheral artery disease (PAD) in lower limbs and who are indicated for endovascular revascularisation was received from Shockwave Medical Inc. (Manufacturer) and Diverse Devices Pty Ltd. (Distributor) by the Department of Health and Aged Care. IVL was proposed as a stand-alone treatment or as a vessel preparation strategy prior to treatment with a drug-coated balloon (DCB) and/or stent insertion.

2. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness, cost-effectiveness and total cost, MSAC supported the creation of a new Medicare Benefits Schedule (MBS) item for intravascular lithotripsy (IVL) for the treatment of moderately or severely calcified symptomatic peripheral artery disease (PAD) that requires endovascular revascularisation. MSAC recalled that it had deferred its advice at its November 2023 meeting but noted there is likely superior procedural effectiveness and non-inferior safety for IVL compared to standard balloon angioplasty when used as a vessel preparation strategy for drug coated balloon or stent in patients with moderately or severely calcified peripheral artery disease (PAD) in lower limbs and who are indicated for endovascular revascularisation. MSAC considered that there was weak but sufficient evidence for superior effectiveness and non-inferior safety compared to standard balloon angioplasty (SBA) when IVL is used as a stand-alone therapy. MSAC noted that the evidence related to use in lower limb only and considered that it was appropriate to restrict use of IVL to lower limb PAD.

MSAC considered the revised economic evaluation showed IVL was cost-effective compared with SBA, inclusive of the cost of the IVL catheter. MSAC considered the financial estimates reasonable but likely overestimated the uptake in clinical practice. MSAC noted the cost of the IVL catheter will not be funded on the MBS.

Category 3 – Therapeutic Procedures

MBS item (number)

PERIPHERAL INTRAVASCULAR LITHOTRIPSY, including associated balloon dilatation and stent insertion, as required, of 1 lower limb, percutaneous or by open exposure, in patients who have symptomatic moderately or severely calcified peripheral artery disease (PAD) requiring endovascular revascularisation, if:

- The service is not provided in association with items 35300, 35303, 35306 or 35309 for the same lesion/s and;
- The service is performed by a specialist or consultant physician practicing in their specialty of vascular surgery or diagnostic radiology who has undertaken appropriate training in the intravascular lithotripsy procedure.
- Providers retain appropriate documentation, ideally with photographic and/or recordings and/or diagnostic imaging evidence, demonstrating the patient's calcification severity and the clinical need for the service, which documentation may be subject to audit.
- If photographic or diagnostic imaging is not retained, the reason for this is clearly documented.

Applicable not more than once in each 3-month period. Excludes aftercare (H)

Multiple Operation Rule

(Anaes.) (Assist.)

Fee: \$736.25 Benefit: 75% = \$552.18

Consumer summary

This is an application from Shockwave Medical Inc (manufacturer) and Diverse Devices Pty Ltd (distributor) requesting Medicare Benefits Schedule (MBS) listing of intravascular lithotripsy (IVL) in patients who have moderately or severely calcified peripheral arterial disease (PAD) in lower limbs.

PAD is a condition in which the build-up of fatty deposits (plaque) in arteries results in narrowing of the arteries in the arms or legs. This in turn reduces blood flow. The plaque build-up can cause arteries to narrow and hard calcium crystals can form within the plaque, which makes the arteries even stiffer. Narrowed and stiff arteries can cause several problems, including reduced blood flow to the body's tissues and the heart having to work harder to pump blood through the arteries. PAD most commonly affects the arteries supplying the legs, causing the circulation to be partially cut off which can cause pain and difficulties with walking. People with PAD are at higher risk of cardiovascular disease, stroke and death.

IVL involves inserting a tiny device into the affected arteries in the lower legs. The device gives off high-pressure shockwaves into the affected arteries, that help to break up the calcification in plaques and improve blood flow to the lower limbs.

MSAC had previously considered this application at its meeting in November 2023. MSAC had concluded that IVL is safe and effective but requested more information and a different approach to how value for money was calculated before it could make a decision.

In this resubmission, the applicant revised the economic model and financial impact analysis as MSAC requested. With this new information, MSAC considered that IVL was good value for money and the overall financial impact was reasonable. MSAC also accepted that data were not available on quality of life or outcomes beyond 2 years, so health outcomes beyond this timeframe remained uncertain. MSAC noted that the cost of the catheter is not covered on the MBS and may not be eligible for funding under the Prescribed List of Medical Devices and Human Tissue Products.

MSAC's advice to the Commonwealth Minister for Health and Aged Care

MSAC supported MBS listing of IVL in patients who have moderately or severely calcified PAD in lower limbs. MSAC concluded that IVL is safe, effective and good value for money.

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

MSAC noted this application requesting MBS listing for providing intravascular lithotripsy (IVL) in patients with moderately or severely calcified peripheral artery disease (PAD) in lower limbs and who are indicated for endovascular revascularisation. IVL was proposed as a standalone treatment or as a vessel preparation strategy before treatment with a drug-coated balloon (DCB) and/or stent insertion.

MSAC recalled that it had previously considered this application at its November 2023 meeting and had deferred its decision on public funding of IVL. MSAC had considered there is likely superior procedural effectiveness and non-inferior safety for IVL compared to standard balloon angioplasty (SBA) when used as a vessel preparation strategy before DCB or stent insertion. MSAC had considered that there was weak evidence for superior effectiveness and non-inferior safety to SBA when IVL is employed as a standalone therapy. MSAC recommended that any resubmission should include a revised clinical algorithm that is not split into two populations since this is not reflective of clinical practice where stenting is provisional depending on the outcome of the IVL as perceived by the clinician in real time. MSAC requested a revised economic assessment for a resubmission using a cost-consequence analysis focused on procedural outcomes and costs, and changes in resource use. MSAC noted the consultation feedback received from individual vascular surgeons and the Royal Australian and New Zealand College of Radiologists, which were supportive of the application.

MSAC noted that the burden of calcification (moderate or severe), and whether IVL will be a standalone procedure or used in conjunction with DCB or stent, are determined in real time at the time of the procedure, so it is not possible to separate these populations. MSAC confirmed that the revised clinical management algorithm and the single MBS item and descriptor (rather than the two separate populations in the original submission) accurately reflect this.

MSAC confirmed that the revised MBS item descriptor was appropriate, including specification of IVL use in lower limbs only. MSAC considered use of the item should be restricted to vascular surgeons or interventional radiologists trained in endovascular techniques. MSAC also confirmed that it was appropriate to restrict use of this item number to not more than once in each 3-month period. The MBS item descriptor supported by MSAC was ratified out of session and has been included on page 2 of this document. MSAC advised that the item descriptor should enable the use of IVL in patients with moderately or severely calcified PAD, either as a standalone procedure or as a vessel preparation strategy prior to treatment with DCB and/or stent insertion. However, MSAC advised that the intent of the IVL item is to cover the costs of the IVL procedure, including DCB and/or stent insertion, should these take place and allow patients to receive benefits for relevant medical devices if they are included on the Prescribed List of Medical Devices and Human Tissue Products (PL). MSAC advised the funding arrangements should not incentivise IVL and associated DCB or stenting to be performed as separate procedures.

MSAC confirmed that clinical data show likely superior procedural effectiveness and non-inferior safety for IVL compared with SBA, at least in the medium term. Alternatives to IVL may be less safe and require reintervention in a proportion of cases, which can lead to stent use to manage cases of vessel dissection or perforation.

MSAC noted that guidelines from the UK National Institute for Health and Care Excellence (NICE) on IVL had been published in January 2024. The NICE guidelines specify that, due to limited data on outcomes, IVL for calcified arteries in PAD should only be used with 'special arrangements' (as opposed to 'standard arrangements', 'use only in research', or 'do not use') for clinical governance, consent, and audit or research. MSAC considered that the 'special arrangements' specified in the NICE guidelines reflected standard practice and clinical governance in Australian healthcare organisations.

MSAC noted the cost-consequence analysis alternative base case developed for the commentary was revised by ESC with updated hospital costs. MSAC considered the revised commentary base case to be an improved estimate over the original submission and resubmission and was unlikely to be improved based on currently available data. MSAC considered the proportion of standalone procedures included in the base case analysis appropriate based on current knowledge of use of IVL in clinical practice.

MSAC considered that although the certainty of the cost-consequence analysis was limited by the uncertainty of long-term clinical outcomes and stenting rates in practice, MSAC considered that IVL was acceptably cost-effective at the proposed price (**\$redacted**), noting the likely superior procedural effectiveness and non-inferior safety for IVL compared with SBA, at least in the medium term. MSAC noted that alternatives to IVL may be less safe and require reintervention in a proportion of cases, due to adverse events such as vessel dissection or perforation. This may lead to the use of other vascular interventions, including stents.

MSAC noted the financial impact analysis indicated net savings to the MBS over 6 years, but overall costs to health budgets (including the MBS) of around \$8.3 million in year 6 due to the net device costs for the IVL procedures. MSAC also noted that the growth in IVL use over 6 years is offset by a reduction in the use of stents (which are on the PL) and re-intervention. However, MSAC considered that utilisation may be overestimated in the base case – IVL takes more time than DCB or stent insertion, so uptake may not be as high in practice. MSAC noted the sensitivity analysis in which uptake rate was reduced by 10%, which reduced the overall financial implications for health budgets to around \$6.7 million in year 6. MSAC considered the overall financial financial implications to be reasonable and recommended a review of utilisation after 2 years.

MSAC noted that there may be no funding mechanism as the device (IVL catheter) may not be eligible for Part A of the PL. MSAC noted the applicant advised the device cost is currently covered via private health insurance or hospital funding on an individual basis. The applicant considered that under the PL reforms, IVL catheters may be eligible to be included on Part C of the PL. MSAC considered that the cost of IVL consumables may be passed on to the patient as an out-of-pocket expense if it is not funded through another mechanism. MSAC requested that its advice regarding the comparative safety, effectiveness and cost-effectiveness be provided to the Medical Devices and Human Tissue Advisory Committee (MDHTAC).

4. Background

The Medical Services Advisory Committee (MSAC) considered IVL for patients with moderately or severely calcified PAD (<u>MSAC 1734</u>) at their November 2023 meeting. After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness, cost-effectiveness and total cost, MSAC deferred its advice for public funding of IVL for the treatment of moderately or severely calcified PAD.

According to the <u>Public Summary Document (PSD)</u>, MSAC considered there is likely superior procedural effectiveness and non-inferior safety for IVL compared to standard balloon angioplasty (SBA) when used as a vessel preparation strategy for DCB or stent. MSAC considered there was weak evidence for superior effectiveness and non-inferior safety compared to SBA when IVL is employed as a stand-alone therapy.

MSAC considered that despite the weak and uncertain evidence, especially for IVL as a standalone procedure, its key concerns related to the inappropriate structure of the economic model, which did not facilitate assessment of IVL's cost effectiveness. However, MSAC acknowledged the clinical need for such a service, as the comparator has several related adverse events.

The key matters of concern raised by MSAC are summarised in Table 1.

Component	Matter of concern	How the resubmission addresses it
Population	MSAC considered the proposed populations to be inappropriate because predetermining beforehand which patients belong to each of the two separate populations is not reflective of Australian clinical practice. MSAC considered that the decision is made in real time and that before IVL, it would be unknown whether the patient would receive IVL as a stand-alone treatment or require further stenting. (PSD, p.3)	Addressed. The PICO was updated in the resubmission to consolidate the two population sets from the original ADAR. The population description was amended by the commentary for consistency with the descriptions of the intervention and comparator, and with the clinical management algorithm.
Clinical algorithm	MSAC recommended that any resubmission should include a revised clinical algorithm that it is not split into two	Addressed.

Table 1 Summary of key matters of concern

Component	Matter of concern	How the resubmission addresses it
	populations since this is not reflective of clinical practice where stenting is provisional depending on the outcome of the IVL as perceived by the clinician in real time. Rather, the clinical algorithm should reflect only one population, namely patients with PAD who have moderately or severely calcified lesions in their lower limb(s). This would result in one proposed MBS item and descriptor and would also serve as a basis for appropriate revisions to the structure of the economic model. (PSD, p.5).	No changes were made to the clinical algorithm nor the MBS item descriptor. The resubmission noted the algorithm in the original ADAR already aligned with MSAC's recommendation for a single population. Consistent with Australian clinical practice, the decision for subsequent intervention after the index balloon dilation procedure is based on clinical judgement (e.g. consideration of level of residual stenosis or presence of a flow-limiting dissection). The original submission proposed only one MBS item; the proposed descriptor aligns with the PICO in the resubmission, though the descriptor is not restricted to PAD in lower limbs. No evidence was provided in the original submission nor the resubmission for use of IVL in upper limb lesions.
Economic analysis	MSAC considered the CUA for the economic model was inappropriate due to the lack of evidence demonstrating an increase in HRQoL or other patent related outcome gains. MSAC considered that a resubmission to address these problems would require a revised clinical care pathway to better capture the decision pathway used by proceduralists to determine use of IVL as a stand-alone or adjunct intervention. This information should serve as the basis for a revised economic model (inclusive of both uses) which is more appropriately a CCA rather than a CUA. MSAC considered that a CCA focusing on costs of the procedure, costs of changes in resource use (i.e. stents and balloons used) with the outcomes being procedural outcomes would be useful. (PSD, p.1).	Addressed. The economic model was revised in the resubmission to a CCA in order take into account the revised clinical care pathway and MSAC's recommendation to focus on costs of the procedure, costs of changes in resource use (i.e. stents and balloons used) with the outcomes being procedural outcomes.
	It [the CCA] should focus on procedure costs and costs of changes in resource use (stents, balloons used, etc.), with the procedural outcome (patency vs lack of patency) as the final outcome. (PSD, p.6)	Addressed, although the CCA does not explicitly consider patency versus lack of patency as the final outcome. The commentary considered the omission of this mechanical outcome to be reasonable, and the use of stents avoided, reinterventions avoided and amputations avoided to be appropriate consequences for the CCA.
Probabilities	Rate of stenting after the intervention:	Partially addressed.
CCA	The ADAR used MBS data instead of trial-based data, but the MBS items were not specific enough to be used reliably, and the ADAR still applied the relative risk data from the trial which then overestimated the percentage of stenting avoided with the use of IVL. (PSD, p.5) MSAC considered the rate of stenting to be a major cause of uncertainty in the economic model and ICER. MSAC noted the pre-MSAC response, which advised that the Australasian	The resubmission applied stenting rates directly from the DISRUPT PAD III RCT. The baseline stenting rate in this trial was lower than seen in the Australian setting and raises applicability concerns. Data from the AVA were used in a sensitivity analysis in the resubmission but were
	MSAC considered the rate of stenting to be a major cause of uncertainty in the economic model and ICER. MSAC noted the pre-MSAC response, which advised that the Australasian Vascular Audit suggests a stenting rate of about 36.6%	applicability concerns. E AVA were used in a ser in the resubmission but inappropriately applied.

Component	Matter of concern	How the resubmission addresses it
	(compared with 4% vs 18% stenting rates used in the DISRUPT PAD III trial). (PSD, p.5)	The commentary provided an alternative base case that applied the relative risk from DISRUPT PAD III to AVA data. However, concerns remain about the relative risk reduction of stenting observed in the RCT, which results in a large decrease in absolute stenting rates that may be unrealistic to expect in clinical practice.
Costs relevant to the CCA	Healthcare resource use and cost: DES costs were used, which are very expensive and not reflective of Australian practice (which uses BMS). (PSD, p.5)	Addressed. BMS costs were used in the economic analysis.
	IVL generator costs and fluoroscopy costs were not included. (PSD, p.5)	Partially addressed. The cost of the IVL generator and multi-use connectors were not captured in the resubmission's economic analysis nor disclosed in the original ADAR or the resubmission. In its pre-MSAC response, the applicant confirmed that the IVL generator and multi-use connectors would continue to be provided to the hospitals on loan, resulting in no extra cost associated with IVL other than what has been captured in the current CCA and financial estimates. Additionally, under conditions of the loan, all maintenance, servicing and additional costs are borne by the manufacturer, and no foreseeable long-term costs will be borne by the health budget or hospitals. The cost of fluoroscopy was not considered, though it is not expected to differ between the intervention and comparator for the index procedure.
Consumables and out-of- pocket costs	MSAC requested that the sponsor clarify the cost of consumables and any potential out-of-pocket costs for patients in the resubmission. (p.6)	Addressed. Costs were clarified and disaggregated in the resubmission's economic and financial analyses. The analyses captured the cost of IVL catheters (assuming only one catheter used per procedure) but the ADAR did not comment on whether this cost may be passed on to patients.
Financial impact	The uncertainties in the economic modelling (such as the use of DES costs to calculate stenting costs and overestimate of stents avoided by the intervention) flowed through to the financial impact. The assumed uptake of between 15% and 50% over time was not based on the evidence presented and resulted in an uncertain financial impact. MSAC noted that the pre-MSAC response stated that this was a minimal financial impact, and MSAC agreed. (PSD, p.5) The resubmission should also produce revised financial estimates which address the issues identified by MSAC. (PSD, p.6).	Partially addressed. The resubmission's financial analysis considered the index procedure only; reintervention costs were not explicitly considered. Costs associated with radiological services (including fluoroscopy) were not considered. Consistent with the economic analysis, the resubmission's financial analysis used trial-based stenting rates (raising

Component	Matter of concern	How the resubmission addresses it
		applicability concerns and noted in the commentary).
		BMS rather than DES costs were (appropriately) applied.
		IVL uptake rates used in the resubmission were identical to the original ADAR.
Guidelines	MSAC noted that there was upcoming updated NICE guidelines on IVL due in January 2024 and any implications of this could also be discussed in a resubmission. (PSD, p.6)	Not addressed. The resubmission did not explicitly refer to the 2024 NICE guidance (IPG780). The commentary included a summary of the NICE recommendations and rationale. NICE considered clinical evidence but not costs, cost-effectiveness nor financial impact.

ADAR = Applicant Developed Assessment Report; AVA = Australasian Vascular Audit; BMS = bare metal stent; CCA = cost-consequence analysis; CUA = cost-utility analysis; DES = drug-eluting stent; HRQoL = health-related quality of life; ICER = incremental costeffectiveness ratio; IVL = intravascular lithotripsy; MBS = Medicare Benefits Schedule; MSAC = Medical Services Advisory Committee; NICE = National Institute for Health and Care Excellence; PAD = peripheral artery disease; PSD = Public Summary Document; RCT = randomised controlled trial.

Source: Compiled from Table 1-1 of MSAC 1734 ADAR resubmission + in-line commentary.

5. Prerequisites to implementation of any funding advice

The only IVL system currently included in the Australian Register of Therapeutic Goods (ARTG) for the treatment of calcified lesions in patients with PAD is manufactured by Shockwave Medical Inc. (sponsored by AA-Med Pty Ltd). The ARTG entries for the single-use transducers (catheters) are shown in Table 2. The ARTG ID for the IVL connector cable is <u>342513</u> and for the Shockwave Medical IVL system (generator and connector cable) is <u>320483</u>.

The Shockwave IVL devices are not restricted to use in peripheral arteries in lower limbs, nor to moderately or severely calcified lesions.

ARTG ID, class and start date	Product name	GMDN	Intended purpose
388192 Class Ilb 9 May 2022	Ultrasonic lithotripsy system transducer, single-use	44138 Ultrasonic lithotripsy system transducer, single-use	The Shockwave S4 Peripheral IVL System is indicated for lithotripsy-enhanced, low-pressure balloon dilatation of calcified, stenotic peripheral arteries, in patients who are candidates for percutaneous therapy. Not for use in the coronary, cerebral, aortic, or common iliac vasculature.
320482 Class IIb 19 Jul 2019	Ultrasonic lithotripsy system transducer, single-use	44138 Ultrasonic lithotripsy system transducer, single-use	The catheter is indicated for lithotripsy enhanced, low pressure balloon dilation of calcified peripheral stenotic arteries in patients who are candidates for percutaneous therapy. The catheters are not indicated for coronary or central vascular systems.

Table 2 Regulatory status in Australia

ARTG = Australian Register of Therapeutic Goods; GMDN = Global Medical Device Nomenclature; IVL = intravascular lithotripsy. Source: Compiled from MSAC 1734 Public Summary Document and Australian Register of Therapeutic Goods, accessed 30 July 2024.

6. Proposal for public funding

The applicant proposed a single new MBS item for peripheral IVL, including associated balloon dilatation of one peripheral artery of one limb. Table 3 presents the proposed item descriptor, which was reproduced from the original Applicant Developed Assessment Report (ADAR). No changes to the descriptor or fee were proposed in the resubmission. The proposal for a single MBS item for peripheral IVL is consistent with advice from MSAC in November 2023 (PSD, p.5).

Table 3 Proposed MBS item

Category 3 – THERAPEUTIC PROCEDURES

MBS item *XXXX

PERIPHERAL INTRAVASCULAR LITHOTRIPSY, including associated balloon dilatation of 1 limb, percutaneous or by open exposure, in patients who have moderately or severely calcified lesions, excluding associated radiological services or preparation, and excluding aftercare

Multiple Operation Rule

(Anaes.) (Assist.)

Fee: \$736.25 Benefit: 75% = \$552.18 85% = \$625.81

Source: Table 1-3 of MSAC 1734 ADAR resubmission + in-line commentary.

Although the PICO population was restricted to PAD in lower limbs, the proposed MBS item descriptor does not restrict use of IVL to lower limb lesions. In October 2023, the Evaluation Subcommittee (ESC) considered that this was appropriate because the ARTG listing does not specify whether IVL should be restricted to upper or lower limb(s).

The randomised controlled trial (RCT) evidence provided in the original ADAR (<u>DISRUPT PAD III</u>) included patients with superficial femoral artery or popliteal artery lesions only. No evidence was provided to support the safety and effectiveness of IVL in upper limb lesions.

The proposed MBS item excludes associated radiological services. MBS item 60509 (fluoroscopy in conjunction with a surgical procedure lasting 1 hour or more; fee \$110.90) is likely to be used during the procedure to guide and check the positioning of the IVL catheter.

Although not mentioned in the resubmission, the ESC previously considered it appropriate to include co-claiming restrictions with angioplasty items (MBS items 35300 and 35303), as the proposed IVL MBS item should replace these services (PSD, p.36).

MSAC noted the proposed item has no frequency restrictions. The original ADAR and the resubmission do not address whether a patient may undergo repeated IVL procedures to the same calcified lesion, though it has been reported in a small number of patients in IVL studies.^{1,2} Repeat IVL procedures are not captured in the economic nor financial analyses.

The proposed service requires the use of one or more single-use Shockwave S4 or M5 catheters (indicated for different vessel diameters). According to the resubmission, each IVL catheter costs

¹ Lopez-Pena G, Musto L, Finch SL, Bown MJ, Davies R, Sohrabi S, Rees O, Lakshminarayan R, Saratzis A on behalf of SHOCC Investigators. (2024) 'SHOCkwave lithotripsy for patients with peripheral arterial disease: the SHOCC study', *J Vasc Soc G B Irel*, 3(3):140-146. doi: 10.54522/jvsgbi.2024.126

² Colacchio, EC, Salcuni M, Gasparre A, Giorgio D, Barile D, Bussetti F, Antonello M, Colacchio G. (2022). 'Midterm results of intravascular lithotripsy for severely calcified common femoral artery occlusive disease: A single-center experience', *J Endovasc Ther*, 15266028221105188. doi: 10.1177/15266028221105188

\$redacted. This cost is currently covered via private health insurance or hospital funding on an individual basis. MSAC noted that the cost of IVL consumables may also be passed on to the patient as an out-of-pocket expense. The resubmission claimed that under the Prescribed List (PL) reforms, there is an opportunity for IVL catheters to be included on Part C of the PL – akin to DCBs – thereby resulting in more equitable access for patients.

The IVL generator and connector cable are multi-use and are currently provided to the hospitals on loan by the manufacturer. MSAC noted that the applicant confirmed in its pre-MSAC response that, under the conditions of the loan, all maintenance, servicing and additional costs are borne by the manufacturer and no foreseeable long-term costs of the IVL generator and connector cables will be borne by the health budget or hospitals.

7. Population

Consistent with advice from MSAC in November 2023 (PSD, p.5), the proposed population considered in the resubmission's economic and financial analyses was patients with PAD in lower limbs with moderate or severe calcification and who are indicated for endovascular revascularisation.

As mentioned previously, the proposed MBS item is not restricted to procedures in lower limbs, nor is the registered indication for Shockwave IVL.

The IVL system is designed to be used in hospitals as an inpatient procedure and is intended to be performed by vascular surgeons or interventional radiologists trained in endovascular techniques.

8. Comparator

The comparator proposed in the resubmission's PICO was SBA as a stand-alone treatment or followed by DCB and/or stent insertion.

The economic and financial analyses considered that subsequent intervention involved receipt of DCB or stent. The commentary noted the analyses did not account for patients who receive both DCB and stent during the index procedure, nor were data provided to support omission of this combination as a relevant treatment option.

There are four existing MBS items related to the comparator SBA (referred to as transluminal balloon angioplasty [TBA]) under category 3 therapeutic procedures. These items are not confined to the peripheral arteries. The MBS item descriptors enable TBA as a treatment alone (items 35300 and 35303) or in combination with stent insertion (items 35306 and 35309 for stent insertion include associated balloon dilatation). Only one MBS item is claimed per course of treatment (either balloon angioplasty or stent insertion).

9. Summary of public consultation input

The MSAC welcomed consultation input received for this application and noted the period for public consultation closed on 11 October 2024.

The MSAC noted consultation input for this reconsideration was received in the form of a letter from The Royal Australian and New Zealand College of Radiologists (RANZCR) with no further input received from other organisations or individuals in the public consultation period.

RANZCR was supportive of public funding, however, they expressed concern at the proposal to determine eligibility for patients through vascular surgeons, believing it will limit patient access. RANZCR also raised concern for the patient potentially incurring further out-of-pocket costs if needing a stent following the procedure. Additionally, RANZCR made the comment that current use of IVL among interventional radiologists is limited, primarily due to cost and lack of infrastructure.

Further consultation input was solicited by the applicant from two vascular surgeons experienced in the use of IVL, who noted the importance of reducing calcification and the safety of IVL compared to SBA.

10. Characteristics of the evidence base

The original ADAR provided evidence for use of IVL to treat moderately or severely calcified PAD based on five relevant studies identified through a systematic literature search. Of these, three were applicable to IVL as a stand-alone treatment (DISRUPT PAD I [NCT02071108], DISRUPT PAD II [NCT02369848] and DISRUPT BTK [NCT02911623]), and two were applicable to IVL as a vessel preparation strategy followed by a DCB and/or stent insertion (DISRUPT PAD III RCT [NCT02923193] and DISRUPT PAD III Observational Study [NCT05881421]).

DISRUPT PAD III RCT was a prospective, multicentre, single-blind, randomised (1:1) trial of IVL versus SBA for vessel preparation prior to DCB treatment or stenting in moderately or severely calcified femoropopliteal arteries. The DISRUPT PAD III Observational Study was a prospective, multicentre, single-arm study for subjects who did not meet the eligibility criteria for the DISRUPT PAD III RCT or for subjects recruited after enrolment once the randomised portion of the trial was completed.

No new studies or longer-term outcomes from previously identified studies were provided in the resubmission.

The National Institute for Health and Care Excellence (NICE) recently published interventional procedures guidance relating to IVL for calcified arteries in PAD (<u>IPG780</u>, January 2024). The evidence considered by NICE included a systematic review and meta-analysis,³ an individual patient-level pooled meta-analysis,⁴ the DISRUPT PAD III RCT, DISRUPT PAD III Observational Study, two retrospective cohort studies (included in the original ADAR as supportive evidence), one prospective single centre registry and two case reports. The DISRUPT PAD I, DISRUPT PAD II and DISRUPT PAD BTK studies were not included in the main evidence summary for NICE because they were considered to be relatively small and were included in the published meta-analyses.

On the basis of the available evidence, NICE recommended that IVL for calcified arteries in PAD should only be used with special arrangements for clinical governance, consent, and audit or research. The NICE committee acknowledged that the evidence suggests that the IVL procedure is associated with a reduced need for a stent, but there is not enough long-term evidence, or evidence about how many amputations will be avoided by the procedure. The NICE committee noted there may be groups of people who would particularly benefit from this procedure, such as

³ Wong CP, Chan LP, Au DM, Chan HWC, Chan YC. (2022). 'Efficacy and safety of intravascular lithotripsy in lower extremity peripheral artery disease: A systematic review and meta-analysis', *Eur J Vasc Endovasc Surg*, 63(3):446-456. doi: 10.1016/j.ejvs.2021.10.035.

⁴ Madhavan MV, Shahim B, Mena-Hurtado C, Garcia L, Crowley A, Parikh SA. (2020) 'Efficacy and safety of intravascular lithotripsy for the treatment of peripheral arterial disease: An individual patient-level pooled data analysis', *Catheter Cardiovasc Interv*, 95(5):959-968. doi: 10.1002/ccd.28729.

those with smaller vessels or with calcified arteries in a location unsuitable for a stent, but more evidence is needed.

The NICE interventional procedure overview noted four relevant ongoing studies with sample sizes of 50 or more. All were non-randomised, single-arm studies with estimated study completion dates in 2024 to 2026. A fifth study (SHOCC; <u>ISRCTN76218607</u>) recently published results at 6 months follow up for 91 patients.⁵ Due to its small size, lack of a control group and short-term follow up, this new observational study adds little to the body of evidence for the safety and effectiveness of IVL.

No new RCTs of IVL for the treatment of PAD were identified by NICE or the commentary.

11. Comparative safety

The safety of IVL was assessed in the original ADAR and was not further considered in the resubmission.

12. Comparative effectiveness

The clinical effectiveness of IVL was assessed in the original ADAR and was not further considered in the resubmission.

Clinical claim

According to the PSD for MSAC 1734 (November 2023):

• MSAC considered there is **likely superior procedural effectiveness and non-inferior safety** for IVL compared to SBA when used as a vessel preparation strategy before stent insertion or treatment with a DCB.

However, MSAC acknowledged the lack of evidence on long-term safety.

- MSAC considered there was **weak evidence for superior effectiveness and non-inferior safety** compared to SBA when IVL is employed as a stand-alone therapy.
- MSAC also noted that the evidence did not demonstrate any patient-reported outcomes such as quality of life benefit, ankle-brachial index scores or walking improvement, nor any survival benefit demonstrated either directly, or from any linked evidence on avoidance of stenting.

13. Economic evaluation

Structure of the economic evaluation

The ADAR resubmission responded to the request from MSAC to present a cost-consequence analysis (CCA) using a decision tree structure. For the purpose of evaluation, the commentary created a graphic representation of the tree structure (Figure 1).

⁵ Lopez-Pena G, Musto L, Finch SL, Bown MJ, Davies R, Sohrabi S, Rees O, Lakshminarayan R, Saratzis A, on behalf of the SHOCC Investigators. (2024) 'SHOCkwave lithotripsy for patients with peripheral arterial disease: the SHOCC study', J Vasc Soc G B Irel, 3(3):140-146. <u>http://doi.org/10.54522/jvsgbi.2024.126</u>



Figure 1 Decision analytic tree used in the cost-consequence analysis

DCB = drug-coated balloon; IVL = intravascular lithotripsy; PAD = peripheral artery disease; SBA = standard balloon angiography. Source: Commentary Figure 1 of MSAC 1734 ADAR resubmission + in-line commentary, reconstructed based on the resubmission model.

The CCA was a partly trial-based analysis, with index procedure outcomes informed by the DISRUPT PAD III RCT and reintervention outcomes informed from identified literature. Outcomes included provisional stents avoided at index procedure, reintervention procedures avoided (assuming 100% stent placement at reintervention) and amputations avoided. Costs included those associated with the initial procedure and subsequent reinterventions over a 2-year time horizon.

A summary of the updates to the economic evaluation is provided in Table 4.

Component	Original ADAR for MSAC 1734	ADAR resubmission for MSAC 1734
Perspective	Australian health care perspective	Australian health care perspective
Population	Patients with symptomatic PAD with moderate to severe calcification	Patients with symptomatic PAD with moderate to severe calcification
Prior testing	Tests to determine severity of PAD and calcification	Not captured in analysis
Intervention and comparator	Base case: IVL vs SBA followed by DCB or stent Scenario: IVL vs SBA as stand-alone treatment	IVL vs SBA as either a stand-alone or vessel preparation (i.e. followed by DCB or stent insertion)
Type(s) of analysis	CCA CUA	Updated to a CCA to focus on costs of the procedure, costs of changes in resource use and avoided outcomes
Clinical outcomes	Provisional stents avoided Dissections avoided Flow-limiting dissections avoided Primary patency progression Major adverse events Quality-adjusted life years	Change in provisional stenting rate (index procedure) Change in reintervention rate (assuming 100% stent placement at reintervention) at 2 years Change in amputation rate at 2 years
Economic outcomes	Procedural costs 2-year reintervention costs Incremental cost of IVL at 2 years ICER	Procedural costs 2-year reintervention costs Incremental cost of IVL at 2 years
Time horizon	2 years (i.e. trial-based) 30 years (lifetime)	30 days (refers to amputations after reintervention only) 2 years
Computational method	Direct trial Markov cohort	Updated to a decision analytic tree consistent with CCA
Generation of the base case	Trial-based Modelled	Trial-based Modelled
Health states	Patency, Loss of Patency, Critical limb Ischaemia, Amputation, Death	Not applicable to the CCA
Cycle length	1 month	Not applicable to the CCA
Sources of evidence	Transition from Patency to Loss of patency was informed from the DISRUPT PAD III RCT and extrapolated beyond the 2-year trial follow-up. Transition probabilities to CLI and amputation was sourced from a literature review.	Rate of stent placement at index procedure was informed by the DISRUPT PAD III RCT. Transition from index procedure to reintervention at 2 years was informed from the literature and clinical advice.
Software	Microsoft Excel	Microsoft Excel

Table 4 Summary of updates to the economic evaluation

ADAR = Applicant Developed Assessment Report; AVA = Australasian Vascular Audit; CCA = cost-consequence analysis; CLI = critical limb ischaemia; CUA = cost-utility analysis; DCB = drug-coated balloon; ICER = incremental cost-effectiveness ratio; IVL = intravascular lithotripsy; MSAC = Medical Services Advisory Committee; PAD = peripheral artery disease; RCT = randomised controlled trial; SBA = standard balloon angioplasty.

Source: Table 3-1 of MSAC 1734 resubmission ADAR + in-line commentary.

The decision tree is structured so that IVL or SBA at the index procedure will result in one of three outcomes. If the index procedure is successful (defined as per the DISRUPT PAD III RCT as residual stenosis \leq 30% without flow-limiting dissection [\geq grade D] prior to DCB or stenting), patients may either receive subsequent treatment with a DCB or no further treatment

(standalone). If the index procedure is a 'failure', patients receive a stent ('index stent') in order to reduce residual stenosis.

For patients who require no further treatment at the index procedure (standalone) but require reintervention within 2 years, the reintervention procedure was assumed to be endovascular (stent placement), based on clinician advice sourced from the applicant.

For patients who require provisional stent placement at the index procedure and go on to require reintervention within 2 years, the reintervention procedure was assumed to be either stent placement via an endovascular approach or stent placement via open surgery.

Inputs to the economic evaluation

According to the PSD for MSAC 1734 (pp.22-23), the economic evaluation in the original ADAR was challenged in the commentary for applying the relative risk of stenting of 0.25 from the DISRUPT PAD III RCT to a high baseline rate of 45% sourced from MBS utilisation data (not specific to PAD). This approach resulted in a large absolute decrease in stenting that was not demonstrated in the RCT. The resubmission CCA instead applied the rates of stenting directly from each arm of the DISRUPT PAD III RCT (4.6% in the IVL arm versus 18.3% in the SBA arm).

The commentary noted that the DISRUPT PAD III RCT imposed restrictions on stent placement that are not used in clinical practice. The DISRUPT PAD III Observational Study found stenting occurred in 35.5% of patients receiving IVL and may be a better indicator of stenting rates after IVL outside a clinical trial setting. The Australasian Vascular Audit (AVA) Report 2021–2023 indicates similar index stenting rates in Australian clinical practice (37.2%).

Given the difficulty justifying a baseline stenting rate that is less than half that observed in Australian practice and a large observational study of IVL, the commentary proposed an alternative base case using the AVA data as the source of the baseline stenting rate in the CCA. The commentary base case differed from the resubmission base case by the following two adaptations:

- the AVA-derived stenting rate of 37.2% was used for the SBA arm and the relative risk from the DISRUPT PAD III RCT was applied to inform the stenting rate in the IVL arm (9.4%)
- the post-stenting target lesion revascularisation (TLR) rate of 30% at 2 years was increased to match that for non-stented patients (35.6%) – in the absence of comparative data supplied by the resubmission, this rate appears to be a conservative option that falls within the range quoted in the applicant's source (30-40% quoted in an editorial).

The probabilities used in the ADAR resubmission base case and the commentary (alternative) base case are summarised in Table 5. The commentary corrected multiple data extraction errors in the ADAR inputs.

The rate for reintervention by open surgery in stented patients was sourced from the COSTLY-TLR study.⁶ Based on identified literature from this study, it was assumed that stented patients who received reintervention at 2 years – regardless of the index procedure– may require amputation 30 days post reintervention. No data for amputation rates were provided for patients without

⁶ Saratzis A, Torsello GB, Cardona-Gloria Y, Van Herzeele I, Messeder SJ, Zayed H, Torsello GF, Chisci E, Isernia G, D'Oria M, Stavroulakis K. (2024). 'Cost analysis of target lesion revascularisation in patients with femoropopliteal in stent re-stenosis or occlusion: The COSTLY-TLR Study' *Eur J Vasc Endovasc Surg*, 68(1):100-107. doi: 10.1016/j.ejvs.2024.02.001

stent placement at the index procedure. The CCA assumed none of these patients proceed to amputation after IVL or SBA, but this assumption was unsupported.

Component	ADAR			Commentary		
	Treatment	Rate	Source	Treatment	Rate	Source
Index					·	
Provisional stent placement	IVL	4.6%	DISRUPT PAD III RCT	IVL	9.4%	RR from DISRUPT PAD III RCT
	SBA	18.3%	DISRUPT PAD III RCT	SBA	37.2%	AVA Public Report – 2021–2023
Treatment followed by DCB (no index stent)	Both IVL and SBA	80%ª	Clinician guidanceª	No change		
Treatment followed by index stent plus DCB	Both IVL and SBA	0%	Clinician guidance	No change		
Reintervention (no ind	lex stent)					
Overall reintervention rate	Both IVL and SBA	35.6% ^b	BASIL 2010 RCT ⁷ (corrected) ^b	No change		
Reintervention by open surgery	Both IVL and SBA	0%	Unsupported assumption	No change		
Reintervention (index	stent)					
Overall reintervention rate	Both IVL and SBA	30%	2018 editorial ⁸ – low end of range	Both IVL and SBA	35.6%	BASIL 2010 RCT – data from non- stented applied to stented patients
Reintervention by open surgery	Both IVL and SBA	58%	COSTLY-TLR study	No change		
Amputation				•		
In patients with index stent	Both IVL and SBA	4% ^c	COSTLY-TLR study (corrected) ^c	No change		
In patients without index stent	Both IVL and SBA	0%	Unsupported assumption	No change		

 Table 5
 Probabilities of procedural outcomes in ADAR resubmission CCA and commentary (alternative) CCA

ADAR = Applicant Developed Assessment Report; AVA = Australasian Vascular Audit; CCA = cost-consequence analysis; DCB = drugcoated balloon; IVL = intravascular lithotripsy; PAD = peripheral artery disease; RCT = randomised controlled trial; RR = relative risk; SBA = standard balloon angiography.

a All non-stented patients received a DCB in the DISRUPT PAD III RCT, but in clinical practice it is expected some patients will undergo a standalone procedure. The model reflects this by allocating 20% of IVL and SBA procedures to standalone, thereby accounting for both PICO sets from the original submission.

b The resubmission CCA used a rate of 18.6%, incorrectly extracted from BASIL 2010 RCT. The rate was corrected in the commentary.

c The resubmission CCA used a rate of 6%, incorrectly extracted from COSTLY-TLR. The rate was corrected in the commentary. Source: Compiled from Table 3-4, Table 3-6, Commentary Table 3 and Commentary Table 5 of MSAC 1734 resubmission ADAR + in-line commentary.

⁷ Bradbury AW, Adam DJ, Bell J, Forbes JF, Fowkes FG, Gillespie I, Ruckley CV, Raab GM; BASIL trial Participants. (2010) 'Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial: An intention-to-treat analysis of amputation-free and overall survival in patients randomized to a bypass surgery-first or a balloon angioplasty-first revascularization strategy', J Vasc Surg, 51(5 Suppl):5S-17S. doi: 10.1016/j.jvs.2010.01.073.

⁸ Rymer JA, Jones WS. (2018) 'Editorial. Femoropopliteal in-stent restenosis: What is the standard of care?', *Circulation: Cardiovascular Interventions*, 11(12):e007559. doi: 10.1161/CIRCINTERVENTIONS.118.007559.

The cost inputs used in the ADAR resubmission CCA are listed in Table 6. The analyses did not include costs for anaesthesia or fluoroscopy services to guide and check the positioning of the catheter during the index procedure. IVL and SBA procedures typically require locoregional anaesthesia. The mean procedure time reported in DISRUPT PAD III RCT was 89.9 minutes for IVL versus 66.5 minutes for the comparator, though the mean fluoroscopy time was similar (16.6 minutes for IVL versus 13.5 minutes for the comparator). The costs of the IVL generator and reusable connector cables (loaned to the hospital funding by the manufacturer) were not captured in the CCA.

Component	Total cost (ADAR)	Total cost (commentary)º	Source
MBS costs			
IVL procedure	\$736.25	\$736.25	Proposed
SBA procedure	\$669.55ª	\$669.55ª	MBS items 35300, 35303 (weighted for utilisation in 2023)
SBA plus stent procedure	\$789.18ª	\$789.18ª	MBS items 35306, 35309 (weighted for utilisation in 2023)
Device costs			-
IVL device	\$redacted	\$redacted	Sponsor – IVL catheter only
SBA device	\$130.00	\$130.00	PL – Part D (various, median value) ^₅
Bare metal stent	\$1,406.01°	\$1,406.01°	PL – Part A (various) weighted for lesion length from trial data
Drug-coated balloon	\$1,245.00	\$1,245.00	PL – Part C (Billing codes BS424, BT255, MI507)
Hospital costs			
Hospital stay (day)	\$2,045.61	\$2,045.61	Tier 2 1005 – Angioplasty; NHCDC Version 10.0, Round 24 (2019-20)
Hospital stay (overnight)	\$7,699.25 ^d	\$9,623.72°	AR-DRG F14C (minus Prosthesis cost component); NHCDC Version 10.0, Round 24 (2019-20) ESC Revised: AR-DRG F14C (minus Prosthesis cost component); NHCDC Version 11.0, Round 25 (2020- 21)
Reintervention by endovascular procedure	\$9,016.28ª	\$10,732°	Cost of stent placement (MBS fee, stent cost and overnight hospitalisation – AR-DRG F14C; NHCDC Version 10.0, Round 24 (2019-20) ESC Revised: Cost of stent placement (MBS fee, stent cost and overnight hospitalisation – AR-DRG F14C; NHCDC Version 11.0, Round 25 (2020-21)
Reintervention by open surgery	n by \$14,449.88 ^d \$16,403.69 ^e ESC Revised: AR-D number of separations, minus ESC Revised: AR-D number of separations, minuber of separations, minus NHCDC Version 10		AR-DRG F14A,B,C, weighted by number of separations, minus prosthesis cost component; NHCDC Version 10.0, Round 24 (2019-20) ESC Revised: AR-DRG F14A,B,C, weighted by number of separations, minus prosthesis cost component; NHCDC Version 11.0, Round 25 (2020- 21)

Table 6	Cost in	puts used	d in ADAI	R resubmission	CCA ar	d commentary	• CCA
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Component	Total cost (ADAR)	Total cost (commentary) [®]	Source
MBS costs			
Amputation	\$60.592.31ª	\$73.419.69°	AR-DRG F11A,B, weighted by number of separations; NHCDC Version 10.0, Round 24 (2019-20)
			ESC Revised: AR-DRG F11A,B, weighted by number of separations; NHCDC Version 11.0, Round 25 (2020-21)

ADAR = Applicant Developed Assessment Report; AR-DRG = Australian-Refined Diagnosis Related Group; CCA = cost-consequence analysis; IVL = intravascular lithotripsy; MBS = Medicare Benefits Schedule; NHCDC = National Hospital Cost Data Collection; PL = Prescribed List; SBA = Standard balloon angioplasty; **Bold Text** = updated cost as per ESC Revised total cost. a Refers to MBS fees prior to July 2024.

b This cost could not be verified by the commentary - SBA devices do not appear to be on Part D of the PL at July 2024.

c Cost was prior to decrease to PL Group benefit in July 2024 (range in vascular BMS benefits changed to \$1,053 - \$1,394).

d The resubmission CCA used a cost of \$6,821.09 for an overnight stay, \$12,803.89 for open surgery and \$55,384.87 for amputation. These costs could not be verified from the NHCDC source cited in the ADAR resubmission CCA Excel file.

Source: Compiled from Table 3-3 and Table 3-5 of MSAC 1734 resubmission ADAR + in-line commentary.

e Commentary alternative base case CCA economic model and estimates updated for ESC using current national efficient price and AR-DRG F11A,B,C – NHCDC Version 11.0, Round 25 (2020-21).

Source: adapted from Table 3-3 and Table 3-5 of MSAC 1734 resubmission ADAR + in-line commentary.

Results of the economic evaluation

Table 7 shows the ADAR resubmission base case (with errors corrected by the commentary) and the alternative base case generated for the commentary (including alternative judgements regarding the inputs selected).

In summary, the changes applied in the commentary (alternative) base case have reduced the incremental cost of IVL by 35% and doubled the index stents avoided compared to the corrected ADAR resubmission base case. Amputations avoided have more than doubled. Reinterventions are at parity because the commentary applied a single TLR rate to both arms of the analysis, regardless of stenting at index procedure.

Item	ADAR corrected ^a			Commentary (alternative) ^b		
Cost outcomes	IVL	SBA	Difference	IVL	SBA	Difference
Index procedure costs						
MBS fees	\$772.55	\$813.97	-\$41.42	\$810.04	\$963.12	-\$153.08
Device	\$redacted	\$130.00	\$ redacted	\$ redacted	\$130.00	\$ redacted
Hospital	\$2,305.68	\$3,080.23	-\$774.55	\$2,754.22	\$4,864.67	-\$2,110.45
Drug-coated balloon	\$950.18	\$813.73	\$136.45	\$902.87	\$625.49	\$277.38
Stent	\$64.68	\$257.30	-\$192.62	\$131.47	\$523.04	-\$391.57
Index procedure total	\$ redacted	\$5,095.23	\$ redacted	\$ redacted	\$7,106.32	\$ redacted
2-year reintervention costs						
Endovascular	\$3,417.74	\$3,105.96	\$311.77	\$3,979.34	\$3,299.72	\$679.62
Open Surgery	\$115.66	\$460.11	-\$344.46	\$316.72	\$1,259.98	-\$943.26
Amputation	\$33.45	\$133.06	-\$99.61	\$97.76	\$388.92	-\$291.16
Reintervention total	\$3,566.84	\$3,699.14	-\$132.30	\$4,393.82	\$4,948.62	-\$554.80
Total costs at 2 years	\$ redacted	\$8,794.37	\$ redacted	\$ redacted	\$12,054.93	\$ redacted
Consequence outcomes						
Index stents	4.6%	18.3%	-13.7%	9.4%	37.2%	-27.8%
Reintervention stents	35.3%	34.6%	0.77%	35.6%	35.6%	0.00%
Amputation	0.06%	0.22%	-0.16%	0.13%	0.53%	-0.40%

Table 7 ADAR base case CCA (corrected), commentary (alternative) base case CCA

ADAR = Applicant Developed Assessment Report; CCA = cost-consequence analysis; IVL = intravascular lithotripsy; MBS = Medicare Benefits Schedule; SBA = standard balloon angiography.

Note: Numbers may not add up due to rounding.

a The following errors were corrected: (1) formula error – inclusion of the sum of all reintervention costs within the formula calculating the cost of amputation; (2) cost input error – use of day stay instead of overnight hospital costs for reintervention by endovascular stent placement; (3) data extraction error for hospital costs – use of incorrect values from the NHCDC Version 10.0, Round 24 (2019-20); (4) data extraction/calculation error for reintervention rates – use of 18.4% instead of 35.6% TLR rate for non-stented patients; (5) data extraction error for amputation rate – use of 6% instead of 4% after reintervention of stented patients. An inconsistency in the SBA cost between this table and other sources (i.e. the Excel model and elsewhere in the ADAR) has also been corrected (appears to be a transcription error).

b Commentary alternative base case CCA economic model and estimates updated for ESC using current national efficient price and AR-DRG F11A,B,C – NHCDC Version 11.0, Round 25 (2020-21).

Source: adapted from Commentary Table 6 of MSAC 1734 resubmission ADAR + in-line commentary.

As seen with the original ADAR CCA (which applied the relative risk from the DISRUPT PAD III RCT to a stenting rate of 45% sourced from MBS utilisation data), when the relative risk from the RCT was applied to a stenting rate of 37.2% sourced from 2021–2023 AVA data, it also produced a large decrease in absolute stenting rates that may be unrealistic to expect in clinical practice. The findings of the commentary (alternative) base case should therefore be considered in light of the uncertainty associated with the relative risk reduction of stenting observed in the RCT.

The DISRUPT PAD III RCT reported reintervention at two years as freedom from clinically driven TLR. No statistically significant difference was found between IVL and SBA. As reintervention rates were not reported in the study publication, reintervention rates in the CCA could not be informed from the RCT and were sourced from the literature instead, according to stent placement at index procedure. However, the source provided in the ADAR resubmission for reintervention in stented patients was a range quoted in an editorial, and this was not considered robust by the commentary. For reintervention in non-stented patients, the resubmission used a study from 2010; the commentary noted that while this may be considered a more reliable source than an editorial, it is not contemporaneous, so may not reflect current clinical practice.

Therefore, the inputs informing any cost offsets inferred due to a reduced risk of reintervention at two years after IVL are not reliable and introduce uncertainty. The assumption used in the base case of the resubmission CCA that only patients who received a stent at index procedure would undergo TLR by open surgery is not supported, and favours IVL.

Sensitivity analyses

The ADAR resubmission presented the results of two sensitivity analyses that used alternative index procedure stenting rates for the comparator (SBA) arm. The first analysis used the stenting rate from the 2022 AVA Public Report and the second derived the stenting rate from MBS utilisation data. The premise of these analyses was not considered reasonable by the commentary. Changing baseline stenting rates in the SBA arm while keeping the stenting rate in the IVL arm at 4.6% (DISRUPT PAD III RCT) ignores the relative risk of stenting from the DISRUPT PAD III RCT. It inflates the absolute value of stents avoided, and the resubmission ADAR provided no rationale to support this approach.

Results of a selection of sensitivity analyses using the commentary (alternative) base case are shown in Table 8. The incremental cost of IVL was most sensitive to the number of IVL catheters used per procedure and the absolute difference in index procedure stenting rates between the intervention and comparator. The incremental cost was also sensitive to reintervention rates being lower in stented patients compared to non-stented patients; the resubmission ADAR provided insufficient data to indicate the expected relative rates of reintervention in these groups.

As index stents avoided is solely a factor of the absolute difference in index procedure stenting rates, index stents avoided is almost eliminated in the sensitivity analysis that uses the DISRUPT PAD III Observational Study stenting rate after IVL. This scenario also involves the highest incremental cost. The commentary noted that it may be reasonable to consider this observational study as a practical demonstration of stenting rates after IVL in clinical practice, which differ little from current stenting rates in Australia.

As the commentary (alternative) base case assumed the same overall TLR rate for stented and non-stented patients, reinterventions avoided were zero in all but one sensitivity analysis. Again, the resubmission ADAR provided insufficient data regarding reintervention rates, this time for stented versus non-stented patients.

Amputations avoided remained less than 1% in all sensitivity analyses.

Tested variable	Source	Commentary base case	Test value	Incremental cost ^c	Stents	Reintervention	Amputations
Commentary base case	I	I		\$redacted	-27.8%	0.00%	-0.40%
Cost inputs							
IVL catheters per patient	DISRUPT PAD II study ^a	1	1.3	\$redacted	-27.8%	0.00%	-0.40%
Probability inputs	L	I					
Stenting							
IVL stenting rates from	IVL: DISRUPT PAD III OS	IVL: 9.4%	IVL: 35.5%	\$redacted	-1.7%	0.00%	-0.02%
DISRUPT PAD III OS	SBA: AVA 2021–2023	SBA: 37.2%	SBA: 37.2%				
Baseline index stenting	IVL: RR from DISRUPT	IVL: 9.4%	IVL: 11.3%	\$redacted	-33.7%	0.00%	-0.48%
rates from MBS utilisation	PAD III RCT	SBA: 37.2%	SBA: 45%				
with RCT RR applied to	SBA: MBS utilisation						
IVL arm		1)//		¢re de ete d	10 70/	0.000/	0.000/
Stenting rates for both	DISRUPT PAD III RCT	IVL: 9.4%	IVL: 4.6%	\$redacted	-13.7%	0.00%	-0.20%
ADAR base case in		SBA: 37.2%	SBA: 18.3%				
resubmission)							
TLR							
TLR rates in stented	Tosaka et al. 2012 ^b	No stent 35.6%	No stent 35.6%	\$redacted	-27.8%	4.73%	-0.21%
patients		Stent 35.6%	Stent 18.6%				
TLR rates in all patients	Tosaka et al. 2012 ^b	No stent 35.6%	No stent 18.6%	\$redacted	-27.8%	0.00%	-0.21%
		Stent 35.6%	Stent 18.6%				
Open TLR in patients with	COSTLY-TLR study of	No stent 0%	No stent 58%	\$redacted	-27.8%	0.00%	-0.40%
no stent at index procedure	stented patients used in	Stent 58%	Stent 58%				
	non-stented patients						

Table 8 Inputs and results (incremental cost and incremental outcomes) of univariate sensitivity analyses using commentary (alternative) base case^c

ADAR = Applicant Developed Assessment Report; AVA = Australasian Vascular Audit; DCB = drug-coated balloon; IVL = intravascular lithotripsy; MBS = Medicare Benefits Schedule; OS = observational study; PAD = peripheral artery disease; RCT = randomised controlled trial; RR = relative risk; SBA = standard balloon angiography; TLR = target lesion revascularisation; ESC = Evaluation Sub-Committee a Number of catheters used per patient in DISRUPT PAD II single arm study sourced from Madhaven et al 2020, suppl. table 2.

b Tosaka et al. 2012 is cited in the Rymer & Jones 2018 editorial and reports on a cohort of stented patients.

c Commentary alternative base case CCA economic model and estimates updated for ESC using current national efficient price and AR-DRG F11A, B, C – NHCDC Version 11.0, Round 25 (2020-21). Source: adapted from Commentary Table 7 of MSAC 1734 resubmission ADAR + in-line commentary.

14. Financial/budgetary impacts

The financial impact analysis in the ADAR resubmission was updated to align with the updates made to the ADAR economic evaluation (i.e. consideration of a single population rather than two separate populations; revised rates of stent and DCB insertion; and use of bare metal stent costs). The financial analysis adopted a market share approach to estimate the net costs of the proposed MBS listing of IVL as either a stand-alone treatment or as a vessel preparation strategy prior to DCB or stent insertion. This approach (which is consistent with the original submission) was considered appropriate by MSAC as IVL is expected to replace or supplement existing MBS items for lower limb PAD endovascular revascularisation. The MBS listing of IVL is not expected to increase the overall number of people requiring endovascular revascularisation.

The data sources and assumptions used to estimate the utilisation of the proposed new MBS listing of IVL are summarised in Table 9. The financial impact analysis considered index treatment only. Utilisation and costs relating to reintervention after the index procedure (including hospitalisation and amputation, etc.) were not considered.

Parameter	Value/source in ADAR resubmission	Commentary on values/sources
Total number of PAD procedures	Based on MBS utilisation data 2017–2023 for MBS items 35300, 35303, 35306, 35309.	These MBS items are not confined to procedures in peripheral arteries nor to lower limbs and could overestimate the number of services for the proposed MBS population. All four items can be used for peripheral veins. Item 35303 can also be used for aortic arch branches and aortic visceral branches while item 35309 can be used for visceral arteries or veins. These items are not restricted to index procedures.
Predicted IVL uptake	Assumption. Y1: 15%, Y2: 30%, Y3: 40%, Y4: 45%, Y5: 50%, Y6: 50%	Uptake assumptions are consistent with the original ADAR, which states that uptake was estimated based on experience in overseas markets and uptake of other adjunct technologies in Australia (e.g. atherectomy). Data were not provided in the original ADAR nor the resubmission for these market experiences; therefore, the estimated uptake rates each year remain uncertain.
PAD procedure annual growth rate	2.7%, calculated from MBS utilisation data 2017–2021 for MBS items 35300, 35303, 35306, 35309. Utilisation was notably lower in 2022 and was not considered representative.	Omission of 2022 data is reasonable. 2.7% is likely to be an underestimate given the monthly growth in services since 2023. Annual growth rate is 3.5% using MBS utilisation data 2018–2021.
Proportion of PAD patients with heavy calcification	14.2%, taken from a real-world study of PAD patients seeking treatment (Schmidt et al. 2016).	14.2% refers to PAD patients with severe calcification only. Omission of moderate calcification is inconsistent with the proposed MBS population. The proportion of PAD patients in Schmidt et al. 2016 with moderate or severe calcification was 34.7%.

Parameter	Value/source in ADAR resubmission	Commentary on values/sources
Proportion of index services that are stand- alone or followed by DCB or stent	Informed by the stenting rate from DISRUPT PAD III RCT (4.6% for IVL vs 18.3% for SBA), and assuming 20% of non-stent procedures were standalone and the remaining 80% received a DCB.	There are applicability concerns regarding use of RCT data from DISRUPT PAD III because the rate of stenting in the SBA arm was lower than reported in practice. The assumption of 20% stand-alone procedures was informed by clinician guidance sought by the applicant, not clinical evidence. No consideration was given to patients who receive a stent and DCB at the index procedure.

ADAR = Applicant Developed Assessment Report; IVL = intravascular lithotripsy; MBS = Medicare Benefits Schedule; PAD = peripheral artery disease; Y = year.

Source: Adapted from Table 4-1 of MSAC 1734 resubmission ADAR + in-line commentary.

The costs applied in the financial estimates were consistent with those used in the resubmission's economic evaluation. The cost to the MBS was appropriately calculated using the 75% benefit; however, the Multiple Operation Rule was not taken into consideration. MBS costs for associated radiological services (fluoroscopy) and anaesthesia were not considered.

The resubmission clarified that the cost per IVL catheter (**\$redacted**) is currently covered via private health insurance or hospital funding. The financial estimates assumed one IVL catheter per procedure, although the commentary noted published evidence (from DISRUPT PAD II and the SHOCC study) that a small proportion of patients may require more than one catheter. Capital and maintenance costs for the IVL generator and connector cables were not considered in the financial estimates as these items are provided on loan to the hospitals by the manufacturer.

The financial implications to the MBS and other health budgets from the proposed listing for IVL are summarised in Table 10 (commentary adjusted estimates). The estimates are based on an annual growth rate of 3.5% for PAD procedures and assume that patients with moderately and severely calcified lesions will be eligible for IVL (the ADAR resubmission captured severely calcified lesions only). The overall net financial impact includes MBS costs (index procedure only), device costs (IVL and SBA, not attributed to any particular budget), PL costs (calculated using stent and DCB benefits), hospitalisation costs and patient costs (based solely on the difference between the MBS schedule fee and the 75% benefit).

Table 10	Financial im	plications	of IVL u	sing comm	nentary	(alternative) base case ^c
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	Table to Timancial implications of the using commentary (alternative) base case.							
Parameter	Year 1 2025	Year 2 2026	Year 3 2027	Year 4 2028	Year 5 2029	Year 6 2030		
Estimated use of the proposed health technology								
Number of people with moderately or severely calcified lesions eligible for IVL	5,617	5,811	6,012	6,220	6,435	6,657		
Number of people who receive IVL	redacted	redacted	redacted	redacted	redacted	redacted		
Cost to the MBS of the p	roposed health	technology	·····		•••••••			
Cost to the MBS of IVL services (75% benefit)	\$492,260	\$1,018,562	\$1,405,041	\$1,635,325	\$1,879,855	\$1,944,855		
Net cost to the MBS of the	ne proposed hea	Ith technology		-		_		
Net cost to the MBS of IVL services (75% benefit)	-\$57,439	-\$118,850	-\$163,946	-\$190,817	-\$219,350	-\$226,934		
Cost of the proposed tec	chnology to othe	r health budget	S					
Device costs for IVL procedures	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted		
Cost to the PL of IVL procedures (stent and DCB) ^b	\$871,629	\$1,803,535	\$2,487,861	\$2,895,619	\$3,328,600	\$3,443,693		
Cost of hospitalisation for IVL procedures ^c	\$2,323,651	\$4,807,992	\$6,632,316	\$7,719,345	\$8,873,617	\$9,180,439		
Cost to patients of IVL services	\$164,072	\$339,491	\$468,305	\$545,060	\$626,563	\$648,228		
Total cost of IVL to other health budgets ^c	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted		
Net cost of the proposed	technology to o	other health bud	gets					
Net device costs for IVL procedures	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted		
Net cost to the PL of IVL procedures (stent and DCB) ^b	-\$96,034	-\$198,708	-\$274,105	-\$319,031	-\$366,736	-\$379,416		
Net cost of hospitalisation for IVL procedures ^c	-\$1,774,966	-\$3,672,677	-\$5,066,223	-\$5,896,571	-\$6,778,285	-\$7,012,656		
Net cost to patients of IVL services	-\$19,127	-\$39,576	-\$54,593	-\$63,541	-\$73,042	-\$75,568		
Total net cost of IVL to other health budgets ^c	\$2,170,857	\$4,491,837	\$6,196,200	\$7,211,751	\$8,290,123	\$8,576,769		
Overall net financial impact of IVL to the MBS and other health budgets ^c	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted	\$ redacted		

DCB = drug-coated balloon; IVL = intravascular lithotripsy; MBS = Medicare Benefits Schedule; PL = Prescribed List; SBA = standard balloon angioplasty. a Commentary estimates apply to PAD patients with moderately and severely calcified lesions and were based on an annual growth rate of 3.5% for PAD procedures. The Multiple Operation Rule was applied in cases of stent insertion (co-claiming with MBS items 35306 and 35309) using MBS fees at 23 July 2024. In contrast, ADAR resubmission estimates applied to PAD patients with severely calcified lesions only and were based on an annual growth rate of 2.7% for PAD procedures. The Multiple Operation Rule was not applied and MBS fees were prior to 1.July 2024.

2.7% for PAD procedures. The Multiple Operation Rule was not applied and MBS fees were prior to 1 July 2024. b The estimates were based on a weighted PL benefit of \$1,406.01 for bare metal stents. However, the Group benefit was reduced in July 2024 and the range in PL benefits was reduced (\$1,053 to \$1,394).

Source: Compiled from Table 4-4, Table 4-19, Table 4-20, Table 4-21, Table 4-22, Table 4-23 and Table 4-25 of MSAC 1734 resubmission ADAR + in-line commentary.

c Commentary alternative base case CCA economic model and estimates updated for ESC using current national efficient price and AR-DRG F11A,B,C – NHCDC Version 11.0, Round 25 (2020-21).

Source: adapted from Commentary Table 4-4, Table 4-19, Table 4-20, Table 4-21, Table 4-22, Table 4-23 and Table 4-25 of MSAC 1734 resubmission ADAR + in-line commentary.

The primary driver for the net cost of the proposed IVL listing across all health budgets is the cost of the IVL device (currently covered via private health insurance or hospital funding). There are minor net savings estimated for the MBS, the PL (attributed to the avoidance of stent insertion) and out-of-pocket patient expenses (assuming the cost of the IVL device will not be passed on to patients). Substantial cost reductions are anticipated for hospitalisation, primarily due to shorter hospital stays resulting from IVL treatment.

The results of the sensitivity analyses performed by the commentary are shown in Table 11. The net financial impact to the MBS and overall health budgets are most sensitive to changes in the IVL uptake rate and changes to the stenting rate per arm at the index procedure. As mentioned earlier, relative stenting rates in the base case were informed by the DISRUPT PAD III RCT, which imposed restrictions on stent placement that are not used outside of a trial setting. The degree to which stenting rates may decrease with IVL in Australian clinical practice, and therefore the net financial impact, is uncertain.

Parameter	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6		
	2025	2026	2027	2028	2029	2030		
Base case analysis								
Net financial impact to MBS	-\$57,439	-\$118,850	-\$163,946	-\$190,817	-\$219,350	-\$226,934		
Net financial impact to	\$2,170,857	\$4,491,837	\$6,196,200	\$7,211,751	\$8,290,123	\$8,576,769		
other health budgets ^a								
Total budget impacta	\$2,113,418	\$4,372,986	\$6,032,254	\$7,020,934	\$8,070,773	\$8,349,835		
Annual growth rate from 3.	5% to 2.7% (co	nsistent with A	DAR)					
Net financial impact to MBS	-\$56,601	-\$116,258	-\$159,196	-\$183,931	-\$209,886	-\$215,553		
Net financial impact to	\$2,139,176	\$4,393,868	\$6,016,670	\$6,951,510	\$7,932,446	\$8,146,622		
other health budgets ^a								
Total budget impact ^a	\$2,082,576	\$4,277,610	\$5,857,474	\$6,767,579	\$7,722,560	\$7,931,069		
Uptake rate of IVL increase	d by absolute '	10%						
Net financial impact to MBS	-\$95,732	-\$158,467	-\$204,933	-\$233,221	-\$263,220	-\$272,321		
Net financial impact to	\$3,618,095	\$5,989,116	\$7,745,250	\$8,814,362	\$9,948,147	\$10,292,123		
other health budgets ^a								
Total budget impact ^a	\$3,522,363	\$5,830,648	\$7,540,317	\$8,581,141	\$9,684,927	\$10,019,802		
Uptake rate of IVL decrease	ed by absolute	10%						
Net financial impact to MBS	-\$19,146	-\$79,234	-\$122,960	-\$148,413	-\$175,480	-\$181,547		
Net financial impact to	\$723,619	\$2,994,558	\$4,647,150	\$5,609,140	\$6,632,098	\$6,861,415		
other health budgets ^a								
Total budget impact ^a	\$704,473	\$2,915,324	\$4,524,190	\$5,460,726	\$6,456,618	\$6,679,868		
Change IVL stenting rate fr	om 9.4% to 35.	5% (from DISR	UPT PAD III OS	<u>S)</u>		-		
Net financial impact to MBS	\$17,574	\$36,364	\$50,162	\$58,383	\$67,113	\$69,434		
Net financial impact to	\$3,952,446	\$8,178,219	\$11,281,327	\$13,130,325	\$15,093,700	\$15,615,593		
other health budgets ^a								
Total budget impacta	\$3,970,021	\$8,214,583	\$11,331,489	\$13,188,708	\$15,160,813	\$15,685,026		
Change IVL stenting rate to 11.3% (RCT RR applied to MBS utilisation) and SBA								
stenting rate to 45% (MBS utilisation)								
Net financial impact to MBS	-\$75,416	-\$156,048	-\$215,258	-\$250,539	-\$288,002	-\$297,960		
Net financial impact to	\$1,767,781	\$3,657,811	\$5,045,715	\$5,872,703	\$6,750,847	\$6,984,270		
other health budgets ^a								
Total budget impact ^a	\$1,692,365	\$3,501,763	\$4,830,457	\$5,622,164	\$6,462,845	\$6,686,310		

Table 11 Sensitivity analyses using commentary (alternative) base case; Updated Post-ESC^a

ADAR = Applicant Developed Assessment Report; IVL = intravascular lithotripsy; MBS = Medicare Benefits Schedule; RCT = randomised controlled trial; RR = relative risk; SBA = standard balloon angioplasty.

Source: Adapted from Commentary Table 8 of MSAC 1734 resubmission ADAR + in-line commentary.

a Commentary alternative base case CCA economic model and estimates updated for ESC using current national efficient price and AR-DRG F11A,B,C – NHCDC Version 11.0, Round 25 (2020-21).

Source: adapted from Commentary Table 8 of MSAC 1734 resubmission ADAR + in-line commentary.

Although not shown in Table 11, changes to the cost of IVL catheters or the number of IVL catheters used per procedure will increase costs to hospitals and/or private health insurers.

15. Other relevant information

Nil

16. Key issues from ESC to MSAC

Main issues for MSAC consideration

Clinical issues:

- The proposed population for the service includes patients with moderately or severely calcified lesions. The eligibility criteria for the service are not well-defined and definitions of moderately or severely calcified lesions are unclear. Therefore, the patient population cannot be accurately defined.
- Until further evidence is available regarding IVL management of upper-limb PAD lesions, MSAC may wish to consider restricting the proposed services to lower-limb PAD patients only.
- There is uncertainty of vascular surgeons' views regarding the device and its use in current practice. Prior to MSAC consideration, ESC requested the department should seek targeted feedback from vascular surgeons.

Economic issues:

- The updated ADAR CCA used index procedure stenting rates from the DISRUPT PAD III RCT: 4.6% for IVL and 18.3% for SBA. However, the baseline rate of 18.3% is substantially lower than 37.2% reported in the Australasian Vascular Audit (AVA) Report 2021–2023. The commentary generated an alternative base case CCA that used the AVA data for baseline stenting on the basis that it reflects local clinical practice. However, applying the trial relative risk of stent placement to AVA baseline rates resulted in a large absolute decrease in stenting, and it may not be reasonable to assume this will be realised in clinical practice where the decision to place a stent is not restricted by pre-specified intraoperative stenting criteria. The pre-ESC response noted the limitations in the evidence and agrees the AVA Report is the best source of clinical practice in Australia.
- The only data in the CCA informed by the DISRUPT PAD III RCT was the index procedure stenting rate. The trial reported on clinically driven target lesion revascularisation (TLR) as a survival outcome, which was not statistically different between IVL and SBA. But as the trial did not report TLR rates, other sources were required for reintervention rates. The data supplied by the resubmission for two-year reintervention rates were not robust (see below two dot points):
- An editorial quoting 30–40% reintervention at two years was used for patients stented at index procedure, but only one of the cited publications was a primary study, and that study reported a TLR rate of 18.6%, which falls outside the quoted range.
- The rate of TLR in non-stented patients was incorrectly reported in the ADAR as being from the DISRUPT PAD III RCT but appeared to be based on rate for open surgery TLR from the BASIL RCT (18.4%), potentially underestimating the TLR rate for non-stented patients. In the alternative base case, the commentary used the overall TLR rate of 35.6% from the BASIL RCT for TLR following IVL.

- ESC revised the commentary alternative base case results to include updated hospital cost inputs. Compared to the resubmission CCA (after correction of errors), the commentary base case (following recalculation by ESC updating hospital costs) had a 49% lower incremental cost of IVL at two years (\$1,887) and twice the index stents avoided (27.8%). Amputations avoided more than doubled but remained low at 0.4%. Reinterventions were at parity because the commentary applied a single TLR rate to both arms of the analysis, regardless of stenting at index procedure. The reliability of these outputs, however, are subject to the serious limitations in the clinical evidence used to inform the CCA inputs.
- The incremental cost of IVL is sensitive to the absolute difference in index procedure stenting rates between IVL and SBA. A sensitivity analysis using a post-IVL index stenting rate of 31.8% from the DISRUPT PAD III observational study increased the incremental cost of IVL to \$4,703.62 and decreased the stents avoided to 1.7%. It may be reasonable to consider this observational study to be a practical demonstration of stenting rates after IVL in clinical practice, without the stenting restrictions imposed on an RCT, and may be similar to current stenting rates in Australia.

Financial issues:

- The ADAR analysis included PAD patients with severe calcification only. This was not consistent with the proposed MBS population and underestimates the overall net financial impact. The commentary provided updated estimates of proportion of PAD patients that included moderate and severe calcification based on registry data. ESC considered that updated estimates for both moderate and severe calcification populations separately would be useful for MSAC's decision making.
- A market share approach was used, based on utilisation data from MBS items for transluminal balloon angioplasty, with or without stent insertion. These items are not confined to use in peripheral arteries nor index procedures, and this is likely to have overestimated the number of IVL services.
- The financial impact analysis considered index treatment only. Utilisation and costs relating to reintervention after the index procedure were not considered.
- The existing MBS items used for the financial impact analysis are not specific to PAD and lower limbs.
- Changes to the cost of IVL catheters (**\$redacted** each) or the number of IVL catheters used per procedure will increase costs to hospitals and/or private health insurers. Capital and maintenance costs for the IVL generator and connector cables (borne by hospitals) were not captured in the economic or financial analyses. The pre-ESC response confirmed IVL generators were provided to hospitals on loan but there was uncertainty around the long-term costs.

ESC discussion

ESC noted that this application was from Shockwave Medical Inc and Diverse Devices Pty Ltd was for Medicare Benefits Schedule (MBS) listing for providing intravascular lithotripsy (IVL), as a stand-alone treatment or as a vessel preparation strategy before stent insertion or treatment with a drug-coated balloon (DCB), in patients with moderately or severely calcified peripheral arterial disease (PAD) in lower limbs and who are indicated for endovascular revascularisation. ESC noted that this application was first considered by MSAC in November 2023, where MSAC deferred its decision on listing IVL.

ESC noted that there was no public consultation feedback provided for this resubmission. ESC considered that it would be helpful for MSAC decision-making if targeted consultation advice could be sought by the department from vascular surgeons to determine vascular surgeons' views regarding the device and use of the device in current practice.

ESC noted the two proposed PICO populations were as follows:

PICO set 1: patients with PAD who have moderately or severely calcified lesions in their lower limb(s), who are indicated for endovascular revascularisation and do not require subsequent treatment following balloon dilation (that is, IVL is a stand-alone treatment). The comparator is standard balloon angioplasty [SBA].

PICO set 2: patients with PAD who have moderately or severely calcified lesions in their lower limb(s) who are indicated for endovascular revascularisation and require subsequent treatment following balloon dilation (that is, IVL is used in combination with other therapy). The comparator is DCB and/or stent insertion.

ESC noted that MSAC previously considered the two PICO populations presented did not accurately reflect Australian clinical practice and that it would be difficult to determine preoperatively which patients would only require stand-alone treatment, therefore MSAC recommended that the populations be merged for a resubmission. ESC noted that the resubmission had merged the two populations as per MSAC recommendations. However, ESC recalled that comparative data was only available for PICO set 2.

ESC noted that, although there were classification systems available for the different degrees of calcification (including from NICE), it was unclear how often these were used in clinical practice and how easy they were to interpret and adopt. ESC considered that it was important to understand the classification distinction between moderate vs. severe calcification and how this distinction is made in clinical practice.

ESC noted the November 2023 PSD where MSAC considered that there is likely superior procedural effectiveness and non-inferior safety for IVL compared to SBA when used as a vessel preparation strategy prior to stent insertion or treatment with a DCB. However, MSAC acknowledged at the time that there was a lack of evidence regarding long-term safety. MSAC also considered that there was weak evidence for superior effectiveness and non-inferior safety compared to SBA when IVL is employed as a stand-alone therapy, when compared to balloon angioplasty. MSAC had noted that the overall evidence did not demonstrate any patient-reported outcomes such as quality of life (QoL) benefit, ankle-brachial index scores or walking improvement, nor any survival benefit demonstrated either directly, or from any linked evidence on avoidance of stenting. ESC noted that the current application did not provide any new evidence. ESC recalled that the previous evidence for comparative effectiveness included variable criteria for inclusion, outcomes, endpoints, follow-up and definition of calcification. The trials involved small numbers and only one randomised control trial (RCT) was included. However, ESC noted that MSAC's deferral of the November 2023 submission was predominately due to uncertainties with the economic model and considered that the previous MSAC concerns about the quality of the evidence had not been altered.

ESC noted the proposed clinical management pathway and that, after the use of IVL, clinical judgement would be used to determine whether other treatments were required for management of the remaining lesion. ESC considered that the initial steps of the clinical management pathway were appropriate but queried the evidence base for the final steps of the pathway, which detailed adjunctive treatments to be used following IV lithotripsy. ESC recalled that there was no comparative data provided that supported stand-alone IVL. Comparative data was only provided for IVL when used in conjunction with, or as an adjunct to, other therapies. Therefore, ESC considered that IVL would most likely be used as an ancillary therapy to DCB or prior to stenting. Additionally, ESC considered that it would be unusual to use atherectomy after IVL (as detailed in the clinical management pathway), and that it would be more appropriately placed as an alternative to IVL.

ESC noted MSAC previously recommended that the ADAR should consider the implications of the impending National Institute for Health and Care Excellence (NICE) guidelines on IVL (updated early 2024). ESC noted that the now updated NICE guidelines for IVL support MSAC's previous conclusions that IVL is likely safe, but that there is a lack of supportive long-term data. The guidelines state that IVL for calcified arteries in PAD should only be used with special arrangements for clinical governance, consent, and audit or research. They also state that clinicians who want to use IVL for calcified arteries in PAD should audit and review clinical outcomes of patients that have the procedure, and that healthcare organisations should regularly review data on outcomes and safety. Finally, NICE encourages further research into IVL for calcified arteries that the resubmission did not specifically address all of the recommendations as per the updated NICE guidelines.

ESC noted that the pre-ESC response stated that bailout stenting placement, which increases costs, was likely to be lower in the IVL group. ESC considered this was reasonable as low-pressure balloon inflation and lithotripsy was less likely to result in occlusive dissection of the artery. ESC considered that stenting rates would be lower in RCTs than in real-world practice.

ESC recalled that all the provided evidence was related to lower limb intervention, however noted that the proposed MBS item descriptor in the resubmission did not specify lower limbs. ESC noted from the pre-ESC response that upper-limb ischaemia is highly unlikely but still possible, therefore ESC considered that the item descriptor should specify "of one lower limb" to ensure the target population is consistent with the evidence presented. ESC also noted that the descriptor did not specify how often the treatment is applicable, which it considered reasonable given that long-term data are not available.

ESC noted MSAC's previous advice to the applicant to revise the economic model to a costconsequence analysis rather than a cost-utility analysis and revisit the cost calculations based on a consolidated PICO set.

ESC noted that, for the economic evaluation, procedures were spilt into an index procedure, where IVL or SBA is used, followed by a two-year reintervention period. At the index stage, the patient has success with an IVL or SBA stent with or without provisional stent placement. A proportion go on to have reintervention, either as endovascular intervention, open surgery or, in a small number of cases, amputation. ESC noted that, due to the limitations of the trial data, rate of stenting at the index procedure is only used in one input in the model.

ESC noted that the evidence concerns carried through to the economic model – a costconsequence analysis (CCA) – which ESC did not consider to be robust enough to accurately predict costs and consequences. ESC noted that there were also errors in the model that required revision by the commentary and further revisions by ESC. ESC noted and agreed that the cost inputs corrected by the commentary were reasonable; however, ESC noted that the commentary alternative base case used outdated hospital costs. The commentary cost inputs and alternative base case were revised with the updated hospital costs and considered by ESC. The results of the recalculated commentary CCA have been updated throughout the ESC report.

ESC noted that the key uncertainty with the economic model was whether the trial stenting rates reflect clinical practice (the baseline rate of stenting in the RCT is lower than what is observed in Australian practice). In their pre-ESC response, the applicant agreed that there were limitations in the evidence but that the stenting rates were reasonable. ESC noted that this assumption favoured the intervention. In a sensitivity analysis, the applicants applied the baseline rate of stenting from the Australasian Vascular Audit (AVA) Report (2021), but then needed to rely on the relative risk (RR) from the DISRUPT PAD III trial to determine the absolute rate of stents. ESC considered that this combination of inputs further contributes to the uncertainty in the economic model, as it is questionable if this is plausible in clinical practice. ESC noted that the stenting

rates have flow-on effects to reintervention rates, which favour the intervention. ESC noted that of the 100 patients, 2 end up with open procedure in the IVL arm and 8 in the SBA arm.

ESC noted that the cost of the device was offset by additional hospital costs, due to the higher stent rate (around 37%) post-SBA. ESC noted that this absolute change is driven by applying the AVA rates from clinical practice to the trial RR (which is uncertain). ESC considered that this combination of inputs produces an absolute change that may not be reflected in clinical practice. ESC noted that the flow-on effects of the stent rates on reintervention is an approximately \$950 difference in open surgery costs, although this is uncertain due to a lack of long-term data.

ESC noted that the commentary presented several sensitivity analyses that tested the rates of stents in both arms of the economic model. Removing the difference in stent rates between the arms resulted in higher incremental costs. ESC considered that uncertainty around the actual rate of stent insertion in clinical practice impacted the certainty of the sensitivity analyses for reintervention.

ESC noted that a market-share approach was used to determine the financial impact. ESC considered that the main issue was that the analysis included patients with severe calcification only, rather than both moderate and severe (the proposed MBS population), underestimating the population and financial impact. ESC noted that the main driver of the financials was the cost of the device (borne by the hospitals) plus hospital costs (which will be higher than what was originally proposed).

ESC noted that several costs had been identified as missing – including reintervention procedures that were not costed (unknown due to a lack of long-term data) and multiple procedures per person that were not considered (which will increase the estimated population; the pre-ESC response estimated that >30% will need another procedure within five years). ESC considered that the estimates should reflect usage and costs for lower limb interventions.

Other missing costs that should have been included were for anaesthesia (the policy paper stated that the procedure time for IVL is an additional 33.4 minutes), fluoroscopy and the capital costs of the IVL generator; the pre-ESC response stated that the generator will be on loan from the applicant to the hospitals, but ESC considered there was uncertainty about the costs over the duration of the loan for the generators. Additionally, ESC noted there were some out-of-pocket costs for consumables that were not considered, such as for the introducer sheath and the guide wire.

ESC advised that inclusion of separate financial impact analyses and costs for both the moderate and severe calcification patients would be useful for MSAC decision making.

Overall, ESC considered IVL to be an intuitively low-risk and clinically effective therapy for peripheral calcium modification. ESC considered that long term data with hard endpoints to support clinical utility and cost benefit of IVL as both an adjunct and stand-alone therapy was not available.

ESC noted that early results from the Disrupt PAD BTK (below the knee) study of the Shockwave IVL system for treatment of calcified below-the-knee PAD demonstrated favourable procedural outcomes, with low angiographic complication rates and a significant reduction in residual stenosis. ESC noted that this ongoing trial is expected to be published in 2025 and considered that this study may be relevant to the current application.

17. Applicant comments on MSAC's Public Summary Document

Nil.

18. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website: <u>visit the</u> <u>MSAC website</u>