South Australian Policy Advisory Committee on Technology (SAPACT)

Health Technology Assessment (HTA) Decision Summary

Government of South Australia

SA Health

Shockwave intravascular lithotripsy for the treatment of severe calcified arterial lesions and stent under-expansion

SAPACT MEETING DATES	28th SAPACT Meeting (27 May 2022)
APPLICATION #	2201
TECHNOLOGY	The Shockwave C2 Coronary intravascular lithotripsy (IVL) System (AA-Med Pty Ltd) combines sound waves with angioplasty to treat calcified plaque in diseased arteries. The system consists of three components: a single-use standard percutaneous transluminal coronary angioplasty balloon catheter, a reusable generator, and a reusable connector cable. The balloon catheter has integrated lithotripsy emitters designed to enhance angioplasty by disrupting calcium before balloon dilation of the stenosis. The lithotripsy pulse waves also facilitate blood passage and enhance the placement of a stent.
TECHNOLOGY CLASSIFICATION	TGA class III high-risk
PATIENT INDICATION (TGA)	The Applicant has requested to use shockwave IVL for both label and off-label indications: (a) TGA intended purpose: The Shockwave C2 Coronary IVL System is indicated for lithotripsy-enhanced, low-pressure balloon dilatation of severely calcified, stenotic de novo coronary arteries prior to stenting. (b) TGA off-label use: For stent under-expansion treatment after percutaneous coronary intervention (PCI).

SAPACT DECISION

☒ Restricted recommendation for clinical use with financial or operational restrictions and under audit conditions.

SAPACT Advisory Recommendations:

SAPACT recommends for the restricted use of shockwave IVL for the treatment of severe calcified arterial lesions and stent under-expansion to three cases per LHN site (SALHN, CALHN and NALHN) in the first year, with a requirement to monitor and report the clinical outcomes back to SAPACT at the completion of three cases at each site.

SAPACT Evidence Review Conclusions

Based on safety and clinical effectiveness, the limited international literature reported that shockwave IVL appeared to be feasible with high procedural success and low major adverse cardiac event (MACE) rates in patients with severe calcified arterial lesions who are not amenable to other conventional treatments. However, no direct comparative studies (including randomised controlled trials [RCT]) compare shockwave IVL to other alternate interventions. In addition, the current published literature did not report on important patient-oriented outcomes, including physical functions and quality of life.

Two studies, each with small sample size, demonstrated the potential of shockwave IVL as a feasible alternative for managing stent under-expansion due to calcific coronary disease.

Current findings need confirmation through high-quality, appropriately powered comparative trials with long-term follow-up and reporting of patient-oriented outcomes.

REGULATORY APPROVALS

☒ **Australia ARTG**: 378470 Shockwave C2 Coronary Intravascular Lithotripsy Catheter - Ultrasonic lithotripsy system transducer, single-use - 22/11/2021	☒ **US FDA**: PMA approval P200039 – 12/02/2021 PMA document states the product is commercially available in 15 jurisdictions, including the European Union and New Zealand. Shockwave IVL is off-label in the United States for both restenosis and/or stent under-expansion treatment.	☒ **EU CE mark**: May 2017

QUALITY OF EVIDENCE

Quality of Evidence	SAPACT staff conducted a comprehensive systematic search for the best available HTA and policy evidence in 6 published and 24 grey literature sources. Given that HTA reports and a systematic review were identified (ECRI 2021, and NICE Guidance 2020 and Sattar 2021), a SAPACT Evidence Review was not required. The search did not identify any Level II evidence (RCT). Case series, matched registry data and case reports formed the clinical evidence. The studies were at risk of bias from short-term follow-up, lack of controls, lack of patient-oriented outcomes and industry sponsorship. Wiens 2021 (n=50) is a non-industry-sponsored real-world retrospective case-series with 1-year follow-up in Canada. Shockwave Medical sponsored the following pivotal single-arm trials (case-series): • Disrupt CAD IV study; n=64 (Saito 2021; 30-days). Disrupt CAD IV study is for Japanese regulatory approval of shockwave IVL. • Disrupt CAD III study; n=384 (Kereiakes 2022; 1-year outcome article and Hill 2020; 30-days outcome article). The Disrupt CAD III study was designed for US FDA regulatory approval of shockwave IVL and is the most extensive long-term (1-year) analysis of coronary IVL. • Disrupt CAD II study; n=120 (Ali 2019); Europe • Disrupt CAD study; n=60 (Brinton 2019); Australia and Europe

	The BASIL RCT trial (ACTRN12620000086965) and the DECALCIFY trial (NCT04960319) are two RCTs pending results publication. Completed in late 2021, the BASIL trial is a Shockwave Medical sponsored RCT (n=60) conducted in New Zealand and compares shockwave IVL plus PCI vs balloon angioplasty plus PCI. The DECALCIFY trial is based in Germany and is ongoing, with a completion date of June 2024. Again, this is a Shockwave Medical supported RCT (n=100) comparing shockwave IVL to rotational atherectomy (RA). **Limited studies for the management of stent under-expansion (off-label)** • Yeoh 2021; n=13 is a case series in the UK. • IntravaScular Lithotripsy for the Management of UndILatable Coronary StEnt (SMILE) Registry; n=34 (Ielasi 2020) is a multicentre, retrospective cohort study in Italy.
CLINICAL NEED	
Burden of Illness	Coronary artery calcification is the build-up of calcium in the arteries, which can cause blood vessels to narrow and lead to the development of heart disease. Heavily calcified coronary lesions are present in about 20% of PCI patients. Coronary calcification limits optimal stent expansion and apposition. Further, heavy calcification exacerbates the safety and effectiveness concerns of PCI.
Need	Without clear clinical evidence of efficacy, conventional debulking modalities to treat calcified plaque, such as high-pressure balloon dilatation, cutting/scoring balloons or rotational atherectomy, are associated with periprocedural complications (e.g. coronary artery dissection and perforation). Shockwave IVL is a novel technology for the de novo preparation of severely calcified coronary lesions with purportedly good outcomes and minimal complications. The differential, non-ablative mechanism of IVL action that modifies calcium using high energy sonic waves in a circumferential, transmural fashion at low balloon inflation pressures without either wire bias or significant thermal energy generation has theoretic appeal. In addition, it may reduce early and late adverse events. • Intervention: Shockwave IVL with or without stent deployment. • Comparator: Alternative interventions include atherectomy, and balloon angioplasty, with or without stent deployment. Shockwave IVL has also been used in peripheral arteries as stand-alone revascularisation or an adjunct to optimise stent deployment.
CLINICAL BENEFIT	
Safety	• **Low 30-day major adverse cardiac event (MACE) rates following IVL (primary outcome):** 0-8.3% (ECRI 2021, Disrupt CAD III and IV studies), compared to 10.4-15.0% for atherectomy (Saito 2021, only hypothetical as no direct comparative studies available) • **Low 1-year MACE:** 13.8% (Disrupt CAD III study, Kereiakes 2022), compared to 16.9% to 24.2% for atherectomy (Saito 2021, only hypothetical as no direct comparative studies available) (cardiac death: 1.1%, MI: 10.5%, ischemia-driven target vessel revascularization: 6.0%) and target lesion failure occurred in 11.9% (ischemia-driven target lesion revascularization (ID-TLR): 4.3%), both driven by non-Q-wave myocardial infarction (MI) (9.2%). Stent thrombosis (definite or probable) occurred in 1.1% of patients (including 1 event [0.3%] beyond 30 days). *MACE: defined as the composite of cardiac death, myocardial infarction (MI), or ischemia-driven target vessel revascularisation; target lesion failure defined as cardiac death, MI, or ischemia-driven target lesion revascularisation (ID-TLR). • **Low rates of periprocedural complications/ adverse events:** 0-8%, including in patients with acute coronary syndrome, stent failure, and left main coronary artery lesions (Wiens 2021) and 8.33% (Sattar 2021. Patients developed complications such as vessel dissection) In ECRI 2021, Hill 2020 reported that 2 of 384 patients experienced severe dissection and abrupt closure or perforation. Aksoy 2019 reported that 6 of 39 patients experienced type b dissections or balloon rupture. Ali 2019 and Brinton 2019 reported that 5% to 6% of patients experienced periprocedural myocardial infarctions. Saito 2021 reported no periprocedural complications. **Stent under-expansion (off-label)** • There is no procedural, periprocedural, or 30-day major adverse cardiac and cerebrovascular event. (Yeoh 2021) • No cardiac death, target lesion revascularisation and stent thrombosis occurred in-hospital and at 30-day follow-up. (SMILE Registry, Ielasi 2020) • Non-fatal periprocedural ST-elevation myocardial infarction occurred in one case (2.5%) due to IVL balloon rupture. (SMILE Registry, Ielasi 2020)
Effectiveness	• **High procedural success (primary outcome, defined as residual stenosis <50% by QCA without in-hospital MACE):** 84%-95% (ECRI 2021), 92.4% (Disrupt CAD III) and 93.8% (Disrupt CAD IV) • **High rates of angiographic and clinical success:** 98% (Wiens 2021; n=50) • Longer-term follow-up is required to determine the **durability of clinical benefit** and the **late impact of optimised stent implantation associated with IVL**. (Disrupt CAD III study) **Stent under-expansion (off-label)** • The average pre-IVL minimal stent area (MSA) was 2.71 mm^2, which improved to 6.44 mm^2 post-IVL treatment, representing an average minimal stent area gain of 238%. (Yeoh 2021) • IVL was successful in 34 cases (87.1%), with significant improvement in minimal stent diameter and minimal stent cross-sectional area

SUITABILITY OF PATIENT GROUP	
Suitability of Patient Group	**Number of patients per year:** 0-10 patients (SALHN); 5-10 patients (CALHN) and 10 patients (NALHN). SA Health The main clinical indication will be patients with severe calcified coronary arteries (evidenced using intravascular ultrasound/optical coherence tomography) requiring PCI for significant angina or acute coronary syndrome. These patients are not amenable to conventional technologies in calcium modification, including rotational atherectomy (rotablade), high-pressure balloon dilatation or cutting balloons. The clinicians from SALHN and CALHN are keen to use IVL off-label for stent under-expansion treatment (evidenced by coronary angiogram/intravascular ultrasound/optical coherence tomography) after PCI. Off-label use has been reported for one CALHN patient who had an under-deployed stent due to concentric calcium that could not be dilated with an ultra-high-pressure balloon. This under deployment resulted in early stent thrombosis and hospital representation. The patient also failed high-pressure ballooning. However, full stent expansion was achieved with the shockwave IVL procedure. A published paper, Mousa 2021, proffered that cracking the calcium preventing stent expansion by using IVL may also be an attractive approach to managing stent under expansion after PCI. However, using IVL for this indication carries the risk of damaging the drug-polymer, increasing the risk of eventual stent thrombosis and restenosis. Hence, the manufacturer does not recommend using IVL in patients with previous stenting within 5 mm of the target lesion. Whether or not the theoretical effect of IVL on the drug-polymer has any clinical impact on a patient's outcome remains to be elucidated.
FINANCIAL CONSIDERATIONS	
Device costs	[Confidential to be redacted] Total costs across SA Health per year (first year): $[redacted] * (per catheter consumable; ex GST) x 30 patients = $[redacted] Total costs across SA Health per year (second year): $[redacted] * (per catheter consumable; ex GST) x 30 patients + $[redacted] x 3 units (generator (capital); ex GST) = $[redacted] *The generator will be provided [redacted] for the first year. [redacted] (communication with distributor Diverse Devices, 5 April 2022). The company will provide maintenance and servicing. No software is required. The company representatives provide staff training free of charge, and there are no other related procedural costs. Comparator cost: [redacted], the Rotablator as usual treatment of choice.
Value for Money	The literature search did not identify any articles addressing the cost-effectiveness of the shockwave IVL. However, Kassimis (2021) article explored the need for cost-effectiveness analysis. Despite the higher cost of the lithotripsy device compared with balloon techniques (cutting, scoring, ultra-high pressure), it may be more cost-effective in the long term. This assumption was based on the need for less use of any additional specialty device, fewer complications, greater procedural success and better long-term clinical results. A comparison with the atherectomy devices (rotational, orbital, laser) may also favour the shockwave IVL because of fewer complications and probably better long-term outcomes. However, lesion characteristics treated with each device (superficial vs deep calcium, circumferential distribution, bifurcations or ostial lesions, reference vessel diameter) may introduce uncertainty. Further, an economic analysis should consider any contraindication to device-specific treatment. To align with all device or procedure assessments in interventional cardiology, Kassimis 2021 suggest that a broad approach incorporating all indirect costs and savings from applying this technique is required. Therefore, thorough cost-effectiveness analysis should include; • the cost of the device, • the cost or saving of other devices used or not used (e.g. more or fewer stents after shockwave IVL than after only non-compliant (NC) or specialty balloons or after atherectomy, more or less NC balloons after shockwave IVL than after atherectomy, more burrs with atherectomy etc.), • cost of any re-intervention required for target lesion failure after shockwave IVL, • cost of any re-intervention following other techniques for treating severe calcification, • cost of any complications, • cost of hospitalisation duration, • cost impact of morbidity and mortality.
Australian Funding Approvals	None identified from Commonwealth Medical Services Advisory Committee (MSAC) and the Commonwealth Prosthesis List Advisory Committee (PLAC). In November 2019, the Australian Health Ministers Council Health Technology Reference Group raised coronary lithotripsy as a nominated topic; however, the Group was shortly disbanded. The applicant advised that the device has been approved for use at specified centres in Victoria, New South Wales, Western Australian, Australian Capital Territory and Tasmania. Interstate experiences [Confidential to be redacted] [redacted]

	[redacted] Overseas experiences UK National Institute for Health and Care Excellence (NICE) Guidance 2020: NICE recommended that the evidence on the safety and efficacy of shockwave IVL for calcified coronary arteries during PCI is limited in quantity and quality. Therefore, special arrangements for clinical governance, consent, and audit or research for this procedure are required for its use.
FEASIBILITY OF ADOPTION	
Organisational Feasibility	Risk assessment The Applicant stated that the risk is considered to be lower than rotational atherectomy. Patient consent The Applicant proposed that PCI consent encompasses all standard techniques; hence, specific consent for this additive technology is not required. Clinical outcomes evaluation and broader retrospective and prospective audit The SALHN Cardiology department will monitor a register of all cases undertaken together with clinical outcomes. In CALHN, the clinicians will evaluate their data as part of the Coronary Angiogram Database of South Australia (CADOSA) registry. In addition, results will be presented regularly at the Cardiology multidisciplinary meetings and as part of the CADOSA data presentation. Also, SAPACT is to be advised of outcomes.
Credentialing and Competency	The CALHN applicant noted no formal credentialing process for the shockwave IVL. Unlike atherectomy, which is associated with a steep learning curve and high operator volume to determine favourable outcomes, IVL requires no specific training as the IVL device is delivered similar to the standard catheter-based PCI. In addition, the ease of use and safety profile meant that once the clinicians feel comfortable with the device after the company provides the necessary initial training, they can use it without company support or seek ongoing support. The SALHN applicant outlined that the only initial training required is for the protocol to deliver the shockwave lithotripsy (i.e. how many shocks to deliver to each lesion being treated, the length of intervals, and the maximum number of shocks). Therefore, only one roll-in patient prior to enrolment is required since minimal training is needed. The shockwave IVL procedure should only be done by clinicians with specific training and accreditation in the procedure. The clinicians should be appropriately credentialed and approved by the SA Health Credentialing and Scope of Practice Committee to use the shockwave IVL (refer to paragraph 3.4.3 New Clinical Procedures, Technologies and Treatments of the SA Health Credentialing Policy Directive).
CONSISTENCY WITH EXPECTED SOCIETAL/ ETHICAL/ LEGAL VALUES	
Values	Consistent with expected societal, ethical and legal values at this time.
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