South Australian Policy Advisory Committee on Technology (SAPACT)

Health Technology Assessment (HTA) Decision Summary

Government of South Australia

SA Health

Impella® temporary heart pumps for treating cardiogenic shock

SAPACT MEETING DATES	31st, 27th and 18th SAPACT Meeting (18 August 2023, 10 December 2021 and 7 June 2019)
APPLICATION #	2313-2128-1903
TECHNOLOGY	Impella CP®, Impella CP with SmartAssist, Impella 5.0® Model 004680 and Impella Introducer Kit (Abiomed Australia Pty Ltd) The Impella is a minimally invasive heart pump that temporarily (≤ 6 hours) maintains blood flow during high-risk percutaneous coronary intervention (PCI) procedures or cardiogenic shock (CS). It allows the heart to rest and pumps blood to vital organs while the physician treats the underlining disease.
TECHNOLOGY CLASSIFICATION	TGA class III high-risk
PATIENT INDICATION (TGA)	TGA intended purpose: The Impella is a circulatory support system for patients with reduced left ventricular function, e.g, postcardiotomy, low output syndrome, CS after acute myocardial infarction, or for myocardial protection after acute myocardial infarction. The Impella may also be used as a cardiovascular support system during coronary bypass surgery on the beating heart, particularly in patients with limited preoperative ejection fraction with a high risk of postoperative low output syndrome.

SAPACT DECISION

☒ Restricted recommendation for clinical use with financial or operational restrictions

Background

SAPACT discussed an updated application at the 31st SAPACT meeting. The application proposes the use of Impella in appropriately selected patients with cardiogenic shock who remain haemodynamically unstable despite optimal medical therapy. The most relevant alternative in Australian clinical practice for these patients is venoarterial extracorporeal membrane oxygenation (VA-ECMO). However, Impella and VA-ECMO provide haemodynamic support through different mechanisms so are not always directly comparable.

SAPACT Evidence Review Conclusions

In patients with cardiogenic shock, the recent international scientific literature showed that while Impella can be associated with serious complications (severe or life-threatening bleeding, peripheral vascular complications, high inpatient mortality and device deployment/retrieval issues), that Impella may have improved safety outcomes compared to VA-ECMO. Used in combination with ECMO to unload the left ventricle (ECPELLA), there were more adverse events such as reported bleeding compared to ECMO alone. The applicant notes that this is likely due to the combination of two mechanical circulatory support devices. Compared with ECMO, Impella is associated with improvements in short-term mortality (30 days) with some studies reporting improvements in long-term mortality (6 to 12 months), and its use for temporary circulatory support is recognised in recent international clinical practice guidelines. Despite a lack of randomised controlled trials (RCTs), the minimally invasive Impella devices are increasingly supported and used by clinicians for cardiogenic shock patients.

The use of mechanical circulatory support devices including Impella is costly. ECMO is one of the most expensive diagnosis-related groups, costing up to $305,463 per episode of care. An economic model for the use of Impella in SA Health cannot be produced with certainty, given the lack of good quality data. Cost analyses from the perspective of US and France show that the use of Impella can be cost saving compared to VA-ECMO. The use of ECPELLA will be more expensive than ECMO alone, due to the use of two interventions.

The total estimated direct cost to SA Health for the use of Impella will be $[redacted]/year for the device (for [redacted] patients), plus capital costs of $[redacted] for the control unit, plus hospital costs.

SAPACT Advisory Recommendations (31st SAPACT meeting)

SAPACT recognises that there is a high level of morbidity and mortality in patients with refractory cardiogenic shock, and that there is a significant unmet need in this population. The evidence-base for this technology is limited to retrospective studies, reflective of the difficulty in undertaking large randomised controlled trials in this population of patients who present with acute symptoms.

SAPACT advises that short-term mechanical circulatory support using Impella is an option for appropriately selected patients with cardiogenic shock who remain haemodynamically unstable despite optimal medical therapy. Recent clinical practice guidelines have identified that temporary mechanical circulatory support, including with Impella, is reasonable when end-organ function cannot be maintained by pharmacologic means to support cardiac function or for short-term therapy in selected patients with CS with potentially reversible underlying cause or who are transplant or ventricular assist device (VAD) candidates. There are two sub-populations:

- patients with refractory cardiogenic shock (for example, associated with acute myocardial infarction, severe Takotsubo cardiomyopathy and myocarditis).
- patients with refractory cardiogenic shock who are on VA-ECMO and require unloading of the left ventricle (ECPELLA).

Patients contraindicated for the use of Impella (e.g. patients with a high likelihood of significant anoxic neurological injury) will be excluded. Impella is not proposed for use in patients undergoing elective high-risk percutaneous coronary intervention (PCI) in the absence of established refractory cardiogenic shock, or patients with right heart failure.

Patients should be selected at the discretion of a dedicated multidisciplinary cardiogenic shock team. The following medical staff are proposed at CALHN:

- Intensive care physician with dedicated cardiogenic shock / ECMO expertise
- Heart Failure / Structural-based (non-Interventional) Cardiologist
- Interventional cardiologist with appropriate training and credentialling for Impella implantation
- Cardiothoracic surgeon (where required), including where cardiothoracic surgery is being considered

A centralised funding model for 10 devices per year is proposed, with indications for use formally agreed through the Statewide Structural/intervention Sub Committee of the Statewide Cardiac Care Clinical Network (SCCCN), Commission on Excellence and Innovation in Health (CEIH).
The lack of high-level evidence available for the use of Impella, and the inconsistent reporting of outcome measures across studies means that some outcomes related to the use of Impella are uncertain. SAPACT agrees with the applicant for retrospective multidisciplinary (MDT) review each use of Impella, with reporting to the SCCCN. This information will be valuable to further refine patient selection and use in the local setting.

- SAPACT should be provided with a report of the MDT reviews of the first 10 patients, including 90-day mortality
- SAPACT should be notified of any proposed changes in the use of this technology

Any use of Impella at SALHN or NALHN should first be agreed with the LHN new technologies and procedures committee, confirming the members of the MDT/Shock team in line with the composition as shown above. SAPACT should be notified of this decision.

SAPACT Advisory Recommendations (27th SAPACT meeting)
Given the little or no evidence of benefit (safety, clinical-effectiveness and cost-effectiveness) of the Impella in treating left ventricular heart failure, at this stage SAPACT supports the applicants' proposed establishment of heart MDTs / shock teams at the Royal Adelaide Hospital (CALHN) and Flinders Medical Centre (SALHN). MDTs members should have equal voice to discuss the clinical need of the addition of the Impella devices to the current range of conventional mechanical circulatory support devices already available for use in SA Health. Until the MDT teams are established **AND** more robust high quality evidence are made available, at this stage, it is very difficult for SAPACT to recommend the use of Impella in SA Health. With the MDT teams set up, SAPACT welcomes further discussions with the chief applicant, demonstrating the evidence-based need for the Impella for statewide clinical use in SA Health.

Previous SAPACT Advisory Recommendations (18th SAPACT meeting)
SAPACT recognised the evidence challenges for the safety, clinical- and cost-effectiveness of the Impella CP and 5.0 cardiac-assist devices for patients with high risk PCI or for patients with CS. The key concerns were (1) weak and inconsistent evidence; (2) lack of benefit in terms of improved mortality rates with the Impella device when compared with IABP; and (3) uncertainty on patient selection.
To address these key concerns, the applicant proposed that the appropriate selection of patients is critical to ensure patient benefit and to avoid the use of the device in futile situations. SAPACT is supportive of the applicant's approach, hence, recommends the deferment of a statewide advisory recommendation, until the applicant, in consultation with the relevant medical departments, develops a (1) proposed collaborative clinical algorithm and patient selection pathway for the optimal use of Impella, ECMO and IABP in SA Health and outlines a (2) clinical outcomes measurement report for SAPACT to consider.
Impella costing data and any other updated published evidence, including the results (to be released in November 2019) of the Commonwealth MSAC Impella, should also be submitted to SAPACT for review.

REGULATORY APPROVALS

☒**Australia ARTG**: 344062 Impella CP – 22/09/2020 365210 Impella CP with SmartAssist* REF 0048-0008 - 10/05/2021; 307717 Impella 5.0 Model 004680 - 2/08/2018; 288729 Introducer Kit for Impella- 03/06/2021	☒ **US FDA**: Impella CP – 4/7/2016 (CS); 12/08/2016 (high-risk PCI); Impella 5.0 – 4/7/2016 (CS); Impella ECP -20/08/2021 (high-risk PCI) Impella ECP is the world's smallest heart pump and is only 3mm (9 French) in diameter upon insertion and removal from body. While in the heart, it expands to support the heart's pumping function, providing flow greater than 3.5 L/min. US FDA: Granted the breakthrough status based in part on positive clinical data from the first 21 patients with high-risk PCI treated with the pump as part of an early feasibility study	☒ **EU CE mark**: Impella CP – 4/2012; Impella 5.0 – 01/2003 for both high-risk PCI and CS; Impella 5.5 with SmartAssist – 04/04/2018 (flow rate of up to 6.0 L/min

Impella CP	• Flow rate of up to 2.5 L/min • Temporary (≤6 hours) for use during high-risk PCI • short term use (up to 5 days)
Impella CP with SmartAssist	• Flow rate of up to 4.3 L/min • Short term use (up to 5 days) • SmartAssist - allows for sustained peak flows of up to 4.3 L/min (>85% of a normal cardiac cycle). It is designed to improve patient outcomes by using real-time intelligence to optimize positioning, managing and weaning of Impella.
Impella 5.0	• Flow rate of up to 5.0 L/min • Short term use (up to 10 days)

QUALITY OF EVIDENCE

Quality of Evidence	2023 The applicant undertook an independent literature review and meta-analysis of relevant studies. In addition, a number of recently published systematic reviews were available. Evidence was available for both included sub-populations, but was restricted to retrospective, non-randomised comparative studies. There was no RCT evidence. In line with standard Australian clinical practice, the comparator is VA-ECMO. As recognised by MSAC in its Public Summary Document, intra-aortic balloon pumps are not commonly used in Australia for cardiogenic shock.

	Cardiogenic shock: The application included 5 retrospective non-randomised comparative studies (Karatolios 2021, Lemor 2020, Schiller 2019, Syntila 2021, Wernly 2021). Some authors in some, but not all, studies declared speaker honoraria from Abiomed. There were a number of recent systematic reviews of Impella for this population, of which 3 compared outcomes with VA-ECMO (Abussina 2022 (no conflicts), Ahmad 2023 (no conflicts), Batchelor 2022 (Abiomed provided minor research support to one author, but had no part in the study design or reporting). There were some differences in included studies across analyses; however, the application included the most recent, largest studies, which had adjusted for potential confounders. Patients with refractory cardiogenic shock who are on VA-ECMO and require unloading of the left ventricle (ECPELLA): The application included 4 retrospective non-randomised comparative studies (Pappalardo 2017, Schrage 2020, Patel 2018, and Radakovic 2022). In 2 studies authors declared no conflicts of interest and in 2 studies some authors declared funding from Abiomed. There were 3 recent systematic reviews for this sub-population (Bhatia 2022, Fiorelli 2021, Iannccone 2022), all of which reported no conflicts of interest. The included studies in the published systematic reviews were similar to those presented in the application. Additional studies in published reviews included conference abstracts and studies which did not adjust for potential confounders. The studies presented in the application are an appropriate representation of the relevant evidence base. 2021 For the evidence update (2019-2021), the comprehensive search strategy and study screening were conducted utilizing the same 30 databases as 2019. No landmark high quality RCT (level I evidence) was identified. HTA reports and published journal studies (small open-label RCTs and several large matched cohort studies formed the bulk of the clinical evidence. The search results found the (1) Commonwealth Medical Services Advisory Committee (MSAC) Public Decision Summary (November 2019) for Impella, and three published journal articles: (2) Karami 2021 IMPRESS open-label RCT n=48; (3) Bochaton 2020 IMPELLA-STIC open-label RCT n=15 and (4) Philipson 2021 FDA MAUDE database. All three journal papers reported no conflicts of interest. The chief applicant provided five published papers to support management of CS using shock teams (Papolos 2021, Thiele 2021, Iannaccone 2020, Taleb 2019, Tehrani 2018). Thiele 2021 is a clinical practice guideline that cited three matched studies (Schrage 2019, Dhruva 2020 and Amin 2020). The National Institute for Health and Care Excellence (NICE) IPG633 Guidance 2018 is scheduled for review in November 2021, however, NICE has advised SAPACT that its 2018 guidance still stands as no decision has been made to update the guidance. The PROTECT IV open-label RCT for high-risk PCI is recruiting, with the primary study completion planned for 2024. Local consultations and inputs with the Chief Applicant and Applicant proxies, LHNs Cardiology Leads, SA Health HTA, Economics Experts, Procurement, Centre for Excellence in Innovation and Health (CEIH), industry, NICE UK and national/interstate HTA groups (Commonwealth Prosthesis List Advisory Committee (PLAC), Victorian Policy Advisory Committee on Technology (VPACT), Queeslandland Policy Advisory Committee on Technology (QPACT), New South Wales (NSW) Health and MonashHealth) also informed the SAPACT Advisory Recommendations. 2019 A comprehensive systematic search for best available HTA and policy evidence was conducted in 6 published and 24 grey literature sources. Since HTA reports were available (NICE Guidance 2018 and Health Quality Ontario 2017), no development of a SAPACT Evidence Review was required. SAPACT found the best available evidence underwhelming. The NICE Evidence Review 2018 was based on 7173 patients from 4 systematic reviews, 3 case-series, 1 RCT and 2 case reports, and seemed to limit the population to those undergoing PCI only. The systematic reviews contained observational as well as randomised evidence. The best quality evidence identified by NICE was the Health Quality Ontario 2017 HTA Report. The Health Quality Ontario Report was well conducted. The evidence included in the Health Quality Ontario Report was generally poor quality. The review separated the literature by population – high risk PCI (11 studies) and CS (7 studies). The study included Impella 2.5, Impella 5.0 and TandemHeart. The timing of the search missed one relevant RCT of Impella CP vs IABP; Ouweneel et al 2016 (Impella CP vs IABP for CS). The extrapolation of the data for the Impella 2.5 to the Impella 3.5 is reasonable (confirmed by the applicant) as it is a conservative assumption i.e. because Impella 3.5 provides a higher flow at 3.5 litres/minute, it should theoretically be superior in benefit but equal in risk (same size of vascular access diameter). In all other respects, the mechanism of action and design are consistent between the two catheters.
CLINICAL NEED	
Burden of Illness	The Australian Institute of Health and Welfare (AIHW) reported a national total of 16,594 separations for heart failure with shock and catastrophic outcomes over a period of 1 year (2014-2015). It is unclear whether this accurately reflects the population in which Impella is intended to be used. CS occurs in 7-10% of patients who have an acute MI, and is associated with a 30 day mortality rate of 37% - 65%. There were 9,166 cases of PCI were performed in in Victoria in 2015. The unadjusted in hospital mortality was 1.6%. Mortality rates were higher for ST-Elevation Myocardial Infarction (STEMI) (5.6%) and CS (40%). Impella devices are increasingly utilized for hemodynamic support in high-risk PCI or CS despite a lack of randomized clinical trial data showing clinical benefit and newer observational data suggesting harm. There are reportedly 65,000 patients implanted with the Impella range of devices worldwide, which is a small number considering that the Impella has been approved in Europe for more than 15 years. In Australia, there are thousands of patients with high-risk PCI.
Need	Cardiogenic shock is the most severe complication of acute myocardial infarction, with a mortality rate of around 50%. Clinicians seem to increasingly prefer and support the use of Impella, likely due to its less traumatic and minimally invasive rapid insertion

	features, compared to ECMO. The clinical need for Impella is uncertain - it is unclear what proportion of patients with CS, or who are undergoing PCI, would require Impella. It is unclear whether Impella would alter patient outcomes.
CLINICAL BENEFIT	
Safety	2023 Patients with cardiogenic shock: From the application, there were fewer bleedings requiring transfusions with IMPELLA compared to VA-ECMO (odds ratio [OR]=0.61 [95% confidence interval (CI): 0.46, 0.80] p=0.0004). Published systematic reviews also reported significant improvements in bleeding (p<0.00001) (Abussina 2022), access site (p<0.0001) or major bleeding (p=0.002) (Ahmad 2023). Other complications were not consistently reported and were not meta-analysed. Results from individual studies showed improvements for Impella for acute ischaemic stroke, acute kidney injury requiring dialysis, acute respiratory failure, acute respiratory failure, limb ischaemia requiring intervention and vascular complications. Published systematic reviews reported a reduced risk of stroke with Impella compared to VA-ECMO (Abussina 2022, Ahmad 2023) and less limb ischaemia (p=0.0001) (Ahmad 2023). Patients with refractory cardiogenic shock who are on VA-ECMO and require unloading of the left ventricle (ECPELLA): From the application, meta-analysis showed that 50.0% of ECPELLA patients and 36.8% of VA-ECMO patients had bleeding requiring transfusion (OR=1.65 [95% CI: 1.15, 2.37] p=0.007). Published systematic reviews showed no significant differences in major bleeding (p=0.11, p=0.16, OR: 0.57 [95%CI: 0.273–1.200 respectively) (Bhatia 2022, Fiorelli 2021, Iannaccone 2022). Other outcomes were not reported consistently across studies and were not meta-analysed. For hemorrhagic stroke and ischemic stroke, there was a similar number of events experienced by patients treated with ECPELLA versus VA-ECMO alone. However, events such as haemolysis, intervention because of access-site related ischemia, laparotomy because of abdominal compartment and renal replacement therapy were more frequent in the ECPELLA arm compared to VA-ECMO. The applicants comment that these safety results are expected given the ECPELLA patients are being treated with two mechanical circulatory support devices as opposed to one. Results from published systematic reviews were in line with these data with higher rates of hemolysis (p<0.001 and p<0.00001), and renal failure requiring continuous renal replacement therapy (p<0.0001, p=0.03) (Bhatia 2022, Fiorelli 2021), and VAD/heart transplant (p=0.0001) (Bhatia 2022). 2021 Philipson 2021 paper retrospectively analysed adverse events and inpatient mortality since introduction of the Impella from the US FDA Manufacturer and User Facility Device Experience (MAUDE) database and the US National Inpatient Sample (NIS) database from 2008 to 2019. The Impella devices recorded were the Impella 2.5, CP, 5.0, 5.5, and RP. Among the 885 complete voluntary reports submitted, there were 1,206 complications coded; 88.2% of reports occurred from 2016 to 2019. Among patients with adverse events reported, bleeding (32.8%), device deployment or retrieval issues (18.2%), vascular complications (15.8%), and death (12.4%) were the most common, and 7.9% of all complications were attributable to operator decision-making or technique. From 2007 to 2017 there was a more than 100-fold increase in percutaneous ventricular assist devices use with an increase and plateau in in-hospital mortality to 31% from 2012 to 2016 based on NIS data. The paper concluded that Impella use had increased substantially over the last decade but remains associated with high inpatient mortality and serious complications based on data from the NIS and MAUDE databases. High Risk PCI Population The Evidence Update 2021 found no new Impella RCTs conducted in high risk PCI population. The evidence analysis was focused on O'Neill 2012 paper. The safety outcomes of the Impella appear to be comparable to IABP. There is no difference in mortality rates between Impella and IABP Evidence suggests there may be slightly more serious bleeding events with the Impella device. The primary safety outcome of the Impella is the composite of major adverse events (MAEs), measured at discharge or 30 days – whichever was longer. The composite MAEs were very difficult to interpret – particularly in the presence of key differences in baseline characteristics and marked differences in procedures. It was also unclear how the composite MAE (e.g. revascularisation) measured at 30 days would be accurately attributed to the Impella device that is in place for 2-8 hours. Most of the differences in patient MAE outcomes occurred out of the hospital. It was unclear how these safety outcomes may be accurately attributed to the devices (IABP or the Impella), to the procedure itself or the individual patient. Cardiogenic Shock Population Karami 2021 published results of long-term 5-year outcome of pivotal IMPRESS trial (versus 6-mth in Ouweneel 2017 paper included in MSAC PSD) in CS. In the same cohort of patients n=48, there was no difference in long-term 5-year all-cause mortality and functional status between Impella and IABP-treated patients, supporting previously published short-term data and in accordance with other long-term CS trials. CS patients treated with IABP or Impella CP had similar survival rates, but IABP supported patients had a numerical higher occurrence of major adverse cardiac and cerebrovascular events (MACCE, including death, myocardial re-infarction, repeat PCI, coronary artery bypass graft (CABG) and stroke). Bochaton 2020 IMPELL-STIC randomised study (n=15; Impella 5.0 + IABP vs IABP group) was concerned over the safety of the Impella, especially in relation to bleeding. Major bleeding occurred in five out of seven patients in the Impella LP5.0 + IABP group and none in the IABP group. It is known from the IABP-SHOCKII study that IABPs are neutral in term of complications, especially bleeding. Available data indicate that the risk-benefit ratio of the Impella strategy in INTERMACS® 3 patients (stable but inotrope dependent) with CS-AMI is questionable. In studies that compared the Impella with an IABP, major bleeding was 2-4 times more frequent with the Impella compared with an IABP. The RCT (Seyfarth 2008) n=25 found no difference between Impella and IABP in terms of mortality and very high rates of mortality (30 day mortality was 46% in each arm). Seyfarth 2008 also reported benefit of Impella over IABP for change of cardiac index, diastolic

	arterial pressure and trending for serum lactate. The Impella CP IMPRESS study (comparing Impella CP with IABP) reported no difference in the primary outcomes of 30 day all-cause mortality (46% vs 50%) and 6 months all-cause mortality (50% vs 50%).
Effectiveness	2023 Patients with cardiogenic shock: From the application, compared to VA-ECMO, Impella reduced in-hospital/30-day mortality (OR=0.51 [95% CI 0.40, 0.66] p<0.00001). There was no difference in long-term mortality (6 month mortality OR=0.71 [95% CI 0.43, 1.19] p=0.19). This improvement in short-term mortality was also reported in published systematic reviews (Abussina 2022, Ahmad 2023, Batchelor 2022). One review also reported an improvement on 6-12 month mortality (risk ratio 0.86 [95% CI 0.76, 0.97], p=0.02) (Batchelor 2022). Patients with refractory cardiogenic shock who are on VA-ECMO and require unloading of the left ventricle (ECPELLA): From the application, 30 day mortality was improved with Impella compared to ECMO (OR 0.71 95% CI [0.50, 1.00] p=0.05, 2 studies). Long-term mortality was also improved (hazard ratio 0.39 [95% CI: 0.19, 0.81] p=0.011, one study). Results from published systematic reviews were in line with these data with reported improvements in short-term mortality (Bhatia 2022, Fiorelli 2021, Iannaccone 2022). 2021 Overall, the Commonwealth MSAC considered that the Impella was non-inferior or less effective compared to IABP (in high-risk PCI and CS groups), and uncertain compared to ECMO (in CS group). High Risk PCI Population The haemodynamic outcomes (cardiac output favoured Impella while the device was in place) were of questionable relevance if they were not associated with an improvement in mortality. The haemodynamic outcomes were also only measured in a subgroup of patients and it was unclear how these patients were selected. Cardiogenic Shock Population The Health Quality Ontario 2017 HTA Report showed clear before and after improvements in haemodynamic outcomes, however, similar to the high risk PCI group, there was no obvious correlation between haemodynamic outcomes and mortality. The patient and clinical relevance were unclear. Bochaton 2020 found that in patients presenting with CS caused by acute myocardial infarction, and stabilized by initial treatment with inotropes and an IABP, the use of the Impella LP5.0 provided no additional short-term haemodynamic support and no improvement in LVEF at 1 month. Therefore, the use of this pump in such patients is probably futile and possibly harmful.
SUITABILITY OF PATIENT GROUP	
Suitability of Patient Group	2023 The applicant has updated the patient selection. The proposed population is restricted to patients with cardiogenic shock. The patient group includes two sub-populations: • Patients with refractory cardiogenic shock (for example, associated with acute myocardial infarction, and also severe Takotsubo cardiomyopathy and myocarditis) who require left ventricular support • Patients with refractory cardiogenic shock who are on VA-ECMO and require unloading of the left ventricle Patients contraindicated for the use of Impella (e.g. patients with a high likelihood of significant anoxic neurological injury) will be excluded. Impella is not proposed for use in patients undergoing elective high-risk PCI, or patients with right heart failure. Patients will be selected at the discretion of a multidisciplinary team including the following medical staff: • Intensive care physician with dedicated CS / ECMO expertise • Heart Failure / Structural-based (non-Interventional) Cardiologist • Interventional cardiologist • Cardiothoracic surgeon (where required), in cases where cardiothoracic surgery is being considered It is expected that up to 10 devices per year will be funded through a centralised funding model. The indications for use will be formally agreed through the Statewide Structural/intervention Sub Committee of the Statewide Cardiac Care Clinical Network (SCCCN), Commission on Excellence and Innovation in Health (CEIH). Any use of Impella outside the agreed indications will be payable by the LHN. Recent clinical practice guidelines provide guidance for the use of Impella in cardiogenic shock: • International Society for Heart and Lung Transplantation/Heart Failure Society of America (Bernhardt 2003) recommends the peri-implant use of Impella for adult patients with CS. Impella is also considered for unloading, in combination with ECMO. • The European Association of Percutaneous Cardiovascular Interventions (EAPCI) and the Association for Acute Cardiovascular Care (ACVC) (Chieffo 2021) recommends Impella CP as an option for short-term therapy in selected patients with CS with potentially reversible underlying cause/transplant/VAD candidates.

	• American College of Cardiology (ACC) and American Heart Association (AHA) (Heidenreich 2022). In the management of cardiogenic shock, temporary mechanical circulatory support is reasonable when end-organ function cannot be maintained by pharmacologic means to support cardiac function. • European Society of Cardiology (McDonagh 2021) describes the use of short-term mechanical circulatory support including ECMO or Impella for patients with cardiogenic shock as a bridge to decision or bridge to bridge or bridge to recovery. Guidelines recognise the lack of direct comparative data, the complexity involved with mechanical circulatory support, including complications related with the use of Impella (e.g. vascular, bleeding, and neurologic complications), and the importance of MDT involvement in patient care. <u>2021</u> Number of patients per year: 10 patients in SALHN and 15 patients in CALHN, anticipating that up to 5 CALHN patients may be from a NALHN in the first instance. In 2019, it was estimated that CALHN would use 6 per year (2 complex PCI, 4 CS). The chief applicant's amended protocol covers patient selection related to heart MDTs/shock teams, with some reference to algorithm for the choice of mechanical circulatory support device. The chief applicant has proposed the use of Impella in: • Patients with acute myocardial infarction CS: Use of shock team to determine eligibility for Impella (published frameworks can be used to help determine the appropriateness of use of Impella – i.e. TUFTS algorithm provided in the protocol) • Patients undergoing very high risk PCI: Discussion with MDT, with ICU input (although clinical urgency may prohibit consultation with the heart team). The use of Impella in this patient group is infrequent (<5%) and patients should require escalation to mechanical support. There is also evidence to suggest net harm can be done to patients undergoing high risk PCI if Impella is used routinely, largely owing to the incremental risks involved. The key challenge is to avoid the use of Impella in those patients who would have tolerated the procedure just as well without mechanical circulatory support. • Patients with non-ischaemic CS with a reversible cause: Rare and are commonly from acute fulminant myocarditis and severe/extensive Takotsubo cardiomyopathy The chief applicant's amended protocol intents to minimise harm by: • Involvement of heart team, or other team based strategies (if urgency precludes standard MDT) • Established National Cardiogenic Shock Initiative (NCSI) pathway for patients with CS • Personnel to have extensive experience • Insertion under direct fluoroscopic imaging • Clinicians to be credentialed Through a collaborative working group across SALHN and CALHN (utilising and reporting to the CEIH Cardiology Statewide Clinical Network), the applicants will ensure that shock teams are operational at each site with standardised construct and operation. The shock team literature is particular about ensuring that treatment decisions are individually tailored but based on optimal clinical data and responses to pharmacotherapy, as well as consideration of futility. In particular, the rapid MDT approach ensures that the best therapy for a particular patient at a particular time is selected, based on consideration of potential benefits and risk. This approach delivers superior outcomes but is not necessarily based on device specific algorithms, but rather selection of the most appropriate device at the time e.g. ECMO, pharmacotherapy/inotropes, balloon pump, or Impella.
FINANCIAL CONSIDERATIONS	
Device costs	<u>Total costs across SA Health per year</u>: $[redacted] x [redacted] = $[redacted] per year based on [redacted] patients. Additional costs include capital costs of the Automated Impella Controller and IMPELLA purge system (one unit, $[redacted]), theatre/cardiac catheter laboratory time, and ICU care. <u>Number of patients per year</u>: 10 patients expected through a centralised funding model. <u>Device costs</u>: $[redacted] (according to the applicant)
Value for Money	ECMO is known to be costly due to the costs of ICU beds and ICU support staff. VA-ECMO is costly, with an AR-DRG cost (A40Z) between $207,356 (application) to $305,463 (Linke 2020). The applicant provided a number of cost analyses from the US showing cost savings for Impella compared to ECMO. In the peer-reviewed literature the total costs for Impella varied between USD91,000 and USD142,000, with a mean overall 34% reduction of costs compared to ECMO. Additionally, a budget impact analysis from the French hospital perspective showed Impella was associated with cost savings compared to VA-ECMO, over a 5-year time horizon (Le Guyader 2021). There were no reported costs for the use of ECPELLA which is expected to be more expensive than ECMO alone due to the use of two interventions. The SA Health Health Economics and Analytics Team (HEATS) had indicated that there is little SA Health specific context /costing it could provide to inform the economic component of the Impella review. The MSAC Decision Summary advised that IABP and ECMO are the comparators for the high-risk PCI group, whereas ECMO is the comparator in the CS group. No local comparative costing data is available from Abiomed sponsor, SA Health Procurement and Economics Units, comparing Impella vs IABP vs ECMO. Given the data paucity, an SA Health economic model cannot be produced with certainty. The value for money of Impella relative to ECMO in SA Health is unclear. MSAC conducted an economic evaluation (November 2019) as part of the HTA review. The Health Quality Ontario (2017) presented two published economic analyses from Europe (Roos 2013) based on registry data (Europella and USpella) and the US (Gregory 2013)

	based on the PROTECT II trial (O'Neill 2012). The Gregory 2013 paper took short term 90-day data from the RCT and extrapolated out to 10 years. The model estimated that Impella was more costly but more effective than IABP. This is in contrast to the Health Quality Ontario economic analysis that reported a range from approximately USD40, 000 per additional QALY to dominated, the latter implying that the Impella was more costly and less effective than IABP. The key difference is that Health Quality Ontario incorporated the difference in the observed mortality rates from the O'Neill study. A local economic simulation analysis for 250 patients exploring adverse events and deaths per day was also conducted by a SAPACT member for the original application in 2019.
Australian Funding Approvals	Commonwealth Medical Services Advisory Committee (MSAC) The MSAC Public Decision Summary for Impella (Application 1523, considered in November 2019) was released in March 2020. It showed that MSAC did not support public funding for Impella® because the evidence was not high quality enough to show that it is safe and effective. The economic evaluation and financial impact were also uncertain. After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness and cost-effectiveness, MSAC did not support public funding of transluminal insertion, management, repositioning and removal of an IMVAD (Impella®) for patients requiring mechanical circulatory support. MSAC considered that the evidence for comparative safety and effectiveness was too uncertain relative to standard care in all three populations (high-risk PCI, CS and right-heart failure), which had flow-on effects to the economic analyses. MSAC considered the financial estimates were also highly uncertain and likely underestimated for all three populations. MSAC considered that additional data from RCTs would be required to give greater certainty regarding comparative safety, effectiveness and cost-effectiveness. Commonwealth Prosthesis List Advisory Committee (PLAC) The MSAC application 1523 stated that it was unclear whether the Impella would be funded on the Prosthesis List and that a submission for the Impella device to PLAC was underway. (Personal communication 29.11.2021) The *Prostheses Application Administration Section* has confirmed that they have not received an application to list the Impella on the Prosthesis List. It is also unclear whether it would meet the criteria for listing on the Prosthesis List. It depends on what it does, how long it stays in the patient and whether there is evidence to demonstrate that it is non-inferior to other treatment options. Interstate experiences Victoria: Victoria Health has not conducted a HTA review on the Impella. Only the Alfred Hospital and the Royal Children's Hospital use ventricular assist devices (VADs) (personal communication, 7 December 2021). MonashHealth conducted a HTA evidence review on the Impella in 2019 and has indicated that it is still not used in their sites (personal communication, 30 November 2021). Queensland: Queensland Health has not conducted a HTA review on the Impella. It is used in Prince Charles Hospital (public) for some years as part of standard care in a fairly select patient population (personal communication, 7 December 2021). As of March 2019, the applicant noted 28 instances of Impella use in the following Australian hospitals: Prince Charles Hospital (Queensland public), Liverpool Hospital (NSW public), and St Vincent's Hospital (NSW private).
FEASIBILITY OF ADOPTION	
Organizational Feasibility	This procedure may be used provided that arrangements are in place for funding, clinical governance, consent and audit by the LHN(s). Statewide model of care approach for the Impella device The applicant proposed that there will be a statewide model of care for shock teams and within this paradigm, there will be an agreed model of care for the consideration of Impella use. Impella insertion is a relatively minor component of the model of care. Detailed pathways will inform frequency of patient review, actions for complications/issues, and criteria for weaning and/or escalation of therapy. Clinical outcomes evaluation and broader retrospective and prospective audit The applicant proposes a retrospective MDT review of all Impella implants as part of quality assurance and reporting. Data will be collected prospectively in a mechanical circulatory support registry and reviewed/reported at least annually. Adverse events will be reported through existing safety and quality reporting systems. Organisational feasibility – differing staff, training/credentialing, resources, department budget etc The applicants proposed that the CEIH Cardiology Statewide Clinical Network may commission the use of Impella in Flinders Medical Centre (SALHN) and Royal Adelaide Hospital (CALHN), as they are sites with cardiothoracic surgery, complex vascular surgery and ECMO capability. Both sites are experienced in large bore femoral arterial access, have extensive Transcatherter Aortic Valve Implantation (TAVI) programs and are committed to support the Impella implementation.
Credentialing and Competency	The insertion procedure for Impella is performed by a cardiac surgeon (for IMPELLA 5.0 or 5.5) or by an interventional cardiologist/intensivist with extensive experience in femoral arterial access and experience in large bore femoral arterial access (for IMPELLA 2.5 or CP). The decision-making as to the need for Impella will be done by the shock team, of which the interventional cardiologist will be a member. The Impella 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 implant the Impella (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.
QUERIES TO	Manager, Health Technology Assessment (HTA) Program SAPACT, Medicines and Technology Programs, SA Department for Health and Ageing Level 8, Citi Centre Building, 11 Hindmarsh Square, Adelaide, SA 5000

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