South Australian Policy Advisory Committee on Technology (SAPACT)

Health Technology Assessment (HTA) Decision Summary

Government of South Australia

SA Health

Haemodialysis Reliable Outflow (HeRO®) graft for end stage renal disease patients with central venous stenosis and catheter dependency

SAPACT MEETING DATES	20th SAPACT Meeting, 22 November 2019
APPLICATION #	1910-SAPSC
TECHNOLOGY	HeRO® graft (Merit Medical Systems Inc, South Jordan, Utah, USA) The HeRO graft is a 6mm (inner diameter) expanded polytetrafluoroethylene (ePTFE) arteriovenous graft (AVG) that is coupled to a 19 Fr/6.33mm (outer diameter) tunneled central venous catheter (CVC). The HeRO graft is a subcutaneous AV access solution, bypassing blockage in veins, to maintain long-term access for haemodialysis patients with central venous stenosis (CVS).
TECHNOLOGY CLASSIFICATION	TGA class III high-risk
PATIENT INDICATION (TGA)	The HeRO graft is a synthetic graft prosthesis intended for use in maintaining long-term vascular access for chronic haemodialysis patients who have exhausted peripheral venous access sites suitable for fistulas or grafts.

SAPACT DECISION

☒ Restricted recommendation for clinical use under the Individual Patient Use (IPU) health technology process.
Re-application may be undertaken in future when new high quality evidence is available.

SAPACT Advisory Recommendations

SAPACT recognised the evidence challenges for the safety, clinical- and cost-effectiveness of the HeRO graft for end stage renal disease patients with central venous stenosis and catheter dependency.

The key concerns were (1) only US-based NHMRC level III and IV low level evidence were available; (2) ambiguous interpretation of exhausted arteriovenous fistula and arteriovenous graft options in the treatment algorithm for considering HeRO graft; and (3) the potential lack of generalisability of the largely African-American data in a systematic review.

The HeRO graft is not a conventional treatment and SA Health clinicians have advised of its use only in very rare and exceptional cases. Hence, SAPACT recommends that clinicians apply through the SA Health IPU health technology process for approval to use the HeRO graft in end stage renal disease patients with central venous stenosis and catheter dependency, who have exhausted arteriovenous fistula and arteriovenous graft options for permanent vascular access. The use of HeRO devices should be judicious, with (1) informed patient consent on risks and benefits; and (2) clinician's reporting of clinical outcomes at 6/12/24-month follow-up to SAPACT and LHN New Technology Committee for review.

Re-application may be undertaken in future with new high quality evidence.

SAPACT Evidence Review

The scientific literature on HeRO graft is limited to US-based NHMRC level III and IV low level evidence. While the published scientific evidence (comparison of two uncontrolled studies) showed that the HeRO graft has reduced access-related infections and reduced rate of interventions required to maintain patency compared to central venous catheters, no direct comparative published evidence were found for other outcomes, including primary and secondary patency rates (main primary outcomes), mortality, ischaemia, thrombosis, dialysis rate and quality of life. Percentage of successful vascular access placed as an outcome measure is also not reported in any study. Compared to arteriovenous graft, the HeRO graft showed similar patency, infection and dialysis rates. Compared to the femoral graft, the HeRO graft showed similar mortality and ischaemia rates, but had a higher intervention rate. High quality RCTs over a wider geographical area with long-term data are required to inform the safety, clinical- and cost-effectiveness of this technology.

REGULATORY APPROVALS

☒ **ARTG**: 11/10/2016 (281244 and 281245); 27/10/2016 (281847)	☒ **US FDA**: 30/01/2008; 510(K) approval	☒ **EU CE mark**: 2011

ARTG ID: 281244 HeRO 1001 – catheter, haemodialysis, implantable – venous outflow component (TGA class III)

The HeRO 1001 is the venous outflow component and has a 5mm inner diameter (ID), 19F (6.3mm) outer diameter (OD), and is 40cm long. It consists of radiopaque silicone with braided nitinol reinforcement (for kink and crush resistance) and a tantalum radiopaque marker band at the tip. It is placed in the central vein with the radiopaque distal tip in the mid to upper right atrium.

281245 HeRO 1002 – graft, vascular, synthetic - arterial graft component (TGA class III)

The HeRO 1002 is the arterial graft component and has a 6mm ID, 7.4mm (OD), and is 53cm long, inclusive of the connector. It consists of an ePTFE haemodialysis graft with PTFE beading to provide kink resistance near the titanium connector (the titanium connector attaches the arterial to the venous outflow component). A standard arterial anastomosis is performed to attach the component to the target inflow artery.

281847 HeRO surgical procedure kit (TGA class IIa)

A collection of various surgical instruments, dressings and necessary materials to perform a general purpose surgical procedure. This device can be presented as a kit, tray or set and does not contain any pharmaceuticals. This device is disposable.

QUALITY OF EVIDENCE

Quality of Evidence	Comprehensive systematic searches were conducted in 8 published scientific databases and 25 grey literature sources. The best available evidence from two systematic reviews (Maqsood 2019 and Shakarchi 2015) and a cost-analysis paper (Shakarchi 2016) informed the SAPACT review. There were no randomised controlled trials (RCTs) included in the systematic reviews, only US-

	based observational studies (NHMRC level III and IV). Maqsood 2019 appraised the included studies to be of poor quality, outdated, small number and have insufficient evidence to establish the role of this mode of haemodialysis. Shakarchi 2015 did not assess quality of included studies. Both Shakarchi 2015 and the Shakarchi 2016 cost-analysis paper are industry-affiliated.
CLINICAL NEED	
Burden of Illness	The Australia and New Zealand Dialysis and Transplant Registry recorded 5,100 new cases of ESRD in 2013, equating to an age-standardised rate of 19 per 100,000 people. ESRD patients have two treatment options: Dialysis (haemodialysis or peritoneal dialysis) or renal transplant. Haemodialysis is a major modality of renal replacement therapy in 70-90% of patients who need vascular access to move blood from the patient to the haemodialysis machine.
Need	It is necessary for ESRD patients with CVS to have adequate vascular access before starting haemodialysis treatments. The evidence-based Kidney Health Australia (KHA)-CARI guidelines 2013 recommended that a native AV fistula is created and used for haemodialysis, as it is superior to an AV graft and to a CVC. When an AV fistula is not possible, an AV graft should be used in preference to a CVC. (Level III evidence) AV grafts have similar patency to AV fistula. Concerns regarding AV grafts for chronic renal failure are fluid dynamics and subsequent aneurysm formation. Short- and long-term tunneled CVCs should be avoided, if possible. Access-related infections are four times higher in CVC patients compared to AVG patients, and eight times higher compared to AVF patients (2007 United States Renal Data System). Costs of care are significantly greater for a patient using a CVC than for a patient using an AVG or an AVF, in that order. For patients who cannot have an AV fistula/AV graft and are catheter dependent, the HeRO graft may be considered an alternative to CVC. The use of HeRO graft in Australia is limited. Compared to a tunneled CVC (e.g. permcaths), the main advantages of the HeRO graft are purportedly the (1) reduced access-related infections (fully subcutaneous device), (2) lesser interventions required to maintain patency and (2) longer permanency of vascular access. Compared to the CVC, the drawbacks for using the HeRO graft are (1) catheter dependence is not removed completely (CVCs are used in the interim while waiting for tissue incorporation, (2) non-immediate cannulation (wait 2-4 weeks after HeRO implant), (3) the need to use needles (no hubs on line) to connect to dialysis tubes.(Perry 2017) Compared to an AVG where one end is connected to the artery (inflow) & the other to the vein (outflow), there is no venous anastomosis for the HeRO graft. The HeRO graft is cannulated just like an AVG, however, only the graft component (HeRO 1002) of the HeRO graft can be cannulated, not the venous outflow component (HeRO 1001).
CLINICAL BENEFIT	
Safety	An analysis of published 2014-15 data and unit costs from the UK National Health System (Ottolini 2016) showed that the use of HeRO devices should be judicious, with outcome expectations reduced. Specifically, the 100-patient cohort managed with the HeRO graft experienced 6 fewer failed devices, 53 fewer access-related infections, and 67 fewer device thrombosis compared to patients managed with tunneled CVC. • **Infection** o HeRO vs CVC (naïve indirect comparison): HeRO graft has lower rate of blood stream infection compared to CVC, hence use of HeRO graft is preferable to catheter dependence. (Maqsood 2019) A lower access-related infection is reported at 0.14 episodes per 1000 (Gage 2012) and 0.7 per 1000 implant days in patients with HeRO graft (Katzman 2009), compared to the infection rate with CVCs at 0.6-6.5 per 1000. (Maqsood 2019) o HeRO vs AVG: Similar infection rates, however noted trial is underpowered. (Maqsood 2019) o HeRO vs femoral graft: Similar at 0.61 vs 0.71 per 1000 implant days. (Schild 2010) o HeRO-related bacteraemia (0.13 - 0.7 events per 1000 days) (Shakarchi 2015) • **Mortality** o HeRO vs femoral graft: Similar. (Schild 2010) • **Ischaemia** o HeRO vs femoral graft: Similar. (Schild 2010) • **Dialysis access associated steal syndrome** (Shakarchi 2015) low at 6.3% (range 1 - 14.7%)
Effectiveness	• **Primary outcome - Patency rates** o **HeRO only** 12-month pooled primary patency 21.9% (9.6 - 37.2%) and secondary patency 59.4% (39.4 - 78%) (Shakarchi 2015). In a study (Wallace 2013), secondary patency was maintained in four patients for a mean duration of 10 months (range, 6–18 months), with an average of 4.0 ± 2.2 thrombectomies per graft. o **HeRO vs CVC** Not reported. o **HeRO vs AVG** Similar - primary patency 34.8% vs 30.6%; secondary patency 67.6% vs 58.4% (time frame not reported; likely 12-months). Intervention rates 2.2/year vs 1.6/year (p=0.1) (Maqsood 2019/Gage 2012) Another paper (Nassar 2014 underpowered RCT) showed 1-yr primary patency 22% vs secondary patency 59%. o **HeRO vs femoral AV graft** primary patency at 12-months 29% vs 18.7% (p=0.67) (Kudlaty 2015); secondary patency at 12-months 53.5% vs 50.6% (Kudlaty 2015); 42% vs 86% (Schild 2010). Higher intervention rates 2.21/year vs 1.17/year (Schild 2010) • **Rate of interventions required to maintain patency of HeRO graft, CVC & conventional AVG** (between 6-12months; naïve indirect comparison) o 1.5 to 3 interventions/yr (Shakarchi 2015); 2.21 interventions per year (Maqsood 2019); 2.5 (Katzman 2009) o CVC: 5.8/yr (Katzman 2009) o Conventional AVG: 1.6 to 2.4/yr (Katzman 2009) o Lower extremity graft: 1.17 /yr (Maqsood 2019)

	• **Dialysis rate** o **HeRO vs AVG** Similar (Gage 2012) • **Quality of life** Paucity of evidence. (Maqsood 2019) • **Lifespan/durability of the HeRO graft** Around 2 years for the ePTFE graft. Rotation of cannulation sites may extend the life of the HeRO Graft. Further, the graft portion can be replaced or revised without removing the Venous Outflow Component.
SA Health outcomes	A female patient received the HeRO graft in January 2019 at FMC. The clinician reported positive outcomes. She is dialysing well, with good clearances, excellent access flow volumes and has not had any re-intervention (October 2019). Another female patient who has difficult access for dialysis and is currently dialysing via a permcath with no other options is currently approved under the IPU process at the FMC for the insertion of the HeRO graft (November 2019).
SUITABILITY OF PATIENT GROUP	
Suitability of Patient Group	The applicant recommended using the HeRO graft in the very small number of ESRD patients with CVS dependent on CVC for dialysis (e.g. [redacted] long-term hemodialysis catheter) who face infection or catheter issues. These patients have reached the end of their haemodialysis life and exhausted all other dialysis options. The HeRO graft would allow patients to have a have an upper extremity AV access even if they have CVS, patients can avoid having a CVC or a lower extremity AV access. The catheter component of the HeRO should be able to pass through the stenosed central vein. The HeRO graft Instructions for Use lists as a caution not to implant the HeRO graft in the same vessel as a bridging catheter, defibrillator or pacemaker lead.
FINANCIAL CONSIDERATION	
Device costs	**<Prices and names to be redacted>** Proposed number of SALHN patients per year = 5 Total cost per HeRO graft device set - $[redacted] ex GST, compared to $[redacted] ex GST [redacted] long-term haemodialysis catheters: • HeRO® 1001 Venous Outflow Component - $[redacted] • HeRO® 1002 Arterial Graft Component - $[redacted] • HeRO® 1003 Accessory Component Kit - $[redacted] HeRO graft costs $[redacted] per procedure compared to $[redacted] per procedure for permcaths.
Value for Money	Even though the initial device and placement costs of the HeRO graft is higher than those for the CVC, savings from the lower device complications (i.e. access-related infections) and longer effective device patency make the HeRO graft more cost-effective (Maqsood 2019). The value of the HeRo graft is supported by another cost analysis paper (Shakarchi 2016). Shakarchi 2016 is a 1-year cost-consequence decision analytic model study funded by the industry which analysed the cost of management with the HeRO graft compared to the tunneled CVC from the perspective of the National Health Service in England. The result was a marginal net positive cost with the HeRO graft compared with the tunneled CVC for the because of lesser complications (i.e. device-related thrombosis and access-related infections). Overall net annual costs are £2600 for each HeRO graft-managed patient compared to tunneled dialysis catheter -managed patients. If the UK National Health Service were to reimburse hemodialysis at a uniform rate regardless of the type of vascular access, net 1-year savings of £1200 per patient are estimated for individuals managed with the HeRO graft. i.e. HeRO grafts are more cost-effective than tunneled CVCs.
Australian Funding Approvals	The Commonwealth Medical Services Advisory Committee (MSAC), Prosthesis List Advisory Committee (PLAC), National Health Technology Reference Group (HTRG) and interstate health technology committees have not reviewed this technology. The technology is not listed on the Prosthesis List. In New South Wales, there are no reported sites using haemodialysis reliable outflow graft for use in patients with catheter (permcath). One NSW district informed that surgeons discussed this technique a few years ago and it was deemed a very complex surgery that would need to be individualised.
Local Consultations	CALHN Nephrology and Vascular Surgery noted that the HeRO graft has been around for a long time in the US. They recommended that CALHN clinicians may like to access the device for use in the rare number of eligible patients under audit conditions.
FEASIBILITY OF ADOPTION	
Organizational Feasibility	This procedure may be used provided that standard arrangements are in place for clinical governance, consent and audit by the LHN(s). In SALHN, the renal physicians and team would consider the appropriateness of use for the HeRO graft before the vascular surgeon implant the graft. All decisions and interventions to place a HeRO graft will be undertaken by vascular surgeons in consultation with renal physicians. Vascular surgeons routinely intervene on CVS using the same endovascular techniques that are required for permcath placement. Vascular surgeons also routinely construct AVF and AVG using open surgical strategies. Placement of the HeRO graft simply combines the open and endovascular skills that vascular surgeons already possess. Interventional radiologists do not have these hybrid skills required for such a procedure. All vascular procedures performed in SALHN are reported to the Australasian Vascular Audit as required by membership of the Australia and New Zealand Society of Vascular Surgery (ANZSVS), peer-reviewed on a monthly basis and mortalities are reviewed by the SA Audit of Perioperative Mortality separately. In CALHN, the CVCs are placed with imaging by an interventional radiologist, whereas the HeRO grafts, AVG and AVFs are inserted by a vascular surgeon with referrals from the nephrologist.

Credentialing and Competency	Costs of training of clinicians and nursing staff will be borne by and conducted by the industry. For all cases a trained Merit representative will be present for the cases until such time as the physician(s) decide the additional support is no longer required. There is the industry's intention to facilitate a highly experienced physician (Dr Hohmann) from the USA to visit Adelaide to assist with hands-off proctoring and training of local physicians in using the device. The HeRO graft procedure should only be done by clinicians with specific training in the procedure and within their scope of practice. The clinician(s) should be appropriately credentialed and approved by the SA Health Credentialing and Scope of Practice Committee to implant the HeRO graft (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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