South Australian Policy Advisory Committee on Technology (SAPACT)

Health Technology Assessment (HTA) Decision Summary

Government of South Australia

SA Health

Micra™ single chamber transcatheter pacing system leadless pacemaker

SAPACT MEETING DATES	16th SAPACT Meeting, 23 November 2018
APPLICATION #	1805
TECHNOLOGY	Micra™ single chamber transcatheter pacing system (Medtronic Australasia Pty Ltd)
TECHNOLOGY CLASSIFICATION	Active implantable medical devices (AIMD)
PATIENT INDICATION (TGA)	TGA-indicated for use in patients who have experienced one or more of the following conditions: • symptomatic paroxysmal or permanent high-grade atrioventricular (AV) block in the presence of atrial fibrillation (AF) • symptomatic paroxysmal or permanent high-grade AV block in the absence of AF, as an alternative to dual chamber pacing, when atrial lead placement is considered difficult, high risk, or not deemed necessary for effective therapy • symptomatic bradycardia-tachycardia syndrome or sinus node dysfunction (sinus bradycardia or sinus pauses), as an alternative to atrial or dual chamber pacing, when atrial lead placement is considered difficult, high risk, or not deemed necessary for effective therapy. Rate-responsive pacing is indicated to provide increased heart rate appropriate to increasing levels of activity.

SAPACT DECISION

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

In 2018, SAPACT received an application referral from SALHN to evaluate the potential use of the Micra leadless pacemaker in SA Health. SAPACT commenced the HTA process, inclusive of the development of a SAPACT Rapid Review based on international scientific and local implementation evidence, consultations with applicant, clinical experts, interstate technology committees, Medtronic, Australasian Cemeteries & Crematoria Association (ACCA); presentation and deliberations at the SAPACT meetings, public decision summary and outcome evaluations.

SAPACT Advisory Recommendations

Best available international evidence on the safety of leadless cardiac pacemaker implantation for bradyarrhythmias showed that there were serious but well-recognised complications. Key issues were (1) the lack of evidence of clinical-effectiveness outcomes (although data on electrical performance of Micra was available), (2) lack of comparative trials (only single-arm low level studies available) and (3) only short-term (up to 24 months) follow-up results. Concerns were also raised on unknown long-term issues such as battery longevity and Micra device retrieval after a prolonged implantation time. Careful attention should also be paid to contraindications for leadless pacing, such as patient habitus and venous abnormalities likely to result in difficulties/complications from the large sheaths required for Micra device delivery.

Specific recommendations for Micra implantation within SA Health

1. It is not appropriate for patients suitable for transvenous lead or epicardial lead placement, nor those requiring AV sequential pacing.
2. As implantation is rare, initial roll-out expertise and resources should be consolidated at two LHNs.
3. Patient selection requires a multidisciplinary team approach, with assessment by both cardiologist and cardiothoracic surgeon participating in transvenous or epicardial lead insertion. Specifically, a SA Health Cardiothoracic Surgeon who removes/explants epicardial leads should review the case file (and the patient if necessary) and conclude that the patient is not suitable for epicardial lead placement. This surgical opinion should be formally documented and occur before the Micra option is offered to the patient. Patients who cannot be treated with a conventional transvenous system be counselled as to the options available to them (i.e. leadless pacing versus epicardial pacing).
4. The clinician implanting the Micra device must be credentialed for this procedure by the LHN.
5. A Patient Information Sheet concerning the risks and benefits of Micra implantation must be drafted by the implanting team and submitted to SAPACT for approval before the program can commence.
6. It is mandatory for the implanting clinician to provide SAPACT with follow-up reports for the first 5 patients within 3-months post-procedure, followed by an annual report for a 5-year period. Reporting parameters include:
   (a) Patient selection and device implantation details for new patients
   (b) Clinical outcomes: [Primary] Safety and clinical-effectiveness if Micra implantation; [Secondary] Acute complication rates
   (c) Adverse events: Death; implant-related complications (e.g. device infection, dislodgement, venous access bleeding site complications cardiac tamponade/perforation); hospital admission with collapse/syncope/cardiac arrest
   (d) Patient outcomes recorded via annual Euro Quality-of-Life 5 Dimensions (EQ-5D)

REGULATORY APPROVALS

☒ **ARTG**: 6/12/2016. 283235 Medtronic Australasia Pty Ltd - Micra single chamber TPS	☒ **US FDA**: 6/4/2016	☒ **EU CE mark**: 14/4/2015

QUALITY OF EVIDENCE	
Quality of Evidence	Besides the published scientific literature, grey literature including international HTA reports, government implementation policy guidance documents (e.g. from NICE, CADTH, HealthPACT, ECRI and EuroScan) and the local Australian implementation experiences were sought. The key document included was the evidence-based NICE Guidance on Micra with its comprehensive Evidence Review. Local Australian implementation clinical outcomes report, findings and communication from Queensland Health, Victoria MonashHealth and WA Health also inform the SAPACT Recommendation. Within the published literature, only case-series (level V evidence) with short-term follow-up (up to 24 months) were available. Specifically, 7 systematic reviews of case-series evidence and an additional 22 case-series and 1 case report were found. The case-series were from the Micra Transcatheter Pacing Study of moderate quality, Micra Post-Approval Registry of moderate quality, 2 other Medtronic studies of moderate quality and others were independent studies of low to moderate quality. There were no comparative trials comparing leadless pacemakers with conventional pacemakers and no economic evaluation on Micra was available.
CLINICAL NEED	
Burden of Illness	In 2016-17, there are 18,000 - 20,000 pacemaker implants in Australia, including procedures to replace existing generators. Single-chamber ventricular pacing (VVI) is indicated for patients with cardiac arrhythmias. These are patients with atrial fibrillation who require a pacemaker due to slow ventricular response, and also patents with bradycardia due to atrioventricular (AV) block or sinus node disease if other pacing modes are not appropriate. Cardiac pacing is used to provide an appropriate heart rate and response to re-establish effective circulation and haemodynamics that are compromised by a slow heart rate. Permanent pacemaker implantation is further considered to alleviate symptoms associated with abradyarrhythmia (e.g. dizziness, light-headedness, syncope, fatigue, poor exercise tolerance) or to prevent the possible worsening of the rhythm disturbance. To date (2018), fewer than 100 of the Micra devices have been implanted in Australia (Koh 2018).
Need	Currently, the endocardial (transvenous) approach and the epicardial (surgical) approach are two conventional ways to treat VVI in patients with cardiac arrhythmias. The transvenous approach has leads positioned in the blood veins (through subclavian vein and superior vena cava into the right ventricle) for the single-chamber pacemaker. The second lead is additionally positioned in the right atrium for the dual-chamber pacemaker. Local anaesthesia (LA) is used in the transvenous approach and conducted in a Cardiac Catheterization Lab. When transvenous lead position is not feasible or contraindicated, leads can be positioned using an epicardial approach in the Surgery Theatre under general anaesthetic (GA) condition. Although pacemaker related issues are rare, complications in both endocardial and epicardial approaches relating to the leads or the surgical pocket made under the skin for implantation have remained the greatest source of morbidity and infection. Leadless pacemakers like Micra may present as a new comparator to the epicardial approach, eliminating the need for a surgical pocket or transvenous leads. Micra implantation takes less than an hour under LA in the Cardiac Catheterization Lab and patient can return home the next day. However, noted that Micra cannot completely resolve the issue of difficult venous access or risk of infection (its perceived advantage). This is because (1) large diameter sheaths are required for delivery of Micra through the femoral venous approach and (2) once implanted in the right ventricle, Micra device cannot be explanted. Only up to 2 Micra devices may be implanted in the right ventricle, more commonly in the septum than in the apex. The Micra device is the size of a vitamin pill (2.5cm x 0.7cm) and the battery lifespan is around 10-12 years, after which the battery should be replaced like in other types of pacemakers. Another similar device, the Nanostim, was found to lose telemetry and pacing due to battery malfunction after two years of implant. A TGA hazard alert was issued in November 2016 to stop implanting the Nanostim.
CLINICAL BENEFIT	
Safety	51 events were reported across an entire cohort of 1,595 patients, of which 99 deaths (2 deaths due to procedure) and 16 cardiac injuries (pericardial effusion in a patient who had undergone 18 repositioning attempts because of inappropriate electrical measurements) were reported. All reported events resolved successfully. The second most commonly reported adverse event was complications at the puncture site which were normally resolved with no additional hospitalisation. Micra Transcatheter Pacing System Post-Approval Registry • Implant success: 99.6% • Major complications to 30 days post-implant: 1.51% • Freedom from major complications:96% A number of the studies undertook post-hoc comparisons of their data with data from separate studies on transvenous pacemakers. Complications, hospitalisations, system revisions and device and lead issues were all reduced in the Micra patients.
Effectiveness	Although data on electrical performance of Micra was available, there is a lack of evidence on clinical-effectiveness of Micra. None of the clinical studies reported clinical- and patient-related outcomes, such as quality of life, exercise capacity, bradycardia, change of medication or syncope or pre-syncope. Early emerging evidence focused on device performance, specifically the electrical

	performance of the leadless pacemaker (appears durable up to 24 months), with no associated statistical analyses. No effects of the implant on cardiac structure and function were reported. In terms of feasibility of device implantation, Micra was feasible in conjunction with atrioventricular junction ablation (at the time of the implant, or within 24 hours of the implant procedure) and in conjunction with left atrial appendage closure.
SUITABILITY OF PATIENT GROUP *based on international and interstate scientific evidence and local consultations with independent SA cardiac experts, applicant and SAPACT members*	
Suitability of Patient Group	SAPACT recommended that the Micra would not replace conventional VVI pacemakers. SAPACT agreed that there should be a multidisciplinary team approach to select patients who need single-chamber ventricular VVI or VVIR pacing and in whom a conventional transvenous or epicardial cardiac pacemaker implantation is not feasible or are contraindicated following a careful risk assessment. In particular, clinicians should have already explored the epicardial surgical approach and rule it out through endorsement with a SA Health Cardiothoracic Surgeon who removes/explants epicardial leads, prior to recommending Micra as a treatment option to patients. Clinicians should also document clear and explicit reasons for every SA Health patient selected for the Micra implantation over the conventional transvenous and epicardial approaches. Only SA Health-approved credentialed clinician(s) are allowed to carry out the Micra implantation.
FINANCIAL CONSIDERATION	
Device costs	About $11,000/Micra device, compared to $1,000-2,000 single chamber pacemakers or $1,000-3,000 for dual-chamber pacemakers. Leads are extra costs. An estimated 10 patients per year in SALHN will use Micra. Transvenous pacemaker implantation procedure average cost: $15,000/separation; $4,100/day Epicardial procedure average cost: $23,000/separation; $3,870/day
Value for Money	No published economic evaluation was identified.
Australian Funding	MSAC and Prosthesis List: Nil; AHMAC Health Technology Reference Group: Reviewed leadless pacemakers in 2015 and recommended that further evidence was required. Interstate jurisdictions were contacted regarding the status of evaluation and use of Micra in public health care. In Queensland, Micra was evaluated by QPACT in 2016 and funded conditionally at the Prince Charles Hospital and Princess Alexandra Hospital through the Queensland Health New Technology Funding and Evaluation Program. Micra is under evaluation. An Evaluation Outcome Report from the Clinicians and a Commissioned Australian Centre For Health Services Innovation (AusHSI) economic evaluation report will be finalised in the next few months. A case-series (Denman Nov 2018) was recently published from the Prince Charles Hospital. In Victoria, the MonashHealth Centre for Clinical Effectiveness confirmed that they have introduced Micra into Monash Health under the Technologies and Clinical Practice Committee (TCPC) under audit conditions. Twenty-four patients received the Micra from June 2016 – June 2018. It would be due for TCPC review soon whether it should be reclassified into standard practice. A case report (Kotschet 2018) and an editorial letter (Koh 2018) were recently published from MonashHealth. In New South Wales (NSW), the Micra Leadless Pacemaker has been approved for use at two NSW Health sites, the Royal Prince Alfred and Blacktown Hospital. This technology is also available at a number of private hospitals including the SAN and the Mater. Limited information was available about patient selection; however they are not widely used at present due to cost.
FEASIBILITY OF ADOPTION	
Organizational Feasibility	For follow-up, patient with Micra would be managed in a similar way to patients with conventional pacemakers. Since this service is rare, at the initial roll-out expertise and resources should be consolidated at a single centre in SA to allow for managed introduction of device and monitoring of patient outcomes.
Credentialing and Competency	The Clinician(s) should be appropriately credentialed and approved by the SA Health Credentialing and Scope of Practice Committee to implant the Micra (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 (relevant when safety, clinical and cost-effectiveness are met)	
Values	Unlike other conventional pacemakers, the ACCA has confirmed that the Micra does not need to be explanted prior to cremation or burial, as it does not pose a significant risk to cremation/cremation operators.
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