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Medical Benefit	Effective Date: 02/01/20	Next Review Date: 11/20
Preauthorization	Yes	Review Dates: 11/19

Preauthorization is required.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient’s contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none"> With a guidelines-based indication for a ventricular pacing system who are medically eligible for a conventional PS 	Interventions of interest are: <ul style="list-style-type: none"> Micra transcatheter pacing system 	Comparators of interest are: <ul style="list-style-type: none"> Single-chamber conventional pacemaker(s) 	Relevant outcomes include: <ul style="list-style-type: none"> Overall survival Disease-specific survival Treatment-related mortality Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> With a guidelines-based indication for a ventricular pacing system who are medically ineligible for a conventional PS 	Interventions of interest are: <ul style="list-style-type: none"> Micra transcatheter pacing system 	Comparators of interest are: <ul style="list-style-type: none"> Medical management Single-chamber pacemaker placement via transiliac venous lead placement Surgically placed epicardial single-chamber pacemaker 	Relevant outcomes include: <ul style="list-style-type: none"> Overall survival Disease-specific survival Treatment-related mortality Treatment-related morbidity

DESCRIPTION

Pacemakers are intended to be used as a substitute for the heart’s intrinsic pacing system to correct cardiac rhythm disorders. Conventional pacemakers consist of two components: a pulse generator and electrodes (or leads). Pacemakers are considered life-sustaining, life-supporting class III devices for patients with a variety of bradyarrhythmias. Even though the efficacy and safety profile of conventional pacemakers are excellent, in a small proportion of patients, they may result in lead complications and the requirement for a surgical pocket. Further, some patients are medically ineligible for conventional pacemakers due to lack of venous access and recurrent infection. Leadless pacemakers are single-unit devices that are implanted in the heart via femoral access, thereby eliminating the potential for complications as a result of leads and surgical pocket. The Micra transcatheter pacing system is the only commercially available leadless pacemaker in the U.S. approved by the Food and Drug Administration.

SUMMARY OF EVIDENCE

For individuals with a guidelines-based indication for a ventricular pacing system who are medically eligible for a conventional pacing system who receive a Micra transcatheter pacing system, the evidence includes a pivotal prospective cohort study and a post approval prospective cohort study. Relevant outcomes are overall survival, disease-specific survival, and treatment-related mortality and morbidity. Results at six months and one year for the pivotal study reported high procedural success (>99%) and device effectiveness (pacing capture threshold met in 98% patients). Most of the system- or procedural-related complications occurred within 30 days. At one year, the incidence of major complication did not increase substantially from six months (3.5% at six months vs. 4% at one year). Results of the post approval study were consistent with a pivotal study and showed a lower incidence of major complications up to 30 days post implantation as well as one year (1.5% and 2.7%, respectively). In both studies, the point estimates of major complications were lower than the pooled estimates from six studies of conventional pacemakers used as a historical comparator. While Micra device eliminates lead- and surgical pocket-related complications, its use can result in potentially more serious complications related to implantation and release of the device (traumatic cardiac injury) and less serious complications related to the femoral access site (groin hematomas, access site bleeding). Considerable uncertainties and unknowns remain in terms of the durability of device and device end-of-life issues. Early and limited experience has suggested that retrieval of these devices is unlikely because in due course, the devices will be encapsulated. There are limited data on device-device interactions (both electrical and mechanical), which may occur when there is a deactivated Micra device alongside another leadless pacemaker or when a leadless pacemaker and transvenous device are both present. While the current evidence is encouraging, overall benefit with the broad use of Micra transcatheter pacing system compared with conventional pacemakers has not been shown. Clinical input supplements and informs the interpretation of the published evidence. Clinical input suggests that some individuals who are eligible for conventional pacing but are concerned about the long-term risk of lead-related issues may prefer initial use of a leadless pacemaker after considering the balance of benefits and harms using shared decision making. The evidence is insufficient to determine the effects of technology on health outcomes.

For individuals with a guidelines-based indication for a ventricular pacing system who are medically ineligible for a conventional pacing system who receive a Micra transcatheter pacing system, the evidence includes subgroup analysis of a pivotal prospective cohort study and a post approval prospective cohort study. Relevant outcomes are overall survival, disease-specific survival, and treatment-related mortality and morbidity. Information on the outcomes in the subgroup of patients from the post approval study showed that the Micra device was successfully implanted in 98% of cases and safety outcomes were similar to the original cohort. Even though the evidence is limited and long-term effectiveness and safety are unknown, the short-term benefits outweigh the risks because the complex trade-off of adverse events for these devices needs to be assessed in the context of the life-saving potential of pacing systems for patients, ineligible for conventional pacing systems. There are little data available regarding outcomes associated with other alternatives to conventional pacemaker systems such as epicardial leads or transiliac placement. Epicardial leads are most relevant for the patient who is already going to have a thoracotomy for treatment of their underlying condition (e.g., congenital heart disease). Epicardial leads are associated with a longer intensive care unit stay, more blood loss, and longer ventilation times compared to conventional pacemaker systems. The evidence for transiliac placement is limited to small case series and the incidence of atrial lead dislodgement using this approach in the literature ranged from seven to 21%. Limitations in the published evidence preclude determining the effects of the technology on net health outcome. Evidence reported through clinical input supports that use of a Micra transcatheter pacing system provides a clinically meaningful improvement in net health outcome and is consistent with generally accepted medical practice particularly for selected patients who are medically ineligible for a pacemaker using pectoral placement system when compared with the limited options available to these individuals. Clinical input noted that the placement of a pacemaker through transiliac or epicardial “approaches require special expertise or necessitate a surgically invasive procedure. Additionally, the long-term performance of transiliac leads or epi-

cardiac leads is suboptimal.” The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

POLICY

The Micra transcatheter pacing system may be considered **medically necessary** in patients when both conditions below are met:

- The patient has symptomatic paroxysmal or permanent high-grade arteriovenous block or symptomatic bradycardia-tachycardia syndrome or sinus node dysfunction (sinus bradycardia or sinus pauses).
- The patient has a significant contraindication precluding placement of conventional single-chamber ventricular pacemaker leads such as any of the following:
 - History of an endovascular or cardiovascular implantable electronic device (CIED) infection or who are at high risk for infection
 - Limited access for transvenous pacing given venous anomaly, occlusion of axillary veins or planned use of such veins for a semi-permanent catheter or current or planned use of an AV fistula for hemodialysis
 - Presence of a bioprosthetic tricuspid valve

The Micra transcatheter pacing system is considered **investigational** in all other situations in which the above criteria are not met.

POLICY GUIDELINES

As per the FDA label, the Micra Model MC1VR01 pacemaker is contraindicated for patients who have the following types of devices implanted:

- An implanted device that would interfere with the implant of the Micra device in the judgment of the implanting physician
- An implanted inferior vena cava filter
- A mechanical tricuspid valve
- An implanted cardiac device providing active cardiac therapy which may interfere with the sensing performance of the Micra device

As per the FDA label, the Micra Model MC1VR01 pacemaker is also contraindicated for patients who have the following conditions:

- Femoral venous anatomy unable to accommodate a 7.8 mm (23 French) introducer sheath or implant on the right side of the heart (for example, due to obstructions or severe tortuosity)
- Morbid obesity that prevents the implanted device to obtain telemetry communication within <12.5 cm (4.9 in)
- Known intolerance to titanium, titanium nitride, parylene C, primer for parylene C, polyether ether ketone, siloxane, nitinol, platinum, iridium, liquid silicone rubber, silicone medical adhesive, and heparin or sensitivity to contrast medical which cannot be adequately pre-medicated

As per the FDA label, the Micra Model MC1VR01 pacemaker should not be used in patients for whom a single dose of 1.0 mg dexamethasone acetate cannot be tolerated because the device contains a molded and cured

mixture of dexamethasone acetate with the target dosage of 272 µg dexamethasone acetate. It is intended to deliver the steroid to reduce inflammation and fibrosis.

For the MRI contraindications for patients with a Micra MRI device, refer to the Medtronic MRI Technical Manual.

For axillary transvenous pacemakers, there is a concern that leads or the generator could be impacted by the recoil of using a firearm (e.g., rifles or shotguns). Thus leadless cardiac pacemakers can provide an alternative for patients who suffer lead fracture or malfunction from mechanical stress and may be considered when axillary venous access is present only on a side of the body that would not allow use of equipment producing such mechanical stress (e.g., a firearm).

MEDICARE ADVANTAGE

For Medicare Advantage leadless pacemakers may have potential coverage when provided through Coverage with Evidence Development (CED) when procedures are performed in Food and Drug Administration (FDA) approved studies.

There may be potential for coverage for leadless pacemakers, in prospective longitudinal studies, that are used in accordance with the FDA approved label for devices that have either:

- An associated ongoing FDA approved post-approval study; OR
- Completed an FDA post-approval study.

Each study must be approved by CMS and as a fully-described, written part of its protocol, must address the following research questions:

- What are the peri-procedural and post-procedural complications of leadless pacemakers?
- What are the long term outcomes of leadless pacemakers?
- What are the effects of patient characteristics (age, gender, comorbidities) on the use and health effects of leadless pacemakers?

Leadless pacemakers are **not medically necessary** when furnished outside of a CMS approved CED study.

MEDICARE ADVANTAGE POLICY GUIDELINES

Registries must be reviewed and approved by CMS. All approved registries will be posted on the CED website located at <https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/index.html>

BACKGROUND

CONVENTIONAL PACEMAKERS

Pacemakers are intended to be used as a substitute for the heart's intrinsic pacing system to correct cardiac rhythm disorders. By providing an appropriate heart rate and heart rate response, cardiac pacemakers can reestablish effective circulation and more normal hemodynamics that are compromised by a slow heart rate. Pacemakers vary in system complexity and can have multiple functions as a result of the ability to sense and/or stimulate both the atria and the ventricles.

Transvenous pacemakers or pacemakers with leads (hereinafter referred to as conventional pacemakers) consist of two components: a pulse generator (i.e., battery component) and electrodes (i.e., leads). The pulse generator

consists of a power supply and electronics that can provide periodic electrical pulses to stimulate the heart. The generator is commonly implanted in the infraclavicular region of the anterior chest wall and placed in a pre-pectoral position; in some cases, a subpectoral position is advantageous. The unit generates an electrical impulse, which is transmitted to the myocardium via the electrodes affixed to the myocardium to sense and pace the heart as needed.

Conventional pacemakers are also referred to as single-chamber or dual-chamber systems. In single-chamber systems, only one lead is placed, typically in the right ventricle. In dual-chamber pacemakers, two leads are placed—one in the right atrium and the other in the right ventricle. Single-chamber ventricular pacemakers are more common.

Annually, approximately 200,000 pacemakers are implanted in the U.S. and one million worldwide.¹ Implantable pacemakers are considered life-sustaining, life-supporting class III devices for patients with a variety of bradyarrhythmias. Pacemaker systems have matured over the years with well-established, acceptable performance standards. As per the Food and Drug Administration (FDA), the early performance of conventional pacemaker systems from implantation through 60 to 90 days have usually demonstrated acceptable pacing capture thresholds and sensing. Intermediate performance (90 days through more than five years) has usually demonstrated the reliability of the pulse generator and lead technology. Chronic performance (five to ten years) includes a predictable decline in battery life and mechanical reliability but a vast majority of patients receive excellent pacing and sensing free of operative or mechanical reliability failures.

Even though the safety profile of conventional pacemakers is excellent, they are associated with complications particularly related to leads. Most safety data on the use of conventional pacemakers come from registries from Europe, particularly from Denmark where all pacemaker implants are recorded in a national registry. These data are summarized in Table 1. It is important to recognize that valid comparison of complication rates is limited by differences in definitions of complications, which results in a wide variance of outcomes, as well as by the large variance in follow-up times, use of single-chamber or dual-chamber systems, and data reported over more than two decades.² As such, the following data are contemporary and limited to single-chamber systems when reported separately.

In many cases when a conventional pectoral approach is not possible, alternative approaches such as epicardial pacemaker implantation and transiliac approaches have been used³. Cohen et al (2001) reported outcomes from a retrospective analysis of 123 patients who underwent 207 epicardial lead implantations⁴. Congenital heart disease was present in 103 (84%) of the patients. Epicardial leads were followed for 29 months (range one to 207 months). Lead failure was defined as the need for replacement or abandonment due to pacing or sensing problems, lead fracture, or phrenic/muscle stimulation. The one, two, and five year lead survival was 96%, 90%, and 74%, respectively. Epicardial lead survival in those placed by a subxiphoid approach was 100% at one year and at ten years, by the sternotomy approach (93.9% at one year and 75.9% at ten years) and lateral thoracotomy approach (94.1% at one year and 62.4% at ten years).

Doll et al (2008) reported results of a randomized controlled trial comparing epicardial implantation vs. conventional pacemaker implantation in 80 patients with indications for cardiac resynchronization therapy.⁵ The authors reported that the conventional pacemaker group had a significantly shorter intensive care unit stay, less blood loss, and shorter ventilation times while the epicardial group had less exposure to radiation and less use of contrast medium. The left ventricular pacing threshold was similar in the two groups at discharge but longer in the epicardial group during follow-up. Adverse events were also similar in the two groups. The following events were experienced by one (3%) patient each in the epicardial group: pleural puncture, pneumothorax, wound infection, Acute Respiratory Distress Syndrome, and hospital mortality.

As a less invasive alternative to the epicardial approach, the transiliac approach has also been utilized. Data using transiliac approach is limited. Multiple other studies with smaller sample size report a wide range of lead longevity.

Harakeet al (2018) reported a retrospective analysis of five patients who underwent a transvenous iliac approach (median age 26.9 years).⁶ Pacing indications included AV block in three patients and sinus node dysfunction in two. After a median follow-up of 4.1 years (range 1.0-16.7 years), outcomes were reported for four patients. One patient underwent device revision for lead position-related groin discomfort; a second patient developed atrial lead failure following a Maze operation and underwent lead replacement by the iliac approach. One patient underwent heart transplantation six months after implant with only partial resolution of pacing-induced cardiomyopathy. Tsutsumi et al (2010) reported a case series of four patients from Japan in whom conventional pectoral approach was precluded due to recurrent lead infections (n=1), superior vena cava obstruction following cardiac surgery (n=2) and a postoperative dermal scar (n=1). The mean follow-up was 24 months and the authors concluded the iliac vein approach was satisfactory and less invasive alternative to epicardial lead implantation. However, the authors reported that the incidence of atrial lead dislodgement using this approach in the literature ranged from seven to 21%. Experts who provided clinical input reported that transiliac or surgical epicardial approach requires special expertise and long-term performance is suboptimal.⁷

Table 1. Reported Complication Rates with Conventional Pacemakers

Complications	Rates, % ^{8-10,a}
Traumatic complications	
RV perforation	0.2-0.8
RV perforation with tamponade	0.07-0.4
Pneumo(hemo)thorax	0.7-2.2
Pocket complications	
Including all hematomas, difficult to control bleeding, infection, discomfort, skin erosion	4.75
Including only those requiring invasive correction or reoperation	0.66-1.0
Lead-related complications	
Including lead fracture, dislodgement, insulation problem, infection, stimulation threshold problem, diaphragm or pocket stimulation, other	1.6-3.8
All system-related infections requiring reoperation or extraction	0.5-0.7

Adapted from Food and Drug Administration executive summary memorandum (2016).¹¹

^a Rates are for new implants only and ventricular single-chamber devices when data were available. Some rates listed in this column are for single- and dual-chamber devices when data were not separated in the publication. Note that Micra transcatheter pacing system is a single-chamber device.

Potential Advantages of Leadless Cardiac Pacemakers Over Conventional Pacemakers

The potential advantages of leadless pacemakers fall into three categories: avoidance of risks associated with intravascular leads in conventional pacemakers, avoidance of risks associated with pocket creation for placement of conventional pacemakers, and an additional option for patients who require a single-chamber pacer.¹²

Lead complications include lead failure, lead fracture, insulation defect, pneumothorax, infections requiring lead extractions and replacements that can result in a torn subclavian vein or the tricuspid valve. In addition, there are risks of venous thrombosis and occlusion of the subclavian system from the leads. Use of a leadless system eliminates such risks with the added advantage that a patient has vascular access preserved for other medical conditions (e.g., dialysis, chemotherapy).

Pocket complications include infections, erosions, and pain that can be eliminated with leadless pacemakers. Further, a leadless cardiac pacemaker may be more comfortable and appealing because unlike conventional pacemakers, patients are unable to see or feel the device or have an implant scar on the chest wall.

Leadless pacemakers may also be a better option than surgical endocardial pacemakers for patients with no vascular access due to renal failure or congenital heart disease.

Leadless Cardiac Pacemakers in Clinical Development

Leadless pacemakers are self-contained in a hermetically sealed capsule. The capsule houses a battery and elec-

tronics to operate the system. Similar to most pacing leads, the tip of the capsule includes a fixation mechanism and a monolithic controlled-release device. The controlled-release device elutes glucocorticosteroid to reduce acute inflammation at the implantation site. Leadless pacemakers have rate-responsive functionality, and current device longevity estimates are based on bench data. Estimates have suggested that these devices may last over ten years, depending on the programmed parameters.¹¹

Three systems are currently being evaluated in clinical trials: (1) the Micra Transcatheter Pacing System (Medtronic), (2) the Nanostim leadless pacemaker (St. Jude Medical); and (3) the WiCS Wireless Cardiac Stimulation System (EBR Systems). The first two devices are free-standing capsule-sized devices that are delivered via femoral venous access using a steerable delivery sheath. However, the fixing mechanism differs between the two devices. In the Micra Transcatheter Pacing System, the fixation system consists of four self-expanding nitinol tines, which anchor into the myocardium; for the Nanostim device, there is a screw-in helix that penetrates about 1 mm into the myocardium, with nylon tines that provide secondary fixation. In both devices, the cathode is steroid eluting and delivers pacing current; the anode is located in a titanium case. The third device, WiCS system differs from the other devices; this system requires implanting a pulse generator subcutaneously near the heart, which then wirelessly transmits ultrasound energy to a receiver electrode implanted in the left ventricle. The receiver electrode converts the ultrasound energy and delivers electrical stimulation to the heart sufficient to pace the left ventricle synchronously with the right.¹¹

Of these three, only the Micra transcatheter pacing system is approved by the FDA and commercially available in the U.S. Multiple clinical studies of Nanostim have been published^{1,13-18} but trials have been halted due to the migration of the docking button in the device. Evidence on Nanostim is not reviewed further because the device is not yet FDA approved.

The Micra is about 26 mm in length and introduced using a 23 French catheter via the femoral vein to the right ventricle. It weighs about 2 grams and has an accelerometer-based rate response.

Nanostim is about 40 mm in length and introduced using an 18 French catheter to the right ventricle. It also weighs about 2 grams and uses a temperature-based rate response sensor.¹⁹

REGULATORY STATUS

In April 2016, the Micra™ transcatheter pacing system (Medtronic) was approved by the FDA through the pre-market approval process for use in patients who have experienced one or more of the following conditions:

- symptomatic paroxysmal or permanent high-grade arteriovenous block in the presence of atrial fibrillation
- paroxysmal or permanent high-grade arteriovenous block in the absence of atrial fibrillation, 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.

Services that are the subject of a clinical trial do not meet our Technology Assessment and Medically Necessary Services Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment and Medically Necessary Services Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

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