Leadless Cardiac Pacemaker

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Place(s) of Service: Inpatient

I. 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 2 components: a pulse generator and electrodes (also referred to as leads). Pacemakers are considered life-sustaining, life-supporting class III devices for patients with variety of bradyarrhythmias. Even though the efficacy and safety profile of conventional pacemakers is excellent, in a small proportion of patients, they may result in complications particularly related to leads and requirement for 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 potential for complications as a result of leads and surgical pocket. Micra Transcatheter Pacing System is the only commercially available leadless pacemaker in the United States approved by the Food and Drug Administration.

For individuals with guidelines-based indication for a ventricular pacing system who are medically eligible to receive a conventional pacing system who are treated with Micra transcatheter pacing system, the evidence includes a pivotal prospective cohort study and a postapproval prospective cohort study. Relevant outcomes are other test performance, treatment-related mortality, and treatment-related morbidity. Results at 6 months and 1 year for the pivotal study reported high procedural success (above 99%) and device effectiveness (pacing capture threshold met in 98% patients). Majority of the system or procedural-related complications occur within 30 days. At 1 year, the incidence of major complication did not increase substantially from 6 months (3.5% at 6 months vs 4% at 1 year). Results of the postapproval study were consistent with pivotal study and showed a lower incidence of major complications at 30 days as well as 1 year (1.5% and 2.7%, respectively). In both studies, the point estimates of major complication were lower than the pooled estimates from 6 studies of conventional pacemakers used as a historical comparator.

While Micra Transcatheter Pacing System eliminates lead- and surgical pocket-related complications, its use can result in potentially more serious complication related to implantation/release of the device (traumatic cardiac injury) and less serious complications related to the femoral access site (groin hematomas and access site bleeding). Considerable uncertainties and unknowns remain in terms of durability of device and end of life device issues. Early and limited experience suggests that retrieval of these devices is unlikely because, in due course, the
devices will be encapsulated. There is 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 broad use of Micra transcatheter pacing system compared to conventional pacemakers has not been shown. The evidence is insufficient to determine the effects of technology on health outcomes.

For individuals with guidelines-based indication for a ventricular pacing system who are medically ineligible for a conventional pacing system who are treated with Micra transcatheter pacing system, the evidence includes subgroup analysis of a pivotal prospective cohort study and a postapproval prospective cohort study. Relevant outcomes are other test performance, treatment-related mortality, and treatment-related morbidity. Information on the outcomes in the subgroup of patients from the postapproval study showed that Micra 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 is unknown, the short-term benefits outweigh the risks as the complex tradeoff of adverse events for these devices need to be assessed in the context of lifesaving potential of pacing systems in patients who are ineligible for conventional pacing systems. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

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 (hereafter referred to as conventional pacemakers) consist of 2 components: a pulse generator (also referred to as battery component) and electrodes (also referred to as leads). The pulse generator consists of a power supply and electronics that can provide periodic electrical pulses to stimulate the heart. It is commonly implanted in the infraclavicular region of the anterior chest wall and generally placed in a prepectoral position, but in some cases a subpectoral position is advantageous. It generates the 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 1 lead is placed, typically in the right ventricle. In dual-chamber pacemakers, 2 leads are placed one in the right atrium and the other in right ventricle. Single-chamber ventricular pacemakers are much more commonly used in practice.

Annually, approximately 200,000 pacemakers are implanted in the United States and 1 million worldwide. Implantable pacemakers are considered life-sustaining, life-supporting class III devices for patients with variety of bradycardiac rhythm supraventricular tachycardias. Pacemaker systems have matured over the years with well-established, acceptable performance. As per the Food and Drug Administration (FDA), the
early performance of conventional pacemaker systems from implant through 60 to 90 days has usually demonstrated acceptable pacing capture thresholds and sensing. Intermediate performance from 90 days through more than 5 years has usually demonstrated reliability of the pulse generator and lead technology. Chronic performance from 5 to 10 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, nevertheless they are associated with complications particularly related to the requirement of leads. Most of safety data on the use of conventional pacemakers comes from registries from Europe, particularly from Denmark where all pacemaker implants are recorded in a national registry. This data is compiled in Table 1. It is important to recognize that valid comparison of complication rates is limited by differences in definitions of complications resulting in a wide variance of outcomes, as well as by the strongly varying time windows of follow-up, use of single chamber or dual chamber systems, and reporting over more than 2 decades. As such, the following data is contemporary and is limited to single-chamber systems when reported separately.

### Table 1. Reported Complication Rates with Conventional Pacemakers

<table>
<thead>
<tr>
<th>Complications</th>
<th>Rates, %a</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Traumatic complications</strong></td>
<td></td>
</tr>
<tr>
<td>RV perforation</td>
<td>0.2 to 0.8</td>
</tr>
<tr>
<td>RV perforation with tamponade</td>
<td>0.07 to 0.4</td>
</tr>
<tr>
<td>Pneumo(hemo)thorax</td>
<td>0.7 to 2.2</td>
</tr>
<tr>
<td><strong>Pocket complications</strong></td>
<td></td>
</tr>
<tr>
<td>Including all hematomas, difficult to control bleeding, infection, discomfort, skin erosion</td>
<td>4.75</td>
</tr>
<tr>
<td>Including only those requiring invasive correction or reoperation</td>
<td>0.66 to 1.0</td>
</tr>
<tr>
<td><strong>Lead-related complications</strong></td>
<td>1.6 to 3.8</td>
</tr>
<tr>
<td>Including lead fracture, dislodgement, insulation problem, infection, stimulation threshold problem, diaphragm or pocket stimulation, other</td>
<td></td>
</tr>
<tr>
<td>All system related infections requiring reoperation or extraction</td>
<td>0.5 to 0.73</td>
</tr>
</tbody>
</table>

Adapted from Food and Drug Administration executive summary memorandum. Even though the safety profile of conventional pacemakers is excellent, nevertheless they are associated with complications particularly related to the requirement of leads. Most of safety data on the use of conventional pacemakers comes from registries from Europe, particularly from Denmark where all pacemaker implants are recorded in a national registry. This data is compiled in Table 1. It is important to recognize that valid comparison of complication rates is limited by differences in definitions of complications resulting in a wide variance of outcomes, as well as by the strongly varying time windows of follow-up, use of single chamber or dual chamber systems, and reporting over more than 2 decades. As such, the following data is contemporary and is limited to single-chamber systems when reported separately.

### Potential Advantages of Leadless Cardiac Pacemakers Over Conventional Pacemakers

The potential advantages of leadless pacemakers fall into 3 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.

- **Lead complications** include lead failure, lead fracture, insulation defect, pneumothorax, infections requiring lead extractions/replacements that can result in a torn subclavian vein or tricuspid valve. In addition, there are potential risk of venous thrombosis and occlusion of the subclavian system from the leads. Use of a leadless system eliminates such potential risks with the added advantage that patient has vascular access preserved for other medical conditions (eg, dialysis or 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 as unlike conventional pacemakers, patients are unable to see or feel or have implant scar on the chest wall with leadless pacemakers.

- Lastly, leadless pacemakers may also be a better option than a surgical endocardial pacemaker 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 electronics 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 glucocorticostereoid 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 shown that these devices may last over 10 years depending on the programmed parameters.

There are 3 systems currently being evaluated in clinical trials: (1) Micra Transcatheter Pacing System (TPS, Medtronic, 2013), (2) Nanostim Leadless Pacemaker System (LPS, St. Jude Medical, 2012); and (3) WiCS system (Wireless Cardiac Stimulation, EBR systems). The first 2 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 2 devices. In the Micra Transcatheter Pacing System, the fixation system consists of 4 self-expanding nitinol tines, which anchor into the myocardium while in the Nanostim LCP, there is a screw-in helix that penetrates about 1 mm into the myocardium, with nylon tines that provide a secondary fixation mechanism. In both devices, the cathode is steroid eluting and delivers pacing current while the anode is located in a titanium case. The third device, WiCS System, is different from other devices that involves implanting a pulse generator subcutaneously near the heart and then wirelessly transmits ultrasound energy to a receiver electrode implanted inside the left ventricle. The receiver electrode converts the ultrasound energy, then delivers electrical stimulation to the heart sufficient to pace the left ventricle synchronously with the right.

Of these 3, only Micra Transcatheter Pacing System is approved by FDA and commercially available in the United States. Multiple clinical studies of Nanostim have been published but trials have been halted due to issues with the migration of the docking button in the device. Evidence on Nanostim is not reviewed further as it is not yet FDA approved.

Transcatheter Pacing System is about 26 mm in length and introduced through 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 through an 18 French catheter to the right ventricle. It is also about 2 grams in weight and uses a temperature-based rate response sensor.13

**Regulatory Status**

In April 2016, Micra® Transcatheter Pacing System (Medtronic) was approved by FDA through the premarket approval process for use in patients who have experienced 1 or more of the following conditions:
• symptomatic paroxysmal or permanent high-grade AV block in the presence of atrial fibrillation (AF)
• 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.

II. Criteria/Guidelines
Micra Transcatheter Pacing System is covered (subject to Limitations and Administrative Guidelines) when conditions A through D are met:
A. Patient has symptomatic paroxysmal or permanent high-grade AV block or symptomatic bradycardia-tachycardia syndrome or sinus node dysfunction (sinus bradycardia or sinus pauses)
B. One of the following criteria (1. or 2.) must be met:
   1. Patient has any of the following that precludes implantation of a single chamber ventricular pacemaker:
      a. Need for persistent anticoagulation therapy
      b. Persistent severe bleeding tendencies
      c. Severe lung disease and positive end-expiratory pressure ventilation that precludes internal jugular and subclavian access
      d. Congenital acquired venous anomalies that preclude transvenous access to the heart
      OR
   2. Presence of any of the following and delay in implanting a single chamber ventricular pacemaker could be life threatening:
      a. Persistent or recurrent local infection at implantation site
      b. Persistent or recurrent active systemic infection with bacteremia
C. Patient does not have any of the following device(s) implanted:
   1. An implanted device that would interfere with the implant of the Micra device in the judgment of the implanting physician
   2. An implanted inferior vena cava filter
   3. A mechanical tricuspid valve
   4. An implanted cardiac device providing active cardiac therapy that may interfere with the sensing performance of the Micra device.
D. Patient does not have any of the following conditions:
   1. Femoral venous anatomy unable to accommodate a 7.8 mm (23 French) introducer sheath
   2. Unable to accommodate implant on the right side of the heart (e.g., due to obstructions or severe tortuosity)
   3. Morbid obesity that prevents the implanted device from obtaining telemetry communication within ≤12.5 cm (4.9 in)
4. Known intolerance to titanium, titanium nitride, parylene C, primer for parylene C, PEEK, siloxane, nitinol, platinum, iridium, liquid silicone rubber, and silicone medical adhesive and heparin.
5. Known sensitivity to contrast media that cannot be adequately premedicated.
6. Cannot tolerate a single dose of 1.0 mg of dexamethasone acetate.

III. Limitations

Micra Transcatheter Pacing System is not covered in all other situations as it has not been shown to improve health outcomes.

IV. Administrative Guidelines

A. Precertification is required for the insertion of a leadless cardiac pacemaker. To pre-certify, complete HMSA’s Precertification Request form and fax or mail the form with the following documentation:
   1. Clinical notes to include specific documentation demonstrating that Section II. A-D criteria have all been met.

B. Applicable codes:

<table>
<thead>
<tr>
<th>CPT Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>33274</td>
<td>Insertion, replacement, or removal and replacement of permanent leadless pacemaker.</td>
</tr>
<tr>
<td>33275</td>
<td>Removal of permanent leadless pacemaker.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-10 Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I44.1-I44.2</td>
<td>Atrioventricular block; second degree and complete</td>
</tr>
<tr>
<td>I45.2</td>
<td>Bifascicular block</td>
</tr>
<tr>
<td>I45.3</td>
<td>Trifascicular block</td>
</tr>
<tr>
<td>I45.5</td>
<td>Other specified heart block; includes sinoatrial block</td>
</tr>
<tr>
<td>I47.2</td>
<td>Ventricular tachycardia</td>
</tr>
<tr>
<td>R00.1</td>
<td>Bradycardia unspecified; includes sinus bradycardia</td>
</tr>
<tr>
<td>I48.0-I48.92</td>
<td>Atrial fibrillation and flutter code range</td>
</tr>
<tr>
<td>I49.3</td>
<td>Ventricular premature depolarization (PVC’s)</td>
</tr>
<tr>
<td>I49.5</td>
<td>Sick sinus syndrome (tachycardia-bradycardia syndrome)</td>
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</tbody>
</table>
V. Background

This evidence review was created in August 2018 with a search of the MEDLINE database through July 18, 2018.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Conventional pace makers systems have been in use for over 50 years and the current available technology has matured with significant similarities of device design across models. Extensive bench testing experience with conventional pacemakers and a good understanding of operative and early postimplant safety and effectiveness is available which limits the need for collection of clinical data to understand their safety and effectiveness with regard to implant, tip fixation, electrical measures, and rate response. As such, a randomized trial comparing the leadless pacemakers with conventional pacemakers was not required by the Food and Drug Administration (FDA).

INDIVIDUALS WITH GUIDELINES-BASED INDICATION FOR A VENTRICULAR PACING SYSTEM WHO ARE MEDICALLY ELIGIBLE TO RECEIVE A CONVENTIONAL PACING SYSTEM

Clinical Context and Therapy Purpose

The purpose of Micra Transcatheter Pacing System in patients with a class I or II guidelines-based indication for implantation of a single chamber ventricular pacemaker is to provide a treatment option that is an alternative to or an improvement on conventional pacing systems.

The question addressed in this evidence review is: Does use of the Micra Transcatheter Pacing System improve the net health outcome in patients with patients with a class I or II guidelines-based indication for implantation of a single-chamber ventricular pacemaker who are medically eligible to receive a conventional pacing systems?

The following PICOTS were used to select literature to inform this review.
Patients
The relevant population of interest is patients with a class I or II guidelines-based indication for implantation of a single chamber ventricular pacemaker who are medically eligible to receive conventional pacing system.

Interventions
The therapy being considered is the Micra Transcatheter Pacing System.

Comparators
The following therapy is currently being used to make decisions about managing patients requiring a pacemaker: a conventional pacemaker.

Outcomes
The general outcomes of interest are treatment-related mortality and morbidity. Specifically, the short-term outcomes include acute complication-free survival rate, electrical performance of the device including pacing capture threshold and adverse events including procedural and postprocedural complications. Long-term outcomes include chronic complication-free survival rate, electrical performance of the device including pacing impedance and pacing thresholds and chronic complications including any system explant, replacement (with and without system explant) and repositions. Further, analysis summary statistics regarding battery length are deemed crucial as well.

Timing
To assess short-term safety, the first 30 days postimplant is generally considered appropriate as majority of device and procedural complications occur within this time frame. To assess long-term efficacy and safety as well issues related to end of life of the device, follow up to 9 to 12 years postimplant with adequate sample size are required to characterize device durability and characterize infrequent complications with sufficient certainty.

Setting
Cardiac pacemaker implant is performed by interventional cardiologists in the electrophysiology laboratory.

Nonrandomized Controlled Trials

Pivotal Trial
The pivotal investigational device exemption (IDE) trial was a prospective single cohort study in which 744 patients with class I or II indication for implantation of a single chamber ventricular pacemaker according to ACC/AHA/HRS 2008 guidelines and any national guidelines were enrolled. The details on the design14 and results of the IDE trial have been published. Trial characteristics and results at 6 months are summarized in Table 2 and 3, respectively. System performance from the pivotal trial has been published but results are not discussed further.

Of the 744 patients, the implantation of the Micra Transcatheter Pacing System was attempted in 725 patients of whom 719 (99.2%) were successfully implanted. The demographics of the trial population were typical for a single chamber pacemaker study performed in the United States with
42% being female and average age was 76 years. Sixty-four percent had a pacing indication associated with persistent or permanent atrial arrhythmias, 72.6% had any atrial fibrillation at baseline, and 27.4% did not have a history of atrial fibrillation. Among those 27.4% (n=199) without atrial fibrillation, 16.1% (n=32) had a primary indication of sinus bradycardia and 3.5% (n=7) had a primary indication of tachycardia-bradycardia.

The IDE trial had 2 primary end points related to safety and efficacy. The trial would have met the safety end point if the lower bound of the 95% confidence interval (CI) for the rate of freedom from major complications related to the Micra Transcatheter Pacing System or implantation procedure exceeded 83% at 6 months. Major complications were defined as those resulting in any of the following: death, permanent loss of device function due to mechanical or electrical dysfunction of the device (eg, pacing function disabled, leaving device abandoned electrically), hospitalization, prolonged Hospitalization by at least 48 hours or system revision (reposition, replacement, explant). The trial would have met the efficacy end point if the lower bound of the 95% CI for the proportion of patients with adequate pacing capture thresholds (PCT) exceeded 80% at 6 months. PCT as an effectiveness objective is a common electrical measure of pacing efficacy and is consistent with recent studies. Pacing capture threshold measured in volts is defined as the minimum amount of energy needed to capture the myocardial tissue electrically. Unnecessary high pacing output adversely shortens the battery life of the pacemaker and is influenced by physiologic and pharmacologic factors. As per FDA, demonstrating that “PCT is less than 2 Volts for the vast majority of subjects will imply that the Micra Transcatheter Pacing System will have a longevity similar to current pacing systems since Micra’s capture management feature will nominally set the safety margin to 0.5 volts above the PCT with hourly confirmation of the PCT.”

Results of the IDE trial are summarized in Table 3. At 6 months, the trial met both the efficacy and safety primary end points including freedom from major complications related to the system or procedure in 96.0% of the patients (95% CI, 93.9% to 97.3%), compared with a performance goal of 83%, and an adequate pacing capture threshold in 98.3% of the patients (95% CI, 96.1% to 99.5%), compared with a performance goal of 80%.

The results of the IDE trial were compared post hoc with a historical cohort of 2667 patients generated from the six previous pacemaker studies conducted between 2005 and 2012 by Medtronic that evaluated performance requirement at 6 months postimplant of right ventricle pacing leads (single-chamber rates obtained by excluding any adverse events that were only related to the right atrial lead from the analysis). Micra Transcatheter Pacing System was associated with fewer complication than the historical control (4.0% vs 7.4%; hazard ratio [HR], 0.49; 95% CI, 0.33 to 0.75; p=0.001). Because there were differences in the baseline patient characteristics between the 2 cohorts (patients in the historical cohort were younger and with lower prevalence of coexisting conditions vs the IDE trial), an additional propensity-matched analysis was also conducted that showed similar result (HR=0.46; 95% CI, 0.28 to 0.74). As per FDA, lower rate of major complication with Micra Transcatheter Pacing System were driven by reductions in access site events (primarily implant site hematoma and implant site infections), pacing issues (primarily device capture and device pacing issues), and fixation events (there were no device/lead dislodgements in the Micra IDE trial).
While the overall rate of complication was low, the rate of major complications related to cardiac injury (ie., pericardial effusion or perforation) was higher in the Micra IDE trial than in the 6 reference Medtronic pacemaker studies (1.6% vs 1.1%, p=0.288). Thus, there appears to be a trade-off between types of adverse events with Micra Transcatheter Pacing System and conventional pacemakers. While adverse events related to leads and pocket are eliminated or minimized with Micra Transcatheter Pacing System, certain adverse events such as groin vascular complications and vascular/cardiac bleeding occur at a higher frequency or are additive (new events) than conventional pacemakers. Of these, procedural complications such as acute cardiac perforations that were severe enough to resulting result in tamponade and emergency surgery were most concerning.

In addition to lack of adequate data on long-term safety, effectiveness, reliability, and incidence of late device failures and battery longevity, there is also inadequate clinical experience with issues related to devices that have reached end of life including whether to extract or leave the device in situ and possibility of device-device interactions. There is no 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. Even though, there have only been few device retrievals and very limited experience with time course of encapsulation of these devices in humans, it is highly likely that these devices will be fully encapsulated by the end of its typical battery life, and therefore device retrieval is unlikely. Current recommendations for end-of-device-life care for a Micra device may include the addition of a replacement device with or without explanation of the Micra device, which should be turned off.

**Post Approval Study**
The FDA approval of the Micra Transcatheter Pacing System is contingent on multiple postapproval studies to ensure reasonable assurance of continued safety and effectiveness of the device. Among these, the Micra Transcatheter Pacing System Post-Approval Study, a global, prospective, observational, multi-center study, enrolled 1830 patients to ensure that data is available for 1741 patients to estimate acute complication rate within 30 day of the implant, 500 patients to estimate 9-year complication free survival rate, and a minimum of 200 patients with a Micra Transcatheter Pacing System revision for characterizing end of device service. As per the protocol, if a subsequent device is placed and the Micra is deactivated or explanted, Medtronic would contact the implanting center and request the patient's clinical data surrounding the revision. All such data would be summarized including the type of system revision, how the extraction was attempted, success rate, and any associated complications.

Study characteristics and results at 1 year (reported in FDA documents and as conference presentation) are summarized in Table 2 and 3, respectively. The postapproval study completed enrollment in early March 2018. The definition of major complication in the postapproval study was same as the Micra IDE trial. It is unclear if any patients who participated in the IDE trial were also enrolled in the post approval study. Results summarized in Table 3 report the data at 30 days published by Roberts et al (2017) and Chami et al (2018) with a mean follow-up of 6.8 months of 1817 patients of whom 465 patients had a follow-up for more than 1 year.
At 30 days, the major complication rate was 1.51% (95% CI, 0.78 to 2.62%). The major complication rate was lower in the postapproval study compared with IDE trial (odds ratio [OR], 0.58; 95% CI, 0.27 to 1.25) although this did not reach statistical difference. The lower major complications was associated with a decrease in events that led to hospitalization, prolonged hospitalization, or loss of device function in the postapproval study compared to the IDE trial.

After a mean follow-up of 6.8 months, the major complication rate was 2.7% (95% CI, 2.0% to 3.6%). Authors compared these results with the same historical cohort of 2667 patients used in the IDE trial and reported a 63% reduction in the risk for major complications through 12 months with Micra Transcatheter Pacing System relative to conventional pacemakers (HR=0.37; 95% CI, 0.27 to 0.52). Additionally, the risk for major complication was lower in the Micra postapproval study than in the IDE trial but it was statistically significant different (HR= 0.71, 95% CI, 0.44 to 1.1). However, details of events classified as major complications were not reported for the historical control or for the IDE trial cohort at 1 year and therefore it is unclear as to which events were decreased in the post approval study or if any events increased with Micra Transcatheter Pacing System.

### Table 2. Summary of Key Nonrandomized Trial Characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Type</th>
<th>Country</th>
<th>Date</th>
<th>Participants</th>
<th>Treatment</th>
<th>Follow-Up, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reynolds et al (2016); NCT02004873</td>
<td>Prospective single cohort</td>
<td>19 countries in North America, Europe, Asia, Australia, and Africa</td>
<td>2013-2015</td>
<td>Patients who met class I or II guidelines-based indications for pacing and suitable candidates for single-chamber</td>
<td>Micra transcatheter pacemaker (n=744)</td>
<td>6</td>
</tr>
<tr>
<td>Roberts et al (2017); Chami et al (2018); NCT02536118 Micra Post Approval Study</td>
<td>Prospective single cohort</td>
<td>23 countries in North America, Europe,</td>
<td>2016-2018</td>
<td>Any patient to be implanted with a Micra</td>
<td>Micra transcatheter pacemaker</td>
<td>1.8&lt;sup&gt;a&lt;/sup&gt; 6.8&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> 30-day results reported by Roberts et al (2017).
<sup>b</sup> Results after a mean follow-up of 6.8 months reported by Chami et al (2018)<sup>22</sup> as an abstract.

### Table 3. Summary of Key Nonrandomized Trial Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Freedom From System- or Procedure-Related Major Complications</th>
<th>Percentage of Patients With Adequate Pacing Capture Thresholds at 6 Months</th>
<th>Major Complications</th>
<th>Major Complications Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reynolds et al (2016)&lt;sup&gt;16&lt;/sup&gt;; 6</td>
<td>N 719&lt;sup&gt;a&lt;/sup&gt;; 300&lt;sup&gt;b&lt;/sup&gt;</td>
<td>96.0% 98.3% (≤2.0 V)</td>
<td>Total major complications: 28 in 25 patients (3.5%) DVT: 1 (0.1%) Pulmonary TE: 1 (0.1%) Events at groin puncture site: 5 (0.7%) Cardiac perforation: 11 (1.6%) Pacing issues: 2 (0.3%)</td>
<td>Death: 1 (0.1%) Loss of device function: 1 (0.1%) Hospitalization: 13 (2.3%) Prolonged hospitalization (≥48 h): 16 (2.6%) System revision: 3 (0.4%)</td>
</tr>
<tr>
<td>Micra, n (%)</td>
<td>95% CI 93.9% to 97.3% 95.4% to 99.6%</td>
<td>95% CI NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>
### Micra, n (%)  
<table>
<thead>
<tr>
<th>Dury et al (2017)</th>
<th>726</th>
<th>NA</th>
<th>726</th>
<th>726</th>
</tr>
</thead>
</table>

| Total major complications: 32 in 29 patients (4.0%) | Death: NR (0.1%) |
| DVT: 1 (0.1%) | Loss of device function: NR (0.1%) |
| Pulmonary TE: 1 (0.1%) | Hospitalization: NR (2.3%) |
| Events at groin puncture site: 5 (0.7%) | Prolonged hospitalization ≥48 h: NR (2.2%) |
| Cardiac perforation: 11 (1.6%) | System revision: (0.7%) |
| Pacing issues: 2 (0.3%) | Loss of device function: NR (0.3%) |

<table>
<thead>
<tr>
<th>95% CI</th>
<th>94.2% to 97.2%</th>
<th>NA</th>
</tr>
</thead>
</table>

### Post-Approval Study  

<table>
<thead>
<tr>
<th>Roberts et al (2017)</th>
<th>795</th>
<th>NA</th>
<th>795</th>
<th>795</th>
</tr>
</thead>
</table>

| Total major complications: 13 in 12 patients (1.51%) | Death: 1 (0.13%) |
| [95% CI: 0.78% to 2.62%] | Hospitalization: 4 (0.50%) |
| DVT: 1 (0.13%) | Prolonged hospitalization ≥48 h: 9 (1.01%) |
| Events at groin puncture site: 6 (0.75%) | System revision: 2 (0.25%) |
| Cardiac effusion/perforation: | |
| Device dislodgement: 1 (0.13%) | |

<table>
<thead>
<tr>
<th>OR (95% CI)</th>
<th>0.58 (0.27 to NA)</th>
<th>NA</th>
<th>NA</th>
<th>NA</th>
</tr>
</thead>
</table>

### Post-Approval Study  

<table>
<thead>
<tr>
<th>Chami et al (2018)</th>
<th>1817</th>
<th>NA</th>
<th>1817</th>
<th>NA</th>
</tr>
</thead>
</table>

| Total major complications: 46 in 41 patients (2.7%) | NA |
| [95% CI: 2.0% to 3.6%] | |
| Pericardial effusions: 8 (0.44%) | |
| Dislodgement: 1 (0.06%) | |
| Procedure-related infections: 3 (0.17%) | |
| Procedure-related deaths: 5 (0.28%) | |
| As per FDA: | |
| Complications: 61 in 53 Deaths: | |
| Procedure-related: 4 | |
| Unknown relatedness: | 3 |

<table>
<thead>
<tr>
<th>HR (95% CI)</th>
<th>0.71 (0.44 to 1.1)*</th>
<th>NA</th>
<th>0.37 (0.27 to NA)</th>
<th>NA</th>
</tr>
</thead>
</table>

---

CI: confidence interval; DVT: deep vein thrombosis; FDA: Food and Drug Administration; HR: hazard ratio; NA: not available; NR: not reported; TE: thromboembolism.

* Total number of patients who received the implant successfully.

† Number of patients for whom data was available for 6-month evaluation.

‡ Device explant, reposition or replacement

§ Calculations performed by BCBSA based on the major complication rate (2.7%; 95% CI 2.0 to 3.6%) reported by Chami et al (2018)

∥ Major complication compared against IDE trial.

¶ Unclear if the complications meet the definition of a major complication as events leading to death, hospitalization, prolonged hospitalization by 48 hours, system revision, or loss of device therapy.
The purpose of the gaps tables (see Tables 4 and 5) is to display notable gaps identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of the evidence supporting the position statement.

### Table 4. Relevance Gaps

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Intervention</th>
<th>Comparator</th>
<th>Outcomes</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reynolds et al (2016)(^{16}) 6 months; Durray et al (2017)(^{23}) 12 months</td>
<td></td>
<td>2. This was a single cohort study; there was no comparator</td>
<td>1. Not sufficient duration for benefit; 2. Not sufficient duration for harms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Roberts et al (2017)(^{21}) Post-Approval Study 30-day; Chami et al (2018)(^{22}) Post-Approval Study 12 months</td>
<td></td>
<td>2. This was a single cohort study; there was no comparator</td>
<td>1. Not sufficient duration for benefit; 2. Not sufficient duration for harms</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

- **Population key:** 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
- **Intervention key:** 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.
- **Comparator key:** 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
- **Outcomes key:** 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
- **Follow-Up key:** 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

### Table 5. Study Design and Conduct Gaps

<table>
<thead>
<tr>
<th>Study</th>
<th>Allocation (^{a})</th>
<th>Blinding (^{b})</th>
<th>Selective Reporting (^{c})</th>
<th>Data Completeness (^{d})</th>
<th>Power (^{e})</th>
<th>Statistic (^{f})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reynolds et al (2016)(^{16}) 6 months; Durray et al (2017)(^{23}) 12 months</td>
<td>1. Participants not randomly allocated; design was prospective single cohort study</td>
<td>3. Not blinded to treatment assignment</td>
<td>4. Not blinded outcome assessment. However, adverse events analyzed by an independent clinical event committee. Trial oversight provided by an independent data and safety monitoring committee.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Roberts et al (2017)(^{21}) Post-Approval Study 30-day; Chami et al (2018)(^{22})</td>
<td>1. Participants not randomly allocated; design was prospective registry</td>
<td>3. Not blinded to treatment assignment</td>
<td>4. Not blinded outcome assessment</td>
<td>5. Outcome assessed by treating physician</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1-year

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

- **Allocation key:** 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
- **Blinding key:** 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
- **Selective Reporting key:** 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
- **Data Completeness key:** 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
Section Summary: Individuals With Guidelines-Based Indication for a Ventricular Pacing System who are Medically Eligible to Receive a Conventional Pacing System

The evidence for use of Micra Transcatheter Pacing System consists of a pivotal prospective cohort study and a postapproval prospective cohort study. Results at 6 months and 1 year for the pivotal study reported high procedural success (above 99%) and device effectiveness (pacing capture threshold met in 98% patients). Majority of the system or procedural-related complications occur within 30 days. At 1 year, the incidence of major complication did not increase substantially from 6 months (3.5% at 6 months versus 4% at 1 year). Results of the postapproval study were consistent with pivotal study and showed a lower incidence of major complications at -30 days as well as 1 year (1.5% and 2.7%, respectively). In both studies, the point estimates of major complication were lower than the pooled estimates from 6 studies of conventional pacemakers used as a historical comparator. While Micra Transcatheter Pacing System eliminates adverse events associated with lead and pocket issue, its use results in additional complication related to the femoral access site (groin hematomas and access site bleeding) and implantation/release of the device (traumatic cardiac injury). Considerable uncertainties and unknowns remain in terms of durability of device and end of life device issues. Early and limited experience suggests that retrieval of these devices is unlikely because in due course of time, the devices will be encapsulated. There is 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.

INDIVIDUALS WITH GUIDELINES-BASED INDICATION FOR A VENTRICULAR PACING SYSTEM WHO ARE MEDICALLY INELIGIBLE FOR A CONVENTIONAL PACING SYSTEM

Clinical Context and Therapy Purpose

The purpose of Micra Transcatheter Pacing System in patients with a class I or II guidelines-based indication for implantation of a single chamber ventricular pacemaker is to provide a treatment option that is an alternative to or an improvement on conventional pacing systems. The question addressed in this evidence review is: Does use of the Micra Transcatheter Pacing System improve the net health outcome in patients with patients with a class I or II guidelines-based indication for implantation of a single chamber ventricular pacemaker who are medically ineligible for a conventional pacing system?

The following PICOTS were used to select literature to inform this review.

Patients

The relevant population of interest is patients with a class I or II guidelines-based indication for implantation of a single chamber ventricular pacemaker who are medically ineligible for a conventional pacing system.

Interventions
The therapy being considered is Micra Transcatheter Pacing System.

Comparators
The following therapy and practice are currently being used to make decisions about managing patients ineligible for a conventional pacemaker: medical management and/or conventional pacemakers.

Outcomes
The general outcomes of interest are treatment-related mortality and morbidity. Specifically, the short-term outcomes include acute complication-free survival rate, electrical performance of the device including pacing capture threshold and adverse events including procedural and postprocedural complications. Long-term outcomes include chronic complication-free survival rate, electrical performance of the device including pacing impedance and pacing thresholds and chronic complications including any system explant, replacement (with and without system explant) and repositions. Further, analysis summary statistics regarding battery length are deemed crucial as well.

Timing
To assess short-term safety, the first 30 days postimplant is generally considered appropriate as majority of device and procedural complications occur within this time frame. To assess long-term efficacy and safety as well issues related to end of life of the device, follow up to 9 to 12 years postimplant with adequate sample size are required to characterize device durability and characterize infrequent complications with sufficient certainty.

Setting
Cardiac pacemaker implant is performed by interventional cardiologists in the electrophysiology laboratory.

Nonrandomized Controlled Trials
No studies that exclusively enrolled patients who were medically ineligible to receive a conventional pacing system were identified.

In the IDE trial, 6.2% or 45 patients received the Micra Transcatheter Pacing System because they were medically ineligible to receive a conventional pacing system such as compromised venous access, the need to preserve veins for hemodialysis, thrombosis, a history of infection, or the need for an indwelling venous catheter. A stratified analysis of these 45 patients was not presented in the published paper or the FDA documents.

In the postapproval registry whose early results have been published only as an abstract, authors reported stratified results of 99 of 1744 patients who had previous cardiac implantable electronic device (CIED) infection. 22 Of these 99, 78 (79%) were classified as medically ineligible to receive a conventional pacemaker in the opinion of physician. A stratified analysis of these 78 patients was not presented in the abstract. Trial characteristics and results are summarized in Tables 6 and 7, respectively. In this cohort of patients with CIED infection, Micra was implanted successfully in 98 patients and the previous CIED was explanted the same day as Micra was implanted in 36% of patients. Major complications were reported in 2% of patients with an average follow-up of 5.5
months. Six deaths were reported but none was related to the Micra Transcatheter Pacing System or the procedure.

### Table 6. Summary of Key Nonrandomized Trial Characteristics in Patients Ineligible to Receive Conventional Pacing Systems and/or Previous Cardiac Implantable Electronic Device Infection

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Type</th>
<th>Country</th>
<th>Dates</th>
<th>Participants</th>
<th>Treatment</th>
<th>Follow-Up, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chami et al (2018)^2^</td>
<td>Prospective single cohort</td>
<td>23 countries in North America, Europe, Asia, Australia, and Africa</td>
<td>2016-2018</td>
<td>Any patient to be implanted with a Micra with a CIED infection</td>
<td>Micra transcatheter pacemaker (N=99)</td>
<td>5.5 (range, 0.4-24.7)</td>
</tr>
</tbody>
</table>

CIED: cardiac implantable electronic device.

### Table 7. Summary of Key Nonrandomized Trial Results in Patients Ineligible to Receive Conventional Pacing Systems and/or Previous Cardiac Implantable Electronic Device Infection

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients With System- or Procedure-Related Major Complications</th>
<th>Average Pacing Threshol</th>
<th>Major Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>99</td>
<td>68</td>
<td>0.64 ± 0.42 V</td>
</tr>
<tr>
<td>Micra, n (%)</td>
<td>2% (2/99)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IVC: in cava filter

The purpose of the gaps tables (see Tables 8 and 9) is to display notable gaps identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of the evidence supporting the position statement.

### Table 8. Relevance Gaps

<table>
<thead>
<tr>
<th>Study</th>
<th>Population^a</th>
<th>Intervention^b</th>
<th>Comparator^c</th>
<th>Outcomes^d</th>
<th>Follow-Up^e</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chami et al (2018)^2^</td>
<td></td>
<td>2. This was a single cohort study; there was no comparator</td>
<td></td>
<td>1. Not sufficient duration for benefit; 2. Not sufficient duration for harms</td>
<td></td>
</tr>
</tbody>
</table>

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

^a Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

^b Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

^c Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

^d Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.

^e Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.
### Table 9. Study Design and Conduct Gaps

<table>
<thead>
<tr>
<th>Study</th>
<th>Allocation*</th>
<th>Blindingb</th>
<th>Selective Reporting</th>
<th>Data Completeness</th>
<th>Power</th>
<th>Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-Approval Registry</td>
<td>prospectively</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

- **Allocation key:** 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
- **Blinding key:** 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
- **Selective Reporting key:** 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
- **Data Completeness key:** 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
- **Power key:** 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
- **Statistical key:** 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

### Section Summary: Individuals with Guidelines-Based Indication for a Ventricular Pacing System who are Medically Ineligible for a Conventional Pacing System

No studies that exclusively enrolled patients who were medically ineligible to receive a conventional pacing system were identified. However, a subgroup of patients in whom use of conventional pacemakers was precluded was enrolled in the pivotal as well as the postapproval trial. Information on the outcomes in these subgroups of patients from the postapproval study showed that Micra 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 is unknown, the short-term benefits outweigh the risks as the complex tradeoff of adverse events for these devices need to be assessed in the context of lifesaving potential of pacing systems in patients who are ineligible for conventional pacing systems on the market.

### SUMMARY OF EVIDENCE

For individuals with guidelines-based indication for a ventricular pacing system who are medically eligible to receive a conventional pacing system who are treated with Micra transcatheter pacing system, the evidence includes a pivotal prospective cohort study and a postapproval prospective cohort study. Relevant outcomes are other test performance, treatment-related mortality, and treatment-related morbidity.

Results at 6 months and 1 year for the pivotal study reported high procedural success (above 99%) and device effectiveness (pacing capture threshold met in 98% patients). Majority of the system or procedural-related complications occur within 30 days. At 1 year, the incidence of major complication did not increase substantially from 6 months (3.5% at 6 months vs 4% at 1 year). Results of the postapproval study were consistent with pivotal study and showed a lower incidence of major complications at -30 days as well as 1 year (1.5% and 2.7%, respectively). In both studies, the point estimates of major complication were lower than the pooled estimates from 6 studies of conventional pacemakers used as a historical comparator. While Micra
Transcatheter Pacing System eliminates lead- and surgical pocket-related complications, its use can result in potentially more serious complication related to implantation/release of the device (traumatic cardiac injury) and less serious complications related to the femoral access site (groin hematomas and access site bleeding). Considerable uncertainties and unknowns remain in terms of durability of device and end of life device issues. Early and limited experience suggests that retrieval of these devices is unlikely because, in due course, the devices will be encapsulated. There is 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 broad use of Micra transcatheter pacing system compared to conventional pacemakers has not been shown. The evidence is insufficient to determine the effects of technology on health outcomes.

For individuals with guidelines-based indication for a ventricular pacing system who are medically ineligible for a conventional pacing system who are treated with Micra transcatheter pacing system, the evidence includes subgroup analysis of a pivotal prospective cohort study and a postapproval prospective cohort study. Relevant outcomes are other test performance, treatment-related mortality, and treatment-related morbidity. Information on the outcomes in the subgroup of patients from the postapproval study showed that Micra 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 is unknown, the short-term benefits outweigh the risks as the complex tradeoff of adverse events for these devices need to be assessed in the context of lifesaving potential of pacing systems in patients who are ineligible for conventional pacing systems. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Supplemental Information

PRACTICE GUIDELINES AND POSITION STATEMENTS
American College of Cardiology Foundation et al
The American College of Cardiology Foundation, American Heart Association, and Heart Rhythm Society’s focused update (2012) on device-based therapy of cardiac rhythm abnormalities incorporated into their joint 2008 guidelines for device-based therapy of cardiac rhythm abnormalities does not include recommendations on leadless cardiac pacemakers.

The 2012 Heart Rhythm Society and American College of Cardiology Foundation expert consensus statement on pacemaker device and mode selection did not include recommendations on leadless cardiac pacemakers.

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS
Not applicable.

MEDICARE NATIONAL COVERAGE
The Centers for Medicare & Medicaid (CMS) cover leadless pacemakers under coverage with evidence development criteria when procedures are performed in studies approved the Food and
Drug Administration (FDA) in “prospective longitudinal studies [and] leadless pacemakers ... are used in accordance with the FDA approved label for devices that have either:

- An associated ongoing FDA approved postapproval 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?”

The following 2 studies are currently approved by CMS: (1) The Micra CED Study (NCT03039712); CMS approval date: 03/09/17; and (2) Micra Transcatheter Pacing System Post-Approval Registry (NCT02536118); CMS approval date: 02/09/17.

**ONGOING AND UNPUBLISHED CLINICAL TRIALS**

Some currently unpublished trials that might influence this review are listed in Table 10.

**Table 10. Summary of Key Trials**

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT03039712</td>
<td>Longitudinal Coverage With Evidence Development Study on Micra Leadless Pacemakers (Micra CED)</td>
<td>37000</td>
<td>Jun 2021</td>
</tr>
<tr>
<td>NCT02610673</td>
<td>WiCS-LV Post Market Surveillance Registry</td>
<td>100</td>
<td>Nov 2021</td>
</tr>
<tr>
<td>NCT02536118</td>
<td>Micra Transcatheter Pacing System Post-Approval Registry</td>
<td>3100</td>
<td>Aug 2026</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

* Denotes industry-sponsored or cosponsored trial.

**VI. Important Reminder**

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA’s determination as to medical necessity in a given case, the physician may request that
HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

VII. References


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Dwight Reynolds, MD; Javier Garcia-Seara, MD; Jacques Mansourati, MD; Jean-Luc Pasquie,
MD; Paul R. Roberts, MD; Kyoko Soejima, MD; Kurt Stromberg, MS; Jonathan P. Piccini, MD,
MHS, FHS. Leadless Pacemaker Implant in Patients with Pre-Existing Infections: Results from the Micra Post-Approval Registry. Paper presented at: Heart Rhythm Scientific Sessions (May 10, 2018) 2018; Boston, Massachusetts.


