ASURIS NORTHWEST HEALTH

Medical Policy Manual Surgery, Policy No. 217

Leadless Cardiac Pacemakers

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Next Review: September 2024
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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

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). 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.

MEDICAL POLICY CRITERIA

Notes: See Policy Guidelines for contraindications for leadless pacemaker systems.

I. A single-chamber transcatheter leadless cardiac pacing system may be considered **medically necessary** in patients when all the Criteria (A. – C.) . below are met:

   A. The device is approved by the Food and Drug Administration (FDA).

   B. The patient has one or more of the following:

      1. Symptomatic paroxysmal or permanent high-grade atrioventricular (AV) block; or

      2. Symptomatic bradycardia-tachycardia syndrome; or

3. Sinus node dysfunction (sinus bradycardia or sinus pauses).

C. The patient has a significant contraindication precluding placement of conventional single-chamber ventricular pacemaker leads, including but not limited to a history or high risk of infection, limited venous access, or presence of a bioprosthetic tricuspid valve.

II. A single-chamber transcatheter leadless pacing system is considered **investigational** for all other indications when Criterion I. is not met.

III. The initial insertion or replacement of a dual chamber leadless pacemaker is considered **investigational.**

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

POLICY GUIDELINES

MICRA™ SYSTEM CONTRAINDICATIONS[1]

Devices

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

Conditions

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 premedicated

Other Contraindications

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.

AVEIR™ SYSTEM CONTRAINDICATIONS[2]

Aveir™ DR Leadless System

As per the FDA label, the Aveir™ Leadless Pacemaker System is contraindicated in the following situations:

- Use of any pacemaker is contraindicated in patients with a co-implanted ICD because high-voltage shocks damage the pacemaker, and the pacemaker could reduce shock effectiveness.
- Single-chamber ventricular demand pacing is relatively contraindicated in patients who have demonstrated pacemaker syndrome, have retrograde VA conduction, or suffer a drop in arterial blood pressure with the onset of ventricular pacing.
- Programming of rate-responsive pacing is contraindicated in patients with intolerance of high sensor-driven rates.
- Use is contraindicated in patients with an implanted vena cava filter or mechanical tricuspid valve because of interference between these devices and the delivery system during implantation.
- Persons with known history of allergies to any of the components of this device may suffer an allergic reaction to this device. Prior to use on the patient, the patient should be counseled on the materials (listed in IFU Product Materials) contained in the device and a thorough history of allergies must be discussed.
- For the MRI contraindications for patients implanted with Aveir™ Leadless Pacemaker, refer to the MRI Procedure Manual.
- There are no contraindications for use of the Aveir™ Link Module.

LIST OF INFORMATION NEEDED FOR REVIEW

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- History and Physical/Chart Notes
- Documentation of symptoms, associated diagnoses and treatments
- Name of FDA-approved leadless device
- Documentation that supports contraindication of placement of conventional single-chamber ventricular pacemaker leads

CROSS REFERENCES

1. Implantable Cardioverter Defibrillator, Surgery, Policy No. 17
2. Intracardiac Ischemia Monitoring, Surgery, Policy No. 208

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 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, tow leads are placed: one in the right atrium and the other in the right ventricle. Single-chamber ventricular pacemakers are more common.

As of 2015, approximately 200,000 pacemakers are implanted in the United States and one million worldwide, annually.[3] 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 has 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 (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, they are associated with complications particularly related to leads. Most 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. 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.[4] As such, the following data are contemporary and limited to single-chamber systems when reported separately.

In many cases when conventional pectoral approach is not possible, alternate approaches such as epicardial pacemaker implantation and trans-iliac approaches have been used[5]. Cohen (2001) reported outcomes from a retrospective analysis of 123 patients who underwent 207 epicardial lead implantations[6]. Congenital heart disease was present in 103 (84%) of the patients. Epicardial leads were followed for 29 months (range 1 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 10 years, by the sternotomy approach (93.9% at one year and 75.9% at 10 years) and lateral thoracotomy approach (94.1% at one year and 62.4% at 10 years).

Doll (2008) reported results of a randomized trial comparing epicardial implantation to conventional pacemaker implantation in 80 patients with indications for cardiac resynchronization therapy.[7] The authors reported that the conventional pacemaker group had 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 alternate to epicardial approach, trans-iliac approach has also been utilized. Data using trans-iliac approach is limited. Multiple other studies with smaller sample size report a wide range of lead longevity.

Harake (2018) reported a retrospective analysis of five patients who underwent a transvenous iliac approach (median age 26.9 years)[8]. Pacing indications included AV block in three patients and sinus node dysfunction in two patients. 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 (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 authors concluded iliac vein approach was satisfactory and less invasive alternative to epicardial lead implantation. However, the authors reported that incidence of atrial lead dislodgement using this approach in the literature ranged from 7% to 21%. Experts who provided clinical input reported that trans-iliac or surgical epicardial approach require special expertise and long term performance is suboptimal.[9]

Table 1. Reported Complication Rates with Conventional Pacemakers

Complications	Rates, %[10-12]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

Complications	Rates, %[10-12]a
All system related infections requiring reoperation or extraction	0.5-0.7

Adapted from Food and Drug Administration executive summary memorandum (2016).[13]

[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.[14]

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 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.

SINGLE CHAMBER 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 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 10 years, depending on the programmed parameters.[13]

Three systems are currently being evaluated in clinical trials: (1) the Micra™ Transcatheter Pacing System (Medtronic), (2) the Aveir™ VR leadless pacemaker (Abbot; formerly Nanostim, 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 Aveir™ device, there is a screw-in helix that penetrates into the myocardium. 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.[13]

Of these three, only the Micra™ and Aveir™ single-chamber transcatheter pacing systems are approved by FDA and commercially available in the United States. Multiple clinical studies of the Aveir™ predecessor device, the Nanostim, have been published[3, 15-19] but trials have been halted due to the migration of the docking button in the device and premature battery depletion. These issues have since been addressed with the Aveir™ device.[20] Aveir™ has a unique mapping capability to assess correct positioning prior to placement and is specifically designed to be retrieved when therapy needs evolve or the device needs to be replaced.[21]

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 two grams and has an accelerometer-based rate response.[22]

The Aveir™ is about 42 mm in length and introduced using a 25 French catheter to the right ventricle. It also weighs about three grams and uses a temperature-based rate response sensor.[23]

REGULATORY STATUS

Micra™ leadless pacing system (Medtronic)

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

- symptomatic paroxysmal or permanent high-grade AV block in the presence of atrial fibrillation
- paroxysmal or permanent high-grade AV 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.

In January 2020, the Micra AV Transcatheter Pacing System Model MC1AVR1 and Application Software Model SW044 were approved as a PMA supplement (S061) to the Micra system described above. The Micra AV includes an enhanced algorithm to provide AV synchronous pacing.

In November 2021, the U.S. FDA issued a letter to health care providers regarding the risk of major complications related to cardiac perforation during implantation of leadless pacing systems.[24] Specifically, the FDA states that "real-world use suggests that cardiac perforations associated with Micra leadless pacemakers are more likely to be associated with serious complications, such as cardiac tamponade or death, than with traditional pacemakers."

Aveir™ DR Leadless Pacemaker system (Abbott)

In March 2022, the Aveir™ VR Leadless Pacemaker was approved by the U.S. FDA through the premarket approval process for use in patients with bradycardia and:

- normal sinus rhythm with only rare episodes of A-V block or sinus arrest
- chronic atrial fibrillation
- severe physical disability.

Rate-modulated pacing is indicated for patients with chronotropic incompetence, and for those would benefit from increased stimulation rates concurrent with physical activity.

In June 2023, the Aveir™ DR Leadless Pacemaker system was approved by the FDA through the premarket approval process. The device is indicated for management of one or more of the following permanent conditions:

- syncope
- pre-syncope
- fatigue
- disorientation.

The device has multiple pacing functions including rate-modulated pacing, atrial pacing, ventricular pacing and dual chamber pacing. Each function has specific indications:

Rate-Modulated Pacing is indicated for patients with chronotropic incompetence, and for those who would benefit from increased stimulation rates concurrent with physical activity.

Atrial Pacing is indicated for patients with:

- Sinus node dysfunction and normal AV and intraventricular conduction systems

Ventricular Pacing is indicated for patients with:

- Significant bradycardia and normal sinus rhythm with only rare episodes of AV block or sinus arrest
- Chronic atrial fibrillation
- Severe physical disability

Dual-Chamber Pacing is indicated for patients exhibiting:

- Sick sinus syndrome
- Chronic, symptomatic second- and third-degree AV block
- Recurrent Adams-Stokes syndrome
- Symptomatic bilateral bundle branch block when tachyarrhythmia and other causes have been ruled out.

MR Conditional: The Aveir Leadless Pacemaker is conditionally safe for use in the MRI environment and according to the instructions in the MRI-Ready Leadless System Manual.

EVIDENCE SUMMARY

Conventional pacemaker systems have been in use for over 50 years and current technology has matured with significant similarities in designs across models. Extensive bench testing

data with conventional pacemakers and a good understanding of operative and early postimplant safety and effectiveness are available, which limits the need for clinical data collection to understand their safety and effectiveness with regard to implantation, tip fixation, electrical measures, and rate response. As such, a randomized controlled trial comparing the leadless pacemakers with conventional pacemakers was not required by the Food and Drug Administration (FDA).

VENTRICULAR PACING FOR INDIVIDUALS WHO ARE MEDICALLY ELIGIBLE FOR A CONVENTIONAL PACING SYSTEM

Micra™ Leadless Pacemaker

Pivotal Trial

The pivotal investigational device exemption (IDE) trial was a prospective single cohort study enrolled 744 patients with a class I or II indications for implantation of a single-chamber ventricular pacemaker based on national guidelines. Details on the design[25], and results of the IDE trial have been published.[26-28] Trial characteristics and results at six months are summarized in Tables 2 and 3, respectively. System performance from the pivotal trial has been published,[29] but results are not discussed further.

Of the 744 patients enrolled, implantation of the Micra™ transcatheter pacing system was successful in 719 (99.2%) of the 725 patients who underwent the procedure. The demographics of the trial population were typical for a single-chamber pacemaker study performed in the U. S., with 42% being female and the 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.[28]

The IDE trial had two primary endpoints related to safety and efficacy. The trial would meet its safety endpoint 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 six 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 (e.g., pacing function disabled, leaving device abandoned electrically), hospitalization, prolonged hospitalization by at least 48 hours, or system revision (reposition, replacement, explant).[1] The trial would meet its efficacy endpoint if the lower bound of the 95% CI for the proportion of patients with adequate pacing capture thresholds (PCT) exceeded 80% at six 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.[1] As per the FDA, demonstrating that “PCT is less than 2 Volts for the vast majority of subjects will imply that the Micra™ system will have 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.”[1]

Safety and efficacy results of the IDE trial are summarized in Table 3. At six months, the trial met both of its efficacy and safety primary endpoints 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%.[28]

Quality of life results of the IDE trial were published in 2018. At baseline and 12 months, 702 (98%) and 635 (88%) participants completed the 36-Item Short Form questionnaire, respectively.[27] The mean 36-Item Short Form Physical Component Scale at baseline was 36.3 (standard deviation [SD] 9.0) and the mean 36-Item Short Form Mental Component Scale was 47.3 (SD 12.5); the general population mean for both scores is 50. Both the Physical Component Scale and Mental Component Scale improved at 12 months post-implant to a mean Physical Component Scale score of 38.6 (SD 9.4, $p< 0.001$) and a mean Mental Component Scale score of 50.7 (SD 12.2, $p< 0.001$) compared with baseline.

IDE trial results were compared post hoc with a historical cohort of 2,667 patients generated from six previous pacemaker studies, conducted between 2005 and 2012 by Medtronic, that evaluated the performance requirement at six months postimplant of right ventricle pacing leads (single-chamber rates obtained by excluding any adverse events only related to the right atrial lead from the analysis). The Micra™ device was associated with fewer complications than the historical control (4.0% vs 7.4%, hazard ratio [HR], 0.49, 95% CI 0.33 to 0.75, $p=0.001$).[28] Because there were differences in baseline patient characteristics between the two cohorts (patients in the historical cohort were younger and had a lower prevalence of coexisting conditions vs the IDE trial), an additional propensity-matched analysis was conducted. It showed similar results (HR 0.46, 95% CI 0.28 to 0.74). As per the FDA, the lower rate of major complications with the Micra™ device was 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 was no device or lead dislodgements in the Micra™ IDE trial).[13]

While the overall rate of complications was low, the rate of major complications related to cardiac injury (i.e., pericardial effusion or perforation) was higher in the Micra™ IDE trial than in the six reference Medtronic pacemaker studies (1.6% vs. 1.1%, $p=0.288$).[13] Thus, there appears to be a trade-off between types of adverse events with the Micra™ transcatheter pacing system and conventional pacemakers. While adverse events related to leads and pocket are eliminated or minimized with the Micra™ device, certain adverse events (e.g., groin vascular complications, vascular or cardiac bleeding) occur at a higher frequency or are additive (new events) compared with conventional pacemakers. Of these, procedural complications (e.g., acute cardiac perforations) that were severe enough to result in tamponade and emergency surgery were most concerning.[13]

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 possible device-device interactions.[30] There are limited data on device-device interactions (both electrical and mechanical) that 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 the 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.[30] Current recommendations for end-of-device-life care for a Micra™ device may include the addition of a replacement device with or without explantation of the Micra™ device, which should be turned off.[31]

Grubman (2017) reported on system revisions including patients from the IDE study (n=720) and the Micra Transcatheter Pacing System Continued Access Study (n=269).[32] The Continued Access study was conducted to allow for continued access of the Micra™ in the same centers as the IDE study while the device was pending the FDA approval. The mean follow-up duration was 13 months (16 months in the IDE patients and two months in the continued access patients). There were 11 system revisions in 10 patients, corresponding to a 1.4% (95% CI 0.7% to 2.6%) actuarial rate of revisions through 24 months. Micra™ was disabled and left in situ in 7 of 11 revisions including five patients in which there was no retrieval attempt, one patient in which retrieval was aborted because of fluoroscopy failure, and one patient in which retrieval was unsuccessful because of inability to dislodge the device. There were three percutaneous retrievals and one retrieval during surgical valve replacement. There were no complications associated with retrievals. The report indicates that there when a transvenous system was implanted with a deactivated Micra™, there were no reported interactions between the two systems, although it is not clear how often this occurred. In the historical controls from the IDE study, there were 123 revisions in 117 patients through 24 months (actuarial rate 5.3%, 95% CI 4.4% to 6.4%). Using propensity score matching, the reduction in system revisions for Micra™ compared to historical controls was significant (HR 0.27, 95% CI 0.14 to 0.54, p<0.001).

Micra™ Post-approval Experience

Three year outcomes from the Micra Coverage with Evidence Development study were published by Crossley (2023).[33] Patients implanted with leadless pacemakers had a 32% lower rate of chronic complications (HR, 0.68; 95% CI, 0.59 to 0.78; p<.001) and a 41% lower rate of any reinterventions compared to patients receiving a transvenous pacemaker (HR, 0.59; 95% CI, 0.44 to 0.78; p=.0002). Use of a leadless system was also associated with a 49% lower rate (p=.01) of upgrades to a dual-chamber system and a 35% lower rate (p=.002) of upgrades to cardiac resynchronization therapy. Heart failure hospitalizations at three years were slightly, but significantly lower in adjusted time-to-event models (HR, 0.90; 95% CI, 0.83 to 0.97; p=.005) in patients receiving a leadless system. All-cause mortality rates at three years between leadless and transvenous systems were not significantly different after accounting for differences in baseline characteristics (HR, 0.97; 95% CI, 0.92 to 1.03; p=.32). No significant differences in the composite endpoint of time to heart failure hospitalization or death were observed for the original full cohort (p = 0.28) or in a subgroup of patients without a history of heart failure (p = 0.98).

Boveda (2023) published a study comparing clinical outcomes between leadless pacemakers (leadless-VVI) and transvenous ventricular pacemakers (transvenous ventricular permanent-VVI) in subgroups of patients at higher risk of pacemaker complications. [34] This study is based on the Micra Coverage with Evidence Development (CED) study. Patients from the Micra CED study were considered in a high-risk subgroup if they had a diagnosis of chronic kidney disease Stages 4-5 (CKD45), end-stage renal disease, malignancy, diabetes, tricuspid valve disease (TVD), or chronic obstructive pulmonary disease (COPD) 12 months prior to pacemaker implant. A pre-specified set of complications and reinterventions were identified using diagnosis and procedure codes. Competing risks models were used to compare

reinterventions and complications between leadless-VVI and transvenous-VVI patients within each subgroup; results were adjusted for multiple comparisons. A post hoc comparison of a composite outcome of reinterventions and device complications was conducted. Out of 27 991 patients, 9858 leadless-VVI and 12 157 transvenous-VVI patients have at least one high-risk comorbidity. Compared to transvenous-VVI patients, leadless-VVI patients in four subgroups [malignancy, HR 0.68 (0.48-0.95); diabetes, HR 0.69 (0.53-0.89); TVD, HR 0.60 (0.44-0.82); COPD, HR 0.73 (0.55-0.98)] had fewer complications, in three subgroups [diabetes, HR 0.58 (0.37-0.89); TVD, HR 0.46 (0.28-0.76); COPD, HR 0.51 (0.29-0.90)) had fewer reinterventions, and in four subgroups (malignancy, HR 0.52 (0.32-0.83); diabetes, HR 0.52 (0.35-0.77); TVD, HR 0.44 (0.28-0.70); COPD, HR 0.55 (0.34-0.89)] had lower rates of the combined outcome. ClinicalTrials.gov ID NCT03039712.

The FDA approval of the Micra™ transcatheter pacing system was contingent on multiple post-approval studies to provide reasonable assurance of continued safety and effectiveness of the device. Among these, the Micra Transcatheter Pacing System Post-Approval Study, a global, prospective, observational, multicenter study, enrolled 1,830 patients to collect data on 1,741 patients to estimate the acute complication rate within 30 days of the implant, 500 patients to estimate the nine-year complication-free survival rate, and a minimum of 200 patients with a Micra™ device revision for characterizing device end of service.[1] 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 concerning 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.[30]

Study characteristics and results at one year (reported in the FDA documents and published) are summarized in Table 2 and 3, respectively. The post-approval study completed enrollment in early March 2018. The definition of a major complication in the post-approval study was the same as the Micra IDE trial. Although some patients who participated in the IDE study consented to also participate in the PAR study, the publication excludes those patients from analysis and therefore includes an independent population. Results summarized in Table 3 summarize the data at 30 days published by Roberts (2017)[35] and El-Chami (2018),[36, 37] with a mean follow-up of 6.8 months for 1,817 patients, of whom 465 patients had a follow-up for more than one 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 post-approval study than in the IDE trial (odds ratio, 0.58, 95% CI 0.27 to 1.25) although this did not reach statistical difference. The lower rate of major complications was associated with a decrease in events that led to hospitalization, prolonged hospitalization, or loss of device function in the post-approval study compared with the IDE trial.[35] A subsequent subgroup analysis of patients who did not receive perioperative anticoagulation treatment, who received interrupted anticoagulation treatment, or who received continuous anticoagulation treatment did not find a significant difference in rates of acute major complications according to anticoagulation strategy (3.1%, 2.6%, and 1.5%, respectively, p=0.29). The most common major complication was pacing problems, including elevated threshold and device capturing issues.[38] A subgroup analysis of patients treated with and without atrioventricular node ablation (AVNA) at the time of Micra™ implantation identified a significantly higher risk of major complications at both 30 days (7.3% versus 2.0%, p<0.001) and 36 months (HR 3.81, 95% CI 2.33 to 6.23, p<0.001) in the AVNA group versus those without AVNA.[39]

After a mean follow-up of 6.8 months, the estimated major complication rate at 12 months was 2.7% (95% CI 2.0% to 3.7%), corresponding to 46 major complications in 41 patients, the majority of which (89%) occurred within 30 days of implantation. The major complications included 14 device pacing issue events, 11 events at the groin puncture site, eight cardiac effusion/perforation events, three infections, one cardiac failure event, one cardiomyopathy event, and one pacemaker syndrome event. Authors compared these results with the same historical cohort of 2,667 patients used in the IDE trial and reported a 63% reduction in the risk for major complications through 12 months with the Micra™ transcatheter pacing system relative to conventional pacemakers (HR 0.37, 95% CI 0.27 to 0.52). Additionally, the risk for major complications was lower in the Micra™ post-approval study than in the IDE trial but it was a statistically significant difference (HR 0.71, 95% CI 0.44 to 1.1).[36] The reduction in major complications compared to historical controls was primarily driven by a significant 74% (95% CI 54 to 85, p=0.0001) relative risk reduction in system revisions and 71% (95% CI 51 to 83, p=0.0001) relative risk reduction in hospitalizations. The reduction in risk compared to the IDE trial was driven by significantly lower pericardial effusion rates in the post-approval study.

Piccini (2021) published initial data from the ongoing Longitudinal Coverage with Evidence Development Study on Micra Leadless Pacemakers (Micra CED).[40] Patients implanted between March 2017 and December 2018 were identified and included from a fee-for-service population with at least 12 continuous months of Medicare enrollment prior to device implantation. A total of 5,746 patients with single-chamber leadless Micra™ pacemakers and 9,662 patients with transvenous pacemakers were analyzed. Patients with a Micra™ pacemaker were more likely to have end-stage kidney disease (p<0.001) and a higher mean Charlson Comorbidity Index score (5.1 versus 4.6, p<0.001). The unadjusted acute 30-day complication rate was higher in the Micra™ subgroup (8.4% versus 7.3%, p=0.02), but no significant difference was found following adjustment for patient characteristics (p=0.49). Pericardial effusion and/or perforation within 30 days of implantation was significantly higher in the Micra™ population in the adjusted model (0.8% versus 0.4%, p=0.004). Patients with Micra™ pacemakers had a 23% lower risk of complications at six months compared to patients receiving a transvenous pacemaker (HR 0.77, 95% CI 0.62 to 0.96, p=0.02) and a 37% reduction in rates of device revision after adjustment for patient baseline characteristics. The 30-day all-cause mortality rate was not significantly different between groups in both unadjusted (p=0.14) and adjusted analyses (p=0.61). The study is ongoing with an estimated study completion date of June 2025. Study characteristics and results are summarized in Tables 2 and 3.

El-Chami (2022) subsequently compared reinterventions, chronic complications, and all-cause mortality at two years in patients implanted with the Micra™ leadless pacemaker or a transvenous pacemaker in the Micra™ Coverage with Evidence Development study.[41] Patients implanted with leadless (n=6,219) or transvenous pacemakers (n=10,212) were identified from Medicare claims data and compared contemporaneously. Patients receiving leadless pacemakers had higher rates of end-stage renal disease (12.0% versus 2.3%) and a higher Charlson comorbidity index (5.1 versus 4.6). Patients with leadless pacemakers received 37% fewer reinterventions (adjusted HR 0.62, 95% CI 0.45 to 0.85, p =0.003), defined as system revision lead revision or replacement, system replacement, system removal, or system switch or upgrade to an alternative device. Patients implanted with leadless pacemakers also experienced fewer chronic complications (2.4% versus 4.8%, adjusted HR 0.69, 95% CI 0.60 to 0.81, p<0.0001). However, patients receiving leadless pacemakers experienced significantly more other complications, driven by higher rates of pericarditis (adjusted, 1.6% versus 0.8%, p<0.0001). Adjusted all-cause mortality at two years was not

significantly different between groups (adjusted HR 0.97, 95% CI 0.91 to 1.04, p=0.37) despite the higher comorbidity index in patients implanted with a Micra™ device. Study interpretation is limited by reliance on claims data. It is unclear whether all patients receiving leadless devices were considered medically eligible for transvenous devices. Study characteristics and results are summarized in Tables 2 and 3.

Hauser (2021) analyzed the Food and Drug Administration's Manufacturers and User Facility Device Experience (MAUDE) database to capture major adverse clinical events (MACE) associated with the Micra™ device compared to the Medtronic CapSureFix transvenous pacing system.[42] In a search of reports from 2016 through 2020, 363 MACE and 960 MACE were identified for the Micra™ and CapSureFix devices, respectively. For the Micra™ device, significantly higher rates of death (26.4% versus 2.4%, p<0.001)), cardiac tamponade (79.1% versus 23.4%; p<.001), and rescue thoracotomy (27.3% versus 5.2%; p<.001) were reported. Micra™ patients were more likely to require cardiopulmonary resuscitation (21.8% versus 1.1%) and to suffer hypotension or shock (22.0% versus 5.8%) compared to CapSureFix recipients (p<0.001). While the overall incidence of myocardial and vascular perforations and tears that may result in cardiac tamponade and death in Micra™ recipients is estimated to be low (<1%), the authors note that Micra™ patients were more likely to survive these events if they received surgical repair (p=0.014). In a subsequent analysis of the MAUDE database focused on rates of Micra™ perforations from 2016 to 2021, Hauser (2022) identified 563 perforations reported within 30 days of implant, resulting in 150 deaths (27%), 499 cardiac tamponades (89%), and 64 pericardial effusions (11%).[43] Emergency surgery was required in 146 patients (26%). Half all perforations were associated with 139 device problems (25%), 78 operator use problems (14%), and 62 combined device and operator use problems (11%). The most common device problem leading to redeployment were non-capture or inadequate electrical values that required implantable pulse generator recapture and reimplantation or replacement. No device or operator use problems were identified for the remaining 282 perforations (50%), but these were associated with 78 deaths, 245 tamponades, and 57 emergency surgeries. The authors concluded that Micra™ implantation should be confined to specialized centers capable of managing emergency complications and that a risk score for perforation should be developed and validated. Importantly, these analyses are limited by the passive nature of the FDA's post-market device surveillance system, which may not capture all voluntary reports from health care professionals, consumers, and patients. Such analyses carry a high risk of ascertainment bias which may lead to overestimation of the true prevalence of adverse events.

Three year outcomes from the Micra Coverage with Evidence Development study were published by Crossley (2023).[44] Patients implanted with leadless pacemakers had a 32% lower rate of chronic complications (HR, 0.68; 95% CI, 0.59 to 0.78; p<.001) and a 41% lower rate of any reinterventions compared to patients receiving a transvenous pacemaker (HR, 0.59; 95% CI, 0.44 to 0.78; p=.0002). Use of a leadless system was also associated with a 49% lower rate (p=.01) of upgrades to a dual-chamber system and a 35% lower rate (p=.002) of upgrades to cardiac resynchronization therapy. Heart failure hospitalizations at 3 years were slightly, but significantly lower in adjusted time-to-event models (HR, 0.90; 95% CI, 0.83 to 0.97; p=.005) in patients receiving a leadless system. All-cause mortality rates at 3 years between leadless and transvenous systems were not significantly different after accounting for differences in baseline characteristics (HR, 0.97; 95% CI, 0.92 to 1.03; p=.32). No significant differences in the composite endpoint of time to heart failure hospitalization or death were observed for the original full cohort (p=.28) or in a subgroup of patients without a history of

Aveir™ Leadless Pacemaker

Pivotal Trial

The pivotal investigational device exemption (IDE) trial of the Aveir™ leadless pacemaker (LEADLESS II - Phase 2) was a multicenter, prospective single cohort study enrolling 200 patients with a guidelines-based indication for single-chamber pacing.[23] Primary results from the IDE trial have been summarized in a published research correspondence[20] and FDA documents.[23] Trial characteristics and results through six months are summarized in Tables 2 and 3, respectively.

Implantation of the Aveir™ leadless pacing system was successful in 196/200 (98%) trial subjects (mean age 75.6 years, 37.5% female). The primary indication for pacing was chronic atrial fibrillation with 2nd or 3rd degree atrioventricular block (52.5%). The trial had two primary endpoints related to safety and efficacy. The trial would meet its safety endpoint if the lower bound of the 97.5% CI for the complication-free rate exceeded 86% at six weeks. A complication was defined as a device-or-procedure-related serious adverse event, including those that prevented initial implantation. The trial would meet its efficacy endpoint if the lower bound of the 97.5% CI for the composite success rate exceeded 85% at six weeks. The confirmatory effectiveness endpoint was considered met if the pacing threshold voltage is ≤ 2.0 V at 0.4 ms and the sensed R-wave amplitude is either ≥ 5.0 mV at the six-week visit or ≥ the value at implant.

Safety and efficacy results of the Aveir™ IDE trial are summarized in Table 3. At six weeks, the trial met both of its confirmatory safety and efficacy endpoints, including freedom from device-or-procedure-related complications in 96% of patients (95% CI 92.2% to 98.2%), compared with a performance goal of 86%, and a composite success rate of 95.9% of patients (95% CI 92.1% to 98.2%), compared with a performance goal of 85%. The six-month complication-free rate was 94.9% (95% CI 90.0% to 97.4%). The most frequent complications included three cardiac tamponade events and three premature deployment events. The rate of cardiac perforation/tamponade/pericardial effusion was 1.5%. No dislodgement events were reported in the Aveir™ cohort.

Confirmatory secondary endpoints included assessment of an appropriate and proportional rate-response during a Chronotropic Assessment Exercise Protocol (CAEP) exercise protocol and an estimated two-year survival rate. The CAEP assessment was initiated in 23 subjects, of which 17 were considered analyzable. The rate-response slope was 0.93 (95%CI 0.78 to 1.08), which fell within the prespecified range of 65% to 135%. The estimated two-year survival rate based on the Nanostim Phase 1 cohort (n=917) was 85.3% (95% CI 82.7% to 87.4%), which exceeded the performance goal of 80%.[44]

Table 2. Summary of Key Nonrandomized Trial Characteristics

Study; Trial	Study; Type	Country	Dates	1. Participants	Treatment	Follow-Up, mo
Micra						
Reynolds (2016)[28] NCT02004873	Prospective single cohort	19 countries in North America, Europe,	2013-2015	Patients who met a class I or II guidelines-based indication for pacing and suitable	Micra™ pacemaker (n=744)	6

Study; Trial	Study; Type	Country	Dates	1. Participants	Treatment	Follow-Up, mo
		Asia, Australia, and Africa		candidates for single-chamber ventricular demand pacing		
Roberts (2017)[35] El-Chami (2018)[36, 37]	Prospective single cohort (Micra Post-Approval Study)	23 countries in North America, Europe, Asia, Australia, and Africa	2016-2018	Any patient to be implanted with a Micra™ device	Micra™ pacemaker (n=795[a] and 1830[b])	1.8[a] 6.8[b]
Piccini (2021)[40]	Prospective single cohort with contemporaneous control group (Micra CED study)	United States	2017-2018	Medicare beneficiaries implanted with a Micra™ device or transvenous device	Micra™ pacemaker (n=5,746) Transvenous pacemaker (n=9,662)	6
El-Chami (2022)[41]	Prospective Medicare registry	United States	2017-2018	Medicare beneficiaries implanted with a Micra™ device or transvenous device	Micra™ pacemaker (n=6,219) Transvenous pacemaker (n=10,212)	24
Aveir						
FDA SSED (2022), PMA P150035[23]	Prospective single cohort	43 sites in the United States, Canada, and Europe	2020-2021	Patients with a guidelines-based indication for single-chamber pacing	Aveir™ pacemaker (n=200)	6

[a] 30-day results reported by Roberts (2017).[35]

[b] Results after a mean follow-up of 6.8 months reported by El-Chami (2018)[36, 37]

Table 3. Summary of Key Nonrandomized Trial Results

Study	Freedom from System- or Procedure-Related Major Complications	Percentage of Patients with Adequate Pacing Capture Thresholds	Major Complications Criteria, n (%)	Major Complications, n (%)
Micra IDE Trial				
	6 Months	**6 Months**	**6 Months**	**6 Months**
Reynolds (2016)[28]				
N	719[a];300[b]	719	725	725
Micra™	96.0%	98.3% (≤2.0 V)	Death: 1 (0.1)	TMCs: 28 in 25 patients (3.5%) • DVT: 1 (0.1)

Study	Freedom from System- or Procedure-Related Major Complications	Percentage of Patients with Adequate Pacing Capture Thresholds	Major Complications Criteria, n (%)	Major Complications, n (%)
			Loss of device function: 1 (0.1) Hospitalization: 13 (2.3) Prolonged hospitalization (≥48 h): 16 (2.6) System revision: 3 (0.4)	• Pulmonary TE: 1 (0.1) • Events at groin puncture site: 5 (0.7) • Cardiac perforation: 11 (1.6) • Pacing issues: 2 (0.3) • Others: 8 (1.7)
95% CI	93.9% to 97.3%	95.4% to 99.6%	NA	NA
	12 Months	**12 Months**	**12 Months**	**12 Months**
Duray (2017)[45]				
N	726	NA	726	726
Micra	96.0%	NR (93%)	Death: NR (0.1) Loss of device function: NR (0.1) Hospitalization: NR (2.3) Prolonged hospitalization (≥48 h): NR (2.2) System revision[c]: NR (0.7) Loss of device function: NR (0.3)	TMCs: 32 in 29 patients (4.0) • 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) • Others: 11 (1.7)
95% CI	94.2% to 97.2%	NA		
Micra Post-Approval Study				
	30 Days	**30 Days**	**30 Days**	**30 Days**
Roberts (2017)[35]				
N	795	NA	795	795

Study	Freedom from System- or Procedure-Related Major Complications	Percentage of Patients with Adequate Pacing Capture Thresholds	Major Complications Criteria, n (%)	Major Complications, n (%)
Micra™	97.3%[d]	87.2% (≤1.0 V) 97.0% (≤2.0 V)	Death: 1 (0.13%) Hospitalization: 4 (0.50) Prolonged hospitalization (≥48 h): 9 (1.01) System revision[c]: 2 (0.25)	TMCs: 13 in 12 patients (1.51% [95% CI 0.78% to 2.62%]) • DVT: 1 (0.13) • Events at groin puncture site: 6 (0.75) • Cardiac effusion/perforation: 1 (0.13) • Device dislodgement: 1 (0.13) • Pacing issues: 1 (0.13) • Others: 3 (0.38)
OR (95% CI)	0.58 (0.27 to 1.25)[e]	NA	NA	NA
	1 Year	**1 Year**	**1 Year**	**1 Year**
El-Chami (2018)[36, 37]				
N	1,817	NA	NA	1,817
Micra™	97.3%[d]	NA	NA	TMCs: 46 in 41 patients (2.7% [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[f]: 61 in 53 (deaths: 4 procedure-related; 3 unknown relatedness; 3 pending adjudication)
HR (95% CI)	0.71 (0.44 to 1.1)[e] 0.37 (0.27 to 0.52)[g]	NA	NA	NA
Micra CED				
	30 Days and 6 Months	**N/A**	**N/A**	**30 Days and 6 Months**

Study	Freedom from System- or Procedure-Related Major Complications	Percentage of Patients with Adequate Pacing Capture Thresholds	Major Complications Criteria, n (%)	Major Complications, n (%)
Piccini (2021)[40]				
N	5,746	N/A	N/A	5,746
Micra™ complication rate, RR or HR (95% CI)	30-d unadjusted: NR 30-d adjusted: 0.3 (-0.6 to 1.3) 6-mo unadjusted: 0.84 (0.68 to 1.03) 6-mo adjusted: 0.77 (0.62-0.96)	NA	N/A	Acute (30 days), n (%) • Overall: 484 (8.4) • Embolism and thrombosis: 145 (2.5) • PE: 202 (3.5) • Events at puncture site: 78 (1.4) • Cardiac effusion/perforation: 47 (0.8) • Device-related: 81 (1.4) • Other: 136 (2.4) 6-months CIF estimates, % (95% CI) • Overall: 3.2 (2.9 to 3.6) • Embolism and thrombosis: <10 events • Device-related: 1.7 (1.5 to 1.9) • Other: 1.6 (1.3 to 1.8)
	24 months[h]	**N/A**	**N/A**	**24 months**[i]
El-Chami (2022)[41]				
N	6,219 (Micra™) 10,212 (transvenous)	N/A	N/A	6,219 (Micra™) 10,212 (transvenous)
Micra™	Adjusted: 3.1%	NA	N/A	Chronic complications CIF Estimates, % (95% CI) • Overall: 4.6 (4.2 to 4.9) • Embolism and thrombosis: ≤10 events • Device-related: 2.4 (2.2 to 2.5) • Other: 2.1 (2.0 to 2.3)

Study	Freedom from System- or Procedure-Related Major Complications	Percentage of Patients with Adequate Pacing Capture Thresholds	Major Complications Criteria, n (%)	Major Complications, n (%)
Transvenous	Adjusted: 4.9%	NA	N/A	Chronic complications CIF Estimates, % (95% CI) • Overall: 6.5 (6.1 to 6.9) • Embolism and thrombosis: 0.2 (0.2 to 0.2) • Device-related: 4.8 (4.7 to 5.0) • Other: 1.4 (1.3 to 1.6)
RR or HR (95% CI)	Adjusted: 0.62 (0.45 to 0.85)	NA	N/A	Relative risk reduction (95% CI) • Overall: 31 (19 to 40) • Embolism and thrombosis: 46 (-17 to 75) • Device-related: 52 (42 to 60) • Other: -48 (-91 to -15)
Aveir IDE Trial				
	6 weeks **6 months**	**6 weeks** **6 months**	**N/A**	**6 weeks** **6 months**
FDA SSED (2022); PMA P15003[23]				
N	200	200		200
Aveir™	0.960 (0.922 to 0.982) 0.933 (0.898 to 0.956)	0.959 (0.921 to 0.982) 0.934 (0.899 to 0.960)	N/A	SADEs: 9 in 8 patients • Cardiac perforation/tamponade: 3 • Premature deployment with migration: 2 • Premature deployment without migration: 1 • Vascular access site bleeding: 1 • Embolism and thrombosis: 1

CED: coverage with evidence development; CI: confidence interval; CIF: cumulative incidence function; DVT: deep vein thrombosis; FDA: Food and Drug Administration; HR: hazard ratio; IDE: investigational device exemption; NA; not available; NR: not reported; OR: odds ratio; PE: pulmonary embolism; PME: premarket approval; RR: relative risk; SADE: serious adverse device effects; TE: thromboembolism; TMC: Total major complication.

[a] Total number of patients who received the implant successfully.

[b] Number of patients for whom data were available for six-month evaluation.

[c] Device explant, reposition, or replacement.

[d] Calculations based on the major complication rate (2.7%, 95% CI 2.0 to 3.6%) reported by El-Chami (2018).

[e] Major complication vs IDE trial.

[f] Unclear if the complications met the definition of a major complication as events leading to death, hospitalization, prolonged hospitalization by 48 hours, system revision, or loss of device therapy.
[g] Major complication vs historical controls.
[h] Device reintervention rate
[i] Chronic complications

Aveir™ Postapproval Experience

Continued FDA approval of the Aveir™ pacing system is contingent on the results of the Aveir VR Real-World Evidence Study.[46] This post-approval study is designed to evaluate the long-term safety of the Aveir™ device in a real-world sample of 2,100 participants. Both acute and long-term safety will be evaluated as post implant complication-free rates at 30-days and 10-years. Ten-year reports are due in March 2032.

Reddy (2023) published the 1-year outcomes from the LEADLESS II IDE trial. [44] Safety and efficacy endpoints at one year were reported. Freedom from device-or-procedure-related complications was reported in 93.2% of patients (95% CI, 88.7% to 95.9%), compared with a performance goal of 83%, and a composite success rate of 95.1% (95% CI, 91.2% to 97.6%), compared with a performance goal of 80%. Most complications (11 of 15) were reported within the first three days post-implantation (four cardiac tamponade events, three premature deployments with or without device migration, two access site bleeding events, one pulmonary embolism, and one case of deep vein thrombosis. Four long-term complications were reported between 3.8 and 9.5 months post-implantation (two cases of heart failure and two cases of pacemaker-induced cardiomyopathy. The investigators estimated the mean device battery longevity is 17.6 ± 6.6 years (95% CI, 16.6 to 18.6).

Garg (2023) published evaluated the safety profile and assessed the complications of the Aveir™ leadless pacing system.[47] A MAUDE database search was conducted for reports received post-FDA approval to capture all adverse events. A total of 64 entries were included. The most commonly encountered problem was high threshold/noncapture (28.1%, 18 events), followed by stretched helix (17.2%, 11 events) and device dislodgement (15.6%, ten events-5 intraprocedural, while five in the postoperative Day 1). Other reported events included high impedance (14.1%, nine events), sensing issues (12.5%, eight events), bent/broken helix (7.8%, five events), premature separation (4.7%, three events), interrogation problem (3.1%, two events), low impedance (3.1%, two events), premature battery depletion (1.6%, one event) and inadvertent MRI mode switch (1.6%, one event) and miscellaneous (15.6%, n = 10). There were eight serious patient injury events-pericardial effusion requiring pericardiocentesis (7.8%, five events) due to cardiac perforation that resulted in two deaths (3.1%) followed by sustained ventricular arrhythmias (4.6%, n = 3).

Tokavanich (2023) published a retrospective case study review comparing the implant efficiency and clinical performance of the Aveir™ VR Leadless Pacemaker (LP) compared to the Micra™ VR LP.[48] A total of 67 patients were included in the study. The Micra™ VR group had shorter time in the electrophysiology lab (41 ± 12 vs. 55 ± 11.5 min, $p = 0.008$) and shorter fluoroscopic time (6.5 ± 2.2 vs. 11.5 ± 4.5 min, $p < 0.001$) compared to the Aveir™ VR group. The Aveir™ VR group had a significantly higher implant pacing threshold compared to the Micra™ VR group (0.74 ± 0.34 mA vs. 0.5 ± 0.18 mA at pulse width 0.4 ms, $p < 0.001$), but no difference was found at three and six months. There was no significant difference in the R-wave sensing and impedance and pacing percentage at implantation, three and six months. Complications of the procedure were rare. The mean projected longevity of the Aveir™ VR group was longer than the Micra™ VR group (18.8 ± 4.3 vs. 7.7 ± 0.75 years, $p < 0.001$). The authors conclude that Implantation of the Aveir™ VR required longer laboratory and

fluoroscopic time, but showed longer longevity at six months follow-up, compare to the Micra™ VR. Limitations include retrospective study design at a single site, small sample size and lack of long-term data.

Shantha (2023) published a retrospective case study review to compare effectiveness and safety between the Aveir-VR and Micra-VR.[49] The first patients (n= 25) to undergo Aveir-VR implant at our institution between June and November 2022, were compared to 25 age- and sex-matched patients who received MICRA-VR implants. In both groups, mean age was 73 years and 48% were women. Leadless pacemaker implant was successful in 100% of patients in both groups. Single attempt deployment was achieved in 80% of AVEIR-VR and 60% of Micra-VR recipients ($p = 0.07$). Fluoroscopy, implant, and procedure times were numerically longer in the Aveir-VR group ($p > 0.05$). No significant periprocedural complications were noted in both groups. Incidence of ventricular arrhythmias were higher in the Aveir-VR group (20%) compared to the Micra-VR group (0%) ($p = 0.043$). At two and eight weeks follow-up, device parameters remained stable in both groups with no device dislodgements. The estimated battery life at 8 weeks was significantly longer in the Aveir-VR group (15 years) compared to the Micra-VR group (8 years) ($p = 0.047$). The authors reported that it took three to four Aveir-VR implants for the learning curve for successful implantation to reach steady state.The authors conclude that the initial experience with Aveir-VR show that it has comparable effectiveness and safety to Micra-VR. Limitations include retrospective study design at a single site, small sample size and lack of long-term data.

The current evidence on the use of the Aveir™ device remains limited by a lack of adequate data on quality of life, long-term safety, effectiveness, reliability, and incidence of late device failures. The Aveir™ pivotal prospective cohort study primary safety and efficacy outcomes at six weeks exceeded performance goals for complication-free rate and composite success rate (96.0% and 95.9%, respectively). Results at six months were similar and at one year were 93.2% and 91.5%, respectively. Incidence of major complications at one year was 6.7% compared to 4.0% in the Micra pivotal trial. The two-year survival estimate of 85.3% is based on Phase 1 performance with the predecessor Nanostim device. While the device is designed to be retrieved when therapy needs evolve or the device needs to be replaced, there is currently inadequate clinical experience with issues related to devices that have reached end-of-life. Two small retrospective case study reports comparing the Aveir device with the Micra device. Both reported fluoroscopy, implant, and procedure times were longer for the Aveir device. Other outcomes were similar. Through six months follow-up , device parameters remained stable in both groups with no device dislodgements. Long term survival data for the currently marketed version of the Aveir™ device has not been reported.

Section Summary: Ventricular Pacing for Individuals Who Are Medically Eligible for a Conventional Pacing System

The evidence for use of the Micra™ transcatheter pacing system consists of a pivotal prospective cohort study, a post-approval prospective cohort study, a Medicare registry, and a retrospective FDA database analysis. 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 complications 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 and 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. Results of the CMS study indicated that acute complication rates were similar for the Micra™ and transvenous pacemakers, after adjustment for baseline and encounter differences, and there was a slightly lower six-month complication rate for the leadless system. While the Micra™ transcatheter pacing system eliminates adverse events associated with lead and pocket issue, its use results in additional complications related to the femoral access site (groin hematomas, access site bleeding) and implantation and release of the device (traumatic cardiac injury). Initial data from a Medicare registry found a significantly higher rate of pericardial effusion and/or perforation within 30 days in patients with the leadless Micra™ pacemaker compared to patients who received a transvenous device; overall six-month complications rates were significantly lower in the Micra™ group in the adjusted analysis (p=0.02). In a real-world study of Medicare patients, 41% lower rate of reinterventions and a 32% lower rate of chronic complications compared with transvenous pacing, with no significant difference in adjusted all-cause mortality at 3 years despite the higher comorbidity index for patients implanted with a Micra device. However, patients receiving the Micra device experienced significantly more other complications, driven by higher rates of pericarditis. No significant differences were noted in the composite endpoint of time to heart failure hospitalization or death for the full cohort (p=.28) or the subgroup without a history of heart failure (p=.98) It is also unclear whether all patients were considered medically eligible for a conventional pacing system. A 2021 analysis of the FDA Manufacturer's and User Facility Device Experience (MAUDE) database revealed significantly higher rates of death, cardiac tamponade, and rescue thoracotomy in Micra™ recipients compared to patients implanted with a transvenous pacemaker (p<0.001), although this study is limited by potential risk of ascertainment bias. A single-arm study of the Micra AV device reported that 85.2% of individuals with complete AV block and normal sinus rhythm successfully achieved a >70% resting AV synchrony (AVS) rate at 1 month postimplant and that AVS rates could be further enhanced with additional device programming. However, clinically meaningful rates of AVS are unknown. Longer-term device characterization is planned in the Micra AV Post-Approval Registry through 3 years.

The evidence for the use of the Aveir™ transcatheter leadless pacing system consists of a pivotal prospective cohort study. Primary safety and efficacy outcomes at six weeks exceeded performance goals for complication-free rate and composite success rate (96.0% and 95.9%, respectively). Results at six months were similar and at one year were 93.2% and 91.5%, respectively. Incidence of major complications was comparable to rates observed in the Micra™ pivotal trial (4.0%). The two-year survival estimate of 85.3% is based on Phase 1 performance with the predecessor Nanostim device.

Considerable uncertainties and unknowns remain in terms of the durability of the devices and end-of-life device issues. Early and limited experience with the Micra™ device has suggested that retrieval of these devices is unlikely because in due course of time, the devices will be encapsulated. There are limited data on device-device interactions (both electrical and mechanical), which might 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 Aveir™ device is specifically designed to be retrieved when therapy needs evolve or the device needs to be replaced, clinical experience with device retrieval has not yet been reported.

OTHER INDICATIONS

Atrioventricular Synchronous pacing

Micra-AV

Wu (2023) published a systematic review and meta-analysis to examine the efficacy and safety of leadless pacemakers for atrioventricular synchronous pacing.[50] The primary efficacy outcome was atrioventricular synchrony after implantation, whereas the secondary efficacy outcome was the change in cardiac output represented by the left ventricular outflow tract velocity time integral (LVOT-VTI). The primary safety outcome was major complications related to the procedures and the algorithm. Eight published studies (464 participants) were included in the qualitative analysis. The pooled atrioventricular synchrony proportion was 78.9% (95% CI 71.9-86.0%), and a further meta-regression did not screen factors that contributed significantly to the heterogeneity. Additionally, a significant increase in atrioventricular synchrony of 11.3% (95% CI 7.0-15.7%, $p < 0.01$) was achieved in patients experiencing programming optimization. LVOT-VTI was significantly increased by 1.9 cm (95% CI 1.2-2.6, $p < 0.01$), compared with the VVI pacing mode. The overall incidence of complications was approximately 6.3%, with major complications related to the algorithm being extremely low. The authors conclude that the leadless pacemakers with atrioventricular synchronous pacing demonstrated favorable safety and efficacy. Future data on long-term performance are required.

Chinitz (2022) conducted a prospective, single-arm study (AccelAV) at 20 sites in the United States and Hong Kong to assess the efficacy of the Micra AV leadless pacemaker in promoting atrioventricular synchrony (AVS) in adults with a history of atrioventricular (AV) block (n=157).[51] This device uses an accelerometer and detection algorithm to mechanically sense atrial contractions to facilitate VDD pacing (ventricle pacing chamber, both atrium and ventricle are sensing chamber and mode of operation is dual (inhibited and triggered) and AVS in individuals with normal sinus function. Micra AV implantation and completion of the 1-month study visit was achieved by 139 individuals, of which 54 (mean age, 77 years; 55.6% female) comprised the intended use population with a predominant heart rhythm of complete AV block with normal sinus rhythm. The primary endpoint was the rate of AVS during a 20-minute resting period at 1 month postimplant in these patients. Atrioventricular synchronous pacing was defined as a ventricular marker preceding a P wave within 300 ms, regardless of the underlying cardiac rhythm. Secondary endpoints included stability of AVS during rest between one and three months, percent AVS during a 24-hr ambulatory period at one months, and change in stroke volume. Quality of life was also measured with the EQ-5D-3L health status assessment. At one month, AVS percentage at rest was 85.4% (95% CI, 81.1% to 88.9%; median, 90.0%) during VDD pacing, with 85.2% of patients achieving >70% resting AVS. At the 3-month visit, 37/54 remained in the same rhythm. Among these subjects, no significant change in AVS synchrony was detected (p=.43) between the 3-month (mean, 84.1%; 95% CI, 78.3% to 88.6%) and 1-month visits (mean, 84.1%; 95% CI, 81.2% to 89.9%). At the 1 month visit, average 24-hour ambulatory AVS was 74.5% (95% CI, 70.4% to 78.2%). EQ-5D-3L health status scores significantly improved by 0.07 points between baseline and 3 months ($p = 0.031$) among patients with complete AV block and normal sinus function. Ambulatory AVS percentage significantly increased from 71.9% to 82.6% ($p < 0.001$) in twenty patients who participated in a substudy at a mean follow-up of 9.5 months designed to characterize the impact of optimized device programming. Improvement in AVS was most evident during elevated sinus rates between 80 and 110 bpm. In the safety cohort (n=152), there were 14 major complications, including four pericardial effusions and two heart failure events. One pericardial effusion resulted in perforation and death in a 92-year-old woman with high

baseline risk. A second death was reported in an 83-year-old man at 127 days postimplant but was not considered system- or procedure-related. No device upgrades and one device explantation and replacement was reported during follow-up. Study interpretation is limited by lack of a comparator group and short duration of follow-up. The ongoing Micra AV Post-Approval Registry (NCT04253184) has follow-up planned through three years. The investigators also noted that the AVS percentage required to maintain a clinical benefit over time is unknown, but likely is not 100%.

VENTRICULAR PACING FOR INDIVIDUALS WHO ARE MEDICALLY INELIGIBLE FOR A CONVENTIONAL PACING SYSTEM.

Nonrandomized Controlled Trials

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

Micra™ Leadless Pacemaker

In the IDE trial, 6.2% or 45 patients received the Micra™ transcatheter pacing system because they were medically ineligible for a conventional pacing system due to 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[28] or the FDA documents.[1, 13, 22, 30]

In the postapproval registry as an abstract, the authors reported stratified results for 105 of 1,820 patients who had previous cardiac implantable electronic device (CIED) infection.[36, 52] Of these, 83 patients (79%) were classified as medically ineligible to receive a conventional pacemaker in the opinion of the physician. A stratified analysis of these 83 patients was not presented in the publication. Trial characteristics and results are summarized in Tables 4 and 5, respectively. In this cohort of patients with CIED infection, the Micra™ device was implanted successfully in 104 patients and the previous CIED was explanted the same day as the Micra™ device was implanted in 37% of patients. Major complications were reported in 3.8% of patients with an average follow-up of 8.5 months. Ten deaths were reported (14% at 12 months) but none were related to the Micra™ transcatheter pacing system or the implantation procedure.

Garg (2020) performed a post-hoc, stratified analysis of data from the Micra™ clinical trials (Micra Post-Approval Registry, Micra Continued Access [CA] Study, Micra Transcatheter Pacing Study, Medtronic Product Surveillance Registry) based on whether the patient was deemed to be ineligible to receive a conventional pacemaker by the implanter.[53] Of the 2,817 patients that underwent an attempted implantation of a Micra™ device, 546 (19%) were considered to be precluded from receiving a transvenous permanent pacemaker, for reasons that included venous access issues or previous device infections. Compared with individuals that were not precluded from a transvenous device, the precluded patients had significantly higher acute mortality and total mortality at 36 months (2.75% vs 1.32%, p=0.022; and 38.1% versus 20.6%, p<0.001, respectively). The major complication rate was not significantly different between the groups. The majority of medically ineligible patients were enrolled in the CA and Post-Approval Registry studies, which unlike the IDE study, did not exclude patients with a life expectancy <12 months.

Table 4. Summary of Key Nonrandomized Trial Characteristics in Patients Ineligible for a Conventional Pacing System and/or Previous CIED Infection

Study; Trial	Study Type	Country	Dates	Participants	Treatment	Follow-Up, mo
El-Chami (2018)[36, 52]	Prospective single cohort (Micra Post-Approval Registry)	23 countries in North America, Europe, Asia, Australia, and Africa	2016-2018	Any patient to be implanted with a Micra™ with a CIED infection	Micra™ pacemaker (n=105)	8.5 (range 0 to 28.5)
Garg (2020)[53]	Post hoc analysis of prospectively collected data from Micra™ studies	Multinational	NR	Any patient in a Micra™ study considered ineligible for a conventional pacing system	Micra™ pacemaker (n=546)	Total major complications: 24 in 22 patients; (4 cases cardiac effusion/perforation, 4 events at groin puncture site, 1 case of thrombosis, 4 cases of pacing issues, 1 case of cardiac rhythm disorder, 3 cases of infection, and 7 other)

CIED: cardiac implantable electronic device

Table 5. Summary of Key Nonrandomized Trial Results in Patients Ineligible for a Conventional Pacing System and/or Previous Cardiac Implantable Electronic Device Infection

Study	No. of Patients With System- or Procedure-Related Major Complications at One Year	Average Pacing Threshold at One Year	Major Complications at 1 Year
El-Chami (2018)[36, 52]			
N	105	82	105
Micra™	4 (4/105)	0.6 V	Total major complications: 6 in 4 patients (patient 1: effusion requiring pericardiocentesis; patient 2: elevated thresholds, complication of device removal [IVC filter entanglement], and subsequent abdominal wall infection, patients 3 and 4: pacemaker syndrome)
Garg (2020)[53]			
N	546	NR	546
Micra™	4 (22/546, reported at 36 months)	NR	Total major complications: 24 in 22 patients; (4 cases cardiac effusion/perforation, 4 events at groin puncture site, 1 case of thrombosis, 4

Study	No. of Patients With System- or Procedure-Related Major Complications at One Year	Average Pacing Threshold at One Year	Major Complications at 1 Year
			cases of pacing issues, 1 case of cardiac rhythm disorder, 3 cases of infection, and 7 other)

IVC: in cava filter; NR: not reported.

Section Summary: Ventricular Pacing for Individuals Who Are Medically Ineligible for a Conventional Pacing System

No studies that exclusively enrolled patients who were medically ineligible for a conventional pacing system were identified. However, a subgroup of patients in whom the use of conventional pacemakers was precluded was enrolled in the pivotal and the postapproval trials of the Micra™ device. 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 are unknown, the short-term benefits may outweigh the risks in the context of the life-saving potential of pacing systems in patients that are ineligible for conventional pacing systems.

USE OF LEADLESS PACEMAKERS EMERGENTLY

Systematic Reviews

Noor (2023) published a SR evaluating the feasibility and outcomes of emergency implantation of LPM in patients referred for urgent PM implantation.[54] In a total of four studies (1276 patients) of which 114 patients (8.9%) were implanted with leadless pacemakers (LPM) and the rest were implanted with either conventional PMs or some other alternatives. In the included studies, 468 (36.6%) patients were males. All four included studies were prospective cohort studies. The authors reported that LPM implantation demonstrated low procedural times, hospital stay, and fluoroscopy time but one study demonstrated more procedure time in an urgent setting, and pacing parameters were comparable in both comparison with other cardiac implantable electronic devices and elective LPM implantation. Quantative analysis was limited by the heterogeneity of studies and the small number of studies included. Other limitations included experience of the operators, possible selection bias. They conclude that randomized controlled trials are needed to evaluate safety and efficacy of LPMs in emergency settings.

DUAL CHAMBER LEADLESS PACEMAKERS

The Aveir DR i2i ™ is currently being evaluated in an open label prospective, multicenter, international, single-arm, pivotal investigational study designed to evaluate the clinical safety and efficacy of the Aveir DR leadless pacemaker in patients who were indicated for a dual-chamber bradycardia pacing pacemaker that stimulates the appropriate chamber of the heart when necessary or DDD(R).[55] The study was initiated February 2, 2022 and is estimated to be complete by November 2025. The primary completion date is September 2023. The study plan is to enroll up to 550 patients from up to 82 sites in the U.S., Canada, Europe and Asia-Pacific, and all patients will be followed for a minimum of 12 months post-implant. (ClinicalTrials.gov identifier NCT05252702).

Knop (2023) published a prospective, multicenter, single-group study to evaluate the safety and performance of a dual-chamber leadless pacemaker system.[56] Patients with a conventional indication for dual-chamber pacing were eligible for participation. The primary safety end point was freedom from complications (i.e., device- or procedure-related serious adverse events) at 90 days. The first primary performance end point was a combination of adequate atrial capture threshold and sensing amplitude at three months. The second primary performance end point was at least 70% atrioventricular synchrony at three months while the patient was sitting. Among the patients (n = 300) enrolled, 190 (63.3%) had sinus-node dysfunction and 100 (33.3%) had atrioventricular block as the primary pacing indication. The implantation procedure was successful (i.e., two functioning leadless pacemakers were implanted and had established implant-to-implant communication) in 295 patients (98.3%). A total of 35 device- or procedure-related serious adverse events occurred in 29 patients. The primary safety end point was met in 271 patients (90.3%; 95% confidence interval [CI], 87.0 to 93.7), which exceeded the performance goal of 78% ($p < 0.001$). The first primary performance end point was met in 90.2% of the patients (95% CI, 86.8 to 93.6), which exceeded the performance goal of 82.5% ($p < 0.001$). The mean (±SD) atrial capture threshold was 0.82 ± 0.70 V, and the mean P-wave amplitude was 3.58±1.88 mV. Of the 21 patients (7%) with a P-wave amplitude of less than 1.0 mV, none required device revision for inadequate sensing. At least 70% atrioventricular synchrony was achieved in 97.3% of the patients (95% CI, 95.4 to 99.3), which exceeded the performance goal of 83% ($p < 0.001$). This study was (Funded by Abbott Medical; Aveir DR i2i ClinicalTrials.gov number, NCT05252702.).

Section Summary

There is not enough evidence to support the use of dual chamber leadless pacemakers for any indication.

PRACTICE GUIDELINE SUMMARY

AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION, AMERICAN HEART ASSOCIATION, AND HEART RHYTHM SOCIETY

The American College of Cardiology Foundation, American Heart Association, and Heart Rhythm Society's (2012) focused update 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.[57]

In 2020, the Heart Rhythm Society (HRS), along with the International Society for Cardiovascular Infectious Diseases (ISCVID) and several other Asian, European and Latin American societies, endorsed the European Heart Rhythm Association (EHRA) international consensus document on how to prevent, diagnose, and treat cardiac implantable electronic device infections.[58] The consensus states that for patients at high risk of device-related infections, avoiding a transvenous system, and implanting an epicardial system, may be preferential. It makes the following statements regarding leadless pacemakers:

- "There is hope that 'leadless' pacemakers will be less prone to infection and can be used in a similar manner [as epicardial systems] in high-risk patients."
- "In selected high-risk patients, the risk of infection with leadless pacemakers appears low. The device also seems safe and feasible in patients with pre-existing CIED infection and after extraction of infected leads."

The Heart Rhythm Society and American College of Cardiology Foundation (2012) expert consensus statement on pacemaker device and mode selection did not include recommendations on leadless cardiac pacemakers.[59]

SUMMARY

There is enough research to show that Micra™ single-chamber transcatheter pacing system may improve health outcomes for patients with a guidelines-based indication for a ventricular pacing system who are medically ineligible for a conventional pacing system. Although evidence is limited and long-term effectiveness and safety are unknown, the short-term benefits may outweigh the risks, in the context of the life-saving potential of this pacing system for patients who are ineligible for conventional pacing systems. Therefore, this pacemaker system may be considered medically necessary for patients who meet the policy criteria.

There is not enough research to show that a leadless pacing system can improve health outcomes for patients who do not meet medical necessity criteria, including the use of the Aveir™ system or a non-FDA-approved system, or in patients who are eligible for a conventional pacing system. There is little evidence regarding the durability of devices, device end-of-life issues, and device-device interactions (both electrical and mechanical), which may occur when there is a deactivated leadless device alongside another leadless pacemaker or when a leadless pacemaker and transvenous device are both present. Therefore, a leadless pacemaker is considered investigational when criteria are not met.

There is not enough evidence to show that dual chamber leadless pacing systems can improve health outcomes for patients. There are currently no FDA approved dual chamber leadless pacemaker devices.

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CODES

Codes	Number	Description
CPT	0795T	Transcatheter insertion of permanent dual-chamber leadless pacemaker, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography, right ventriculography, femoral venography) and device evaluation (eg, interrogation or programming), when performed; complete system (ie, right atrial and right ventricular pacemaker components)
	0796T	Transcatheter insertion of permanent dual-chamber leadless pacemaker, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography, right ventriculography, femoral venography) and device evaluation (eg, interrogation or programming), when performed; right atrial pacemaker component (when an existing right ventricular single leadless pacemaker exists to create a dual-chamber leadless pacemaker system)
	0797T	Transcatheter insertion of permanent dual-chamber leadless pacemaker, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography, right ventriculography, femoral venography) and device evaluation (eg, interrogation or programming), when performed; right ventricular pacemaker component (when part of a dual-chamber leadless pacemaker system)
	0798T	Transcatheter removal of permanent dual-chamber leadless pacemaker, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography, right ventriculography, femoral venography), when performed; complete system (ie, right atrial and right ventricular pacemaker components)
	0799T	Transcatheter removal of permanent dual-chamber leadless pacemaker including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography, right ventriculography, femoral venography), when performed; right atrial pacemaker component
	0800T	Transcatheter removal of permanent dual-chamber leadless pacemaker, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography, right ventriculography, femoral venography), when performed; right ventricular pacemaker component (when part of a dual-chamber leadless pacemaker system)
	0801T	Transcatheter removal and replacement of permanent dual-chamber leadless pacemaker, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography, right ventriculography, femoral venography) and device evaluation (eg, interrogation or programming), when performed; dual-chamber system (ie, right atrial and right ventricular pacemaker components)
	0802T	Transcatheter removal and replacement of permanent dual-chamber leadless pacemaker, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography, right ventriculography, femoral venography) and device evaluation (eg, interrogation or programming), when performed; right atrial pacemaker component
	0803T	Transcatheter removal and replacement of permanent dual-chamber leadless pacemaker, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography, right ventriculography, femoral venography) and device evaluation (eg, interrogation or programming), when performed; right ventricular pacemaker component (when part of a dual-chamber leadless pacemaker system)
	0804T	Programming device evaluation (in person) with iterative adjustment of implantable device to test the function of device and to select optimal

Codes	Number	Description
		permanent programmed values, with analysis, review, and report, by a physician or other qualified health care professional, leadless pacemaker system in dual cardiac chambers
	0823T	Transcatheter insertion of permanent single-chamber leadless pacemaker, right atrial, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography and/or right ventriculography, femoral venography, cavography) and device evaluation (eg, interrogation or programming), when performed
	0824T	Transcatheter removal of permanent single-chamber leadless pacemaker, right atrial, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography and/or right ventriculography, femoral venography, cavography), when performed
	0825T	Transcatheter removal and replacement of permanent single-chamber leadless pacemaker, right atrial, including imaging guidance (eg, fluoroscopy, venous ultrasound, right atrial angiography and/or right ventriculography, femoral venography, cavography) and device evaluation (eg, interrogation or programming), when performed
	0826T	Programming device evaluation (in person) with iterative adjustment of the implantable device to test the function of the device and select optimal permanent programmed values with analysis, review and report by a physician or other qualified health care professional, leadless pacemaker system in single-cardiac chamber
	33274	Transcatheter insertion or replacement of permanent leadless pacemaker, right ventricular, including imaging guidance (eg, fluoroscopy, venous ultrasound, ventriculography, femoral venography) and device evaluation (eg, interrogation or programming), when performed (new eff 1/1/19)
	33275	Transcatheter removal of permanent leadless pacemaker, right ventricular, including imaging guidance (eg, fluoroscopy, venous ultrasound, ventriculography, femoral venography), when performed
HCPCS	C1605	Pacemaker, leadless, dual chamber (right atrial and right ventricular implantable components), rate-responsive, including all necessary components for implantation

Date of Origin: *December 2018*