Clinical Policy Title: Melody transcatheter pulmonary valve replacement

Clinical Policy Number: CCP.1264

Effective Date: January 1, 2017
Initial Review Date: October 19, 2016
Most Recent Review Date: November 6, 2018
Next Review Date: November 2019

Related policies:
- CCP.1192 Transcatheter aortic and mitral valve replacement and repair
- CCP.1210 Heart valve transplant

ABOUT THIS POLICY: AmeriHealth Caritas has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas’ clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by AmeriHealth Caritas when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas’ clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas’ clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas will update its clinical policies as necessary. AmeriHealth Caritas’ clinical policies are not guarantees of payment.

Coverage policy

AmeriHealth Caritas considers the use of Melody™ transcatheter pulmonary valve (Medtronic Inc., Mounds View, Minnesota) to be clinically proven and, therefore, medically necessary as an adjunct to surgery in pediatric and adult members with the following clinical indications (Stout, 2018; U.S. Food and Drug Administration, 2015):

- Existence of a full (circumferential) right ventricular outflow tract conduit that was equal to or greater than 16 mm in diameter when originally implanted.
- Dysfunctional right ventricular outflow tract conduit with a clinical indication for intervention, and either:
  - Regurgitation: ≥ moderate regurgitation.
  - Stenosis: mean right ventricular outflow tract gradient ≥ 35 mmHg.

Limitations:

All other uses of the Melody transcatheter pulmonary valve are not medically necessary.
For Medicare members only:

AmeriHealth Caritas considers the use of the Melody transcatheter pulmonary valve to be not medically necessary (Local Coverage Determinations L33777 and L35094).

Alternative covered services:

Members should fully discuss alternatives with his or her physician to select the method that best meets expectations and lifestyle.

Background

Congenital heart defects are the most common type of birth defect, affecting eight out of every 1,000 newborns. More than one million adults are living with these conditions. They can affect the interior septa, valves, and blood vessels to and from the heart (National Heart Lung Blood Institute, 2015).

The most common valve defect is pulmonary valve stenosis. It involves narrowing of the pulmonary valve, which can affect blood flow from the right ventricle into the pulmonary artery. The right ventricular outflow tract is the portion of the right ventricle through which blood passes to enter the great arteries. It is an important anatomical feature in many corrective surgeries for congenital heart defects, as dilation of this region can cause pulmonary valve insufficiency (National Heart Lung Blood Institute, 2015).

Pulmonary valve stenosis can range from mild to severe. Most children who have this defect have no signs or symptoms other than a heart murmur and often require no treatment. More severe or complex cases may require open-heart surgery or a heart transplant. Surgical repair is effective in the short term, but valves and conduits have limited durability. Calcification and scar formation can lead to right ventricular outflow tract dysfunction, which, when severe, results in a blocked or regurgitant pulmonary heart valve. Percutaneous catheter-based procedures have emerged in the past 20 years, and are often the preferred way to repair many simple heart defects (National Heart Lung Blood Institute, 2015).

Melody transcatheter pulmonary valve:

The Melody transcatheter pulmonary valve is an artificial heart valve made from a bovine jugular vein valve that is sewn into a small metal frame (Medtronic Inc., 2017). The Medtronic Ensemble™ Transcatheter Valve Delivery System (Medtronic Inc., Mounds View, Minnesota) is a thin, hollow, and long catheter that percutaneously delivers the Melody transcatheter pulmonary valve into the heart while the heart is beating. The Melody transcatheter pulmonary valve is first compressed onto a balloon at the tip of the delivery catheter. Through a small incision typically in the groin, the Melody transcatheter pulmonary valve is directed through a vein to the failing pulmonary heart valve. The small balloon is then inflated to open up the Melody transcatheter pulmonary valve, and the catheter is removed from the body. The Melody transcatheter pulmonary valve immediately becomes the new pulmonary heart valve.
The U.S. Food and Drug Administration (2015) approved the Melody transcatheter pulmonary valve models PB1016 and PB1018 and Ensemble Transcatheter Valve Delivery System models NU1018, NU1020, and NU1022 for the following uses:

- Existence of a full (circumferential) right ventricular outflow tract conduit ≥ 16 mm in diameter when originally implanted.
- Dysfunctional right ventricular outflow tract conduit with a clinical indication for intervention, and either at least moderate regurgitation or a mean right ventricular outflow tract gradient ≥ 35 mmHg.

The purported benefits of the Melody transcatheter pulmonary valve are minimal invasiveness and a potential reduction in the risks of bleeding and infection. It may delay the time when a patient needs additional open heart surgery and reduce the total number of open heart surgeries a patient needs (U.S. Food and Drug Administration, 2015).

**Searches**

AmeriHealth Caritas searched PubMed and the databases of:
- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality.
- The Centers for Medicare & Medicaid Services.

We conducted searches on September 20, 2018. Search terms were: “Heart defects, congenital” (MeSH) and free text terms “Melody transcatheter pulmonary valve,” “pulmonary valve,” and “transcatheter pulmonary valve.”

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews**.
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

A systematic review analyzed 12 observational studies (n = 677 patients), including 10 studies of the Melody valve, implanted for regurgitation, stenosis, or both (Virk, 2015). No studies directly compared percutaneous procedure to surgery. The evidence suggests percutaneous pulmonary valve implantation offers an acceptable mortality risk and a relatively low incidence of major procedural complications. The
most common complications were stent fracture and infective endocarditis. There are no known contraindications to the Melody transcatheter pulmonary valve.

Several factors likely contribute to variation in outcomes. These factors include right ventricular outflow tract etiology and valve pathology, operator experience, and procedure protocol. Other factors that may correlate with improved outcomes include: pre-procedural stenting of the right ventricular outflow tract valve-conduit size matching using pre-procedural right ventricular outflow tract measurement; compliance with antibiotic prophylaxis; compliance with anti-platelet therapy; and adequate dental hygiene. Test angioplasty might be indicated to detect pre-existing coronary artery compression, which can lead to a fatal outcome. Percutaneous pulmonary valve implantation has a learning curve, and protocols that improve outcomes are still being developed. Long-term patient survival, valve durability, and effectiveness in postponing surgery are unclear. The American Heart Association recognizes transcatheter pulmonary valves as an emerging treatment option, but lack of outcome data on surgical pulmonary valve replacement prevents a comparison of outcomes to transcatheter pulmonary valves; these valves are only suitable for patients with non-native right ventricular outflow tracts (Bhatt, 2015).

Policy updates:

In 2017, we added one new systematic review and meta-analysis (Chatterjee, 2017) and one post-marketing surveillance study based on adverse event data reported to the U.S. Food and Drug Administration’s Manufacturer and User Facility Device Experience database (Hill, 2017). The new information suggests improvement in long-term outcomes, particularly reduced re-intervention rates, which are associated with procedural experience and widespread adoption of pre-stenting in patients with failing pulmonary conduits or dysfunctional surgical bioprosthetic valves. The new information confirms previous findings, and warrants no policy changes.

In 2018, we added one systematic review (Abdelghani, 2018), two retrospective chart reviews comparing patient characteristics and outcomes of transcatheter and surgical pulmonary valve replacement (Li, 2018; Zablah, 2017), and one updated evidence-based guideline (Stout, 2018). The American College of Cardiology/American Heart Association guideline lists the following indications for the Melody valve in adults with congenital heart disease (Stout, 2018):

- Right ventricle-to-pulmonary artery conduit and moderate or greater pulmonary regurgitation or moderate or greater stenosis with reduced functional capacity or arrhythmia.
- Asymptomatic adults with right ventricle-to-pulmonary artery conduit and severe stenosis or severe regurgitation with reduced right ventricular ejection fraction or right ventricular dilation.

While the incidence of infective endocarditis continues to be of concern in Melody valve recipients, it can be managed medically, especially in those with streptococcal infection and no right ventricular outflow tract obstruction (Abdelghani, 2018). Comparisons of patient characteristics and outcomes of transcatheter and surgical pulmonary valve replacement procedures suggest that both procedures can effectively improve right ventricular volume despite having differences in baseline and referral characteristics (Li, 2018; Zablah, 2017). These results confirm the need for careful patient selection and risk
assessment in determining the optimal candidates for the Melody valve, and no policy changes are warranted. We added a statement of not medically necessary to the Medicare coverage section (Local Coverage Determinations L33777 and L35094).

Policy ID changed from CP# 04.03.08 to CCP.1264.

**Summary of clinical evidence:**

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
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<tbody>
<tr>
<td>Abdelghani (2018)</td>
<td><strong>Key points:</strong></td>
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<tr>
<td>Infective endocarditis after Melody valve implantation in the pulmonary position</td>
<td>• Systematic review of nine studies (n = 851) patients and 2,060 patient-years of follow up.  Sixty-nine patients developed infective endocarditis over the first three years of follow up.  Cumulative incidence = 3.2% to 25.0%; annualized incidence rate = 1.3% to 9.1% per patient-year.  Most common findings were positive blood culture (93%), fever (89%), and new, significant, and/or progressive right ventricular outflow tract obstruction (79%); vegetations detectable on echocardiography (34%).  Of 69 patients with infective endocarditis, death (8.7%) and surgical and/or transcatheter reintervention (52%) occurred. Both outcomes were more common in patients with new/significant right ventricular outflow tract obstruction (P = .042) and in patients with non-streptococcal infective endocarditis (P = .001).</td>
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<td>Li (2018)</td>
<td><strong>Key points:</strong></td>
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<td>Comparison of valvar and right ventricular function following transcatheter and surgical pulmonary valve replacement</td>
<td>• Retrospective review of echocardiograms obtained at three time points: before, immediately after pulmonary valve replacement, and most recent at Yale-New Haven Hospital who underwent transcatheter (n = 32) or surgical (n = 30) pulmonary valve replacement; median age = 19 years, median follow up 25 months.  Transcutaneous group had predominant right ventricular outflow tract obstruction (74% versus 10%, P &lt; .001) and less severe pulmonary insufficiency (61% versus 100%, P &lt; .001) than the surgical group.  Post-intervention, both groups had a decline in right ventricle size, but the surgical group had a transient postoperative decline in the surgical group.</td>
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<td>Chatterjee (2017)</td>
<td><strong>Key points:</strong></td>
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<td>Transcatheter pulmonary valve Implantation</td>
<td>• Systematic review and meta-analysis of 19 observational studies (1,044 total patients) with a pooled follow-up of 2,271 person-years.  Procedural success rate: 96.2% (95% confidence intervals [CI] 94.6% to 97.4%).  Conduit rupture rate: 4.1% (95% CI 2.5% to 6.8%).  Coronary complication rate: 1.3% (95% CI 0.7% to 2.3%).  Pooled endocarditis rate: 1.4 per 100 person-years (95% CI 0.9 to 2.0).  Incidence of re-intervention: 4.4 per 100 person-years overall (95% CI 3.0 to 5.9) with a marked reduction in studies reporting ≥ 75% pre-stenting (2.9 per 100 person-years [95% CI 1.5 to 4.3] versus 6.5 per 100 person-years [95% CI 4.6 to 8.5]; P&lt;0.01).</td>
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<td>Hill (2017)</td>
<td><strong>Key points:</strong></td>
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<td>Post-market surveillance to</td>
<td>• Post-market surveillance analysis of adverse events associated with Melody valve</td>
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### Citation and Key Points

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| detect adverse events associated with Melody valve implantation | Implantation reported to U.S. Food and Drug Administration’s Manufacturer and User Facility Device Experience database, and a structured literature review of on- and off-label uses. Results were compared to those described in the prospective Investigational Device Exemption and Post-Market Approval Melody transcatheter pulmonary valve trials.  
  - On-label uses: 631 adverse events; most frequent events were similar to those described in the prospective trials (e.g., stent fracture \( n = 210 \) and endocarditis \( n = 104 \)).  
  - Off-label uses: 84 adverse events.  
  - Post-market passive surveillance does not demonstrate a high frequency of previously unrecognized serious adverse events with "on-label" Melody valve implantation.  
  - Further study is needed to evaluate safety of "off-label" uses. |
| Zablah (2017) | Comparison of patients undergoing surgical versus transcatheter pulmonary valve replacement: criteria for referral and mid-term outcome | **Key points:**  
- Retrospective chart review of 30 patients who underwent surgical \( (n = 15) \) or percutaneous \( (n = 15) \) pulmonary valve replacement at one center from 2013 to 2015.  
- At referral, the surgical group had significantly larger right ventricular volumes than the transcutaneous group. Biventricular function was not significantly different.  
- Surgical group patients were mostly referred based on cardiac magnetic resonance volumetric criteria, whereas the transcutaneous group patients were mostly referred due to exercise intolerance with only occasional abnormalities on cardiac magnetic resonance.  
- One year after intervention, both groups had near-normal biventricular volumes and function irrespective of characteristics at referral. |
| Bhatt (2015) for the American Heart Association | Congenital heart disease in the older adult: a scientific statement from the American Heart Association | **Key points:**  
- Transcatheter valve implantation has dramatically changed the treatment paradigm, and possibly the threshold for pulmonary valve implantation, although current size limitations and the requirement for a conduit or other fixed structure in the right ventricular outflow tract may limit use in the patient without prior surgery.  
- Available transcatheter valves are only suitable for patients with non-native right ventricular outflow tracts, although transcatheter valves with broader applicability are in early trials.  
- Early complications associated with transcatheter therapy at least are known.  
- Contemporary morbidity, mortality, and durability of surgical pulmonary valve replacement are not known; therefore, there is no contemporaneous benchmark against which to compare transcatheter valve implantation. |
| Virk (2015) | Percutaneous pulmonary valve implantation: a systematic review of clinical outcomes | **Key points:**  
- Systematic review of 12 observational studies \( (n = 677 \) patients); 10 studies evaluated the Melody valve. Indications were regurgitation, stenosis, or mixed. No studies directly compared percutaneous procedure to surgery. Results reported as (incidence, 95% CI).  
- Pooled peri-procedural mortality (1.4%, 0.7 to 2.8).  
- Procedural complications: coronary artery compression (1.2%, 0.6 to 2.5); valve embolization (2.4%, 1.3 to 4.3), conduit rupture (2.6%, 1.5 to 43), and pulmonary artery obstruction (1.2%, 0.5 to 2.6).  
- Conversion to surgery (2.8%, 1.7 to 4.6).  
- Most common complications at latest follow up: stent fracture (12.4%, 7.6 to 19.6) and |
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<td></td>
<td>Infective endocarditis (4.9%, 3.2 to 7.6).</td>
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<td>- Stent fracture severity was strongly associated with restenosis and subsequent re-intervention.</td>
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<td>- Outcomes of infective endocarditis ranged from resolution with medical treatment to death despite surgical valve explantation. Poor compliance with antibiotic prophylaxis, premature discontinuation of anti-platelet therapy, and inadequate dental hygiene may have contributed.</td>
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**References**

**Professional society guidelines/other:**


**Peer-reviewed references:**


**Centers for Medicare & Medicaid Services National Coverage Determinations:**

No National Coverage Determinations identified as of the writing of this policy.

**Local Coverage Determinations:**

L33777 Noncovered Services.

L35094 Services That Are Not Reasonable and Necessary.

**Commonly submitted codes**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
<th>Comments</th>
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<tbody>
<tr>
<td>33477</td>
<td>Transcatheter pulmonary valve implantation, percutaneous approach, including pre-stenting of the valve delivery site, when performed</td>
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<thead>
<tr>
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<th>Comments</th>
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<tbody>
<tr>
<td>I37.0</td>
<td>Nonrheumatic pulmonary valve stenosis</td>
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<tr>
<td>I37.1</td>
<td>Nonrheumatic pulmonary valve insufficiency</td>
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<tr>
<td>I37.2</td>
<td>Nonrheumatic pulmonary valve stenosis with insufficiency</td>
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<tr>
<th>HCPCS Level II Code</th>
<th>Description</th>
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