Transcatheter Pulmonary Valve Implantation

Policy # 00576
Original Effective Date: 10/18/2017
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Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- Benefits are available in the member’s contract/certificate, and
- Medical necessity criteria and guidelines are met.

Based on review of available data, the Company may consider transcatheter pulmonary valve implantation, when performed according to Food and Drug Administration (FDA)—approved indications for patients with prior repair of congenital heart disease and right ventricular outflow tract dysfunction, who are not good candidates for open repair due to one or more of the following conditions to be eligible for coverage:
  - High risk for surgery due to concomitant medical comorbidities; or
  - Poor surgical candidate due to multiple prior thoracotomies for open heart surgery.

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers transcatheter pulmonary valve implantation for all other indications to be investigational.

Background/Overview
Description of Disease
Congenital heart disease, including tetralogy of Fallot, pulmonary atresia, and transposition of the great arteries, is generally treated by surgical repair at an early age. This involves reconstruction of the right ventricular outflow tract (RVOT) and pulmonary valve by means of a surgical homograft or a bovine-derived valved conduit. These repairs are prone to development of pulmonary stenosis or regurgitation over long periods of follow-up.

Because individuals with surgically corrected congenital heart disease repair are living longer into adulthood, RVOT dysfunction following initial repair has become more common. Calcification of the RVOT conduit can lead to pulmonary stenosis, while aneurysmal dilatation can result in pulmonary regurgitation. RVOT dysfunction can lead to decreased exercise tolerance, potentially fatal arrhythmias, and/or irreversible right ventricular dysfunction.

Interventions for RVOT dysfunction often require repeat open heart surgery, resulting in numerous open heart procedures for patients who live into adulthood. Treatment options for pulmonary stenosis are open surgery with valve replacement, balloon dilatation, or percutaneous stenting. Interventions for pulmonary
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Regurgitation are primarily surgical, either reconstruction of the RVOT conduit or replacement of the pulmonary valve through open surgery. The optimal timing of these interventions is not well understood.

Transcatheter pulmonary valve replacement offers a potentially less invasive treatment option for patients with prior surgery for congenital heart disease and RVOT dysfunction. It is possible that the use of less invasive valve replacement techniques can spare patients from multiple repeat open heart procedures over long periods of follow-up.

**Description of Technology**
The Melody Transcatheter Pulmonary Valve (TPV) and the Ensemble Transcatheter Valve Delivery System are used together for percutaneous replacement of a dysfunctional pulmonary valve. The Melody valve consists of a section of bovine jugular vein with an intact native venous valve. The valve and surrounding tissue is sutured within a platinum-iridium stent scaffolding. The transcatheter delivery system consists of a balloon-in-balloon catheter with a retractable sheath and distal cup into which the valve is placed. The procedure is performed on the beating heart without use of cardiopulmonary bypass.

The Melody valve is first crimped to fit into the delivery system. It is introduced through the femoral vein and advanced into the right side of the heart and put into place at the site of the pulmonary valve. The inner balloon is inflated to open the artificial valve, and then the outer balloon is inflated to position the valve into place.

**FDA or Other Governmental Regulatory Approval**
U.S. Food and Drug Administration (FDA)

On January 25, 2010, the Melody®‡ TPV and the Ensemble®‡ Transcatheter Valve Delivery System (Medtronic, Minneapolis, MN) were approved by the U.S. FDA under the humanitarian device exemption program for use as an adjunct to surgery in the management of pediatric and adult patients with the following clinical conditions:

- Existence of a full (circumferential) RVOT conduit that is 16 mm or greater in diameter when originally implanted, and
- Dysfunctional RVOT conduits with clinical indication for intervention, and either:
  - Regurgitation: moderate-to-severe regurgitation, or
  - Stenosis: mean RVOT gradient ≥35 mm Hg

In 2015, approval of the Melody device was amended to a premarket approval (PMA) because FDA determined that the device represented a breakthrough technology. The PMA was based, in part, on 2 prospective clinical studies, the Melody TPV Long-term Follow-up Post Approval Study (PAS) and the Melody TPV New Enrollment PAS.

On February 29, 2016, the Edwards Sapien XT™‡ Transcatheter Heart Valve (Pulmonic) (Edwards Lifesciences), composed of a stainless steel frame with bovine pericardial tissue leaflets and available in
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23- and 26-mm sizes, was approved by FDA through the PMA process “for use in pediatric and adult patients with a dysfunctional, non-compliant RVOT conduit with a clinical indication for intervention and:

- Pulmonary regurgitation ≥ moderate and/or
- Mean RVOT gradient ≥ 35 mmHg.”

FDA product code: NPV.

Centers for Medicare and Medicaid Services (CMS)
There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

Rationale/Source
The published literature on transcatheter pulmonary valve implantation (TPVI) consists of small case series, which have generally reported on short-term outcomes. Some of the larger, representative publications are discussed in this literature review.

Studies Using Valves Approved by the U.S. Food and Drug Administration
The only device that currently has U.S. FDA approval for TPVI is the Melody valve (Medtronic, Minneapolis, MN). Approved indications include RVOT dysfunction, defined as pulmonic regurgitation (moderate or greater) or pulmonic stenosis (mean gradient, ≥35 mm Hg). In addition, a circumferential RVOT conduit should exist that is 16 mm or greater in diameter when originally implanted.

U.S. Melody TPV Trial
The multicenter U.S. Melody TPV trial was a multicenter, prospective uncontrolled trial designed to assess the safety, procedural success, and short-term effectiveness of the Melody TPV. It was the pivotal trial on which FDA approval of the Melody valve was based. The investigators planned to follow 150 patients over a 5-year period. Eligibility criteria included a dysfunctional RVOT conduit or a dysfunctional bioprosthetic pulmonary valve, plus evidence of heart failure. For patients with New York Heart Association (NYHA) class I heart failure, a Doppler mean gradient of 40 mm Hg or greater or severe pulmonary regurgitation was required, and for patients with NYHA class II to IV heart failure, a mean gradient of 35 mm Hg or greater or moderate pulmonary regurgitation was required. These inclusion criteria generally were indications for pulmonary valve replacement. The primary outcomes were defined as procedural success, adverse events (AEs) from the procedure, and effectiveness, as measured by the proportion of patients with acceptable valve function at 6 months.

Trial results have been published in several reports. Short- and medium-term outcomes for 136 patients who underwent attempted TPVI were reported by McElhinney et al in 2010. A total of 124 (91.2%) of 136 patients had successful implantation. In 12 patients, implantation was not possible due to anatomic or other intraprocedural findings. One (0.7%) death occurred as a result of the procedure, and serious AEs occurred in 8 (6%) of 136 patients. AEs included coronary artery dissection, conduit rupture/tear, wide complex tachycardia, respiratory failure, femoral vein thrombosis, and perforation of the pulmonary artery.
Ninety-four patients with successful implantation had reached the 6-month follow-up time point at the time of publication. Acceptable valve function, defined as mild pulmonary regurgitation or less on echocardiography, was present in more than 90% of patients. Right ventricular (RV) pressure and RVOT gradient improved following the procedure, and 71 (75.5%) of 94 were in NYHA class I heart failure at 6 months. During follow-up, stent fractures were diagnosed in 25 (20.2%) of 124 patients, and 9 (7.3%) of 124 required implantation of a second valve.

Cheatham et al reported on outcomes up to 7 years following TPVI for the 148 patients who received and were discharged with a TPV in the U.S. Melody TPV trial (of 171 patients enrolled). Of the 171 patients enrolled, 167 underwent catheterization, 150 had a Melody valve implanted, and 148 of those survived to discharge with the Melody valve in place. On echocardiogram at discharge, pulmonary regurgitation was absent/trivial or mild in 140 patients and 5 patients, respectively, which represented a significant improvement from baseline. Over a median follow-up of 4.5 years (range, 0.4-7.0 years), 4 deaths occurred. During the follow-up period, 32 patients required a reintervention on RVOT, 25 of which were TPV reinterventions. A total of 11 patients required Melody valve explantation. Among the 113 patients who were alive and free from reintervention at a median of 4.5 years postimplantation, the most recent RVOT gradient was unchanged from early after valve implantation. Functional outcomes generally improved during the study: before TPVI, 14% of patients were in NYHA class I and 17% were in class III or IV. At every postimplantation annual evaluation, at least 74% of patients were in class I and no more than 1% to 2% were in class III or IV.

A secondary publication from the U.S. Melody TPV trial focused on the change in exercise function following TPVI. Patients completed a standardized cardiopulmonary regimen 2 months before TPVI and 6 months after TPVI. Results of pre- and postexercise parameters were available for 94 to 114 patients, depending on the specific outcome. Numerous physiologic outcome measures were reported, with some showing a statistically significant change between the 2 time points, and others not. For example, there was a significant increase in the percent predicted maximal workload from 65.0% at baseline to 68.3% at follow-up (p<0.001) and a significant decrease in the ratio of minute ventilation to CO2 production from 30.8 at baseline to 29.1 at follow-up (p<0.001). In contrast, there were no significant changes in peak oxygen consumption or in spirometric measures of pulmonary function. This trial reported modest benefits in exercise parameters for patients treated with TPVI. The results are limited by the lack of a control group and by the large number of patients who did not have completed exercise results available (approximately one-third of total).

Melody TPV Long-term Follow-up Post Approval Study
Armstrong et al published 1-year follow-up results of the Melody TPV Long-term Follow-up PAS, a prospective study designed to evaluate the short-term hemodynamic changes following device implantation. The study used historical controls from the Melody pivotal investigational device exemption (IDE) trial described above to investigate whether the short-term effectiveness of the device was noninferior to results shown in the IDE trial. PAS enrolled 120 subjects, 101 of whom underwent attempted TPVI. Patient selection was based on the criteria used in the IDE trial, but did not include the age (≥5 years of age) and weight (≥30 kg) limitations. Procedure-related significant AEs occurred in 16 patients (13.3% of total cohort;
15.8% of those who had an attempted TPVI, the most common of which was a confined conduit tear. Procedural success occurred in 99 subjects (98% of those with an attempted TPVI). At 1-year follow-up, the proportion of patients in NYHA class I heart failure increased from 35% at baseline to 89%. Of the 99 patients implanted for at least 24 hours, 87 had acceptable TPV hemodynamic function confirmed at 6 months (96.7% of those with evaluable echocardiographic data, 87.9% of entire cohort) and 82 had acceptable TPV hemodynamic function at 1 year (94.3% of those with evaluable echocardiographic data, 82.8% of the entire cohort). Following the procedural period, serious device-related AEs occurred in 8%, most commonly endocarditis (n=3 patients).

Gillespie et al evaluated results of TPVI after a Ross procedure in a retrospective review of pooled findings from the U.S. Melody TPV trial and PAS and an additional European registry, the manufacturer-sponsored Melody TPV Post-Market Surveillance Study conducted in Canada and Europe (NCT00688571). In the pooled sample (total N=358 patients), 67 (19%) had a prior Ross procedure. A Melody valve was successfully implanted in 56 (84%) of 67 Ross patients who underwent catheterization with intent for TPVI. Six (9%) patients had symptomatic coronary artery compression after TPVI or did not undergo implantation due to the risk of compression. RV hemodynamics generally improved after TPVI, but RVOT reinterventions were required in 12 of 55 patients discharged from the implant hospitalization with the Melody valve in place.

**Additional Noncomparative Studies**

A number of publications have reported on series of patients treated with TPVI. Some of the larger series are discussed in detail.

Lurz et al reported on 163 patients who underwent attempted TPVI from 4 clinical centers in Europe. Eligibility for the procedure included elevated RV systolic pressure, increased RVOT dimensions, and either symptoms or evidence of severe RV dysfunction. Procedural success was achieved in 155 (95.1%) of 163 patients. Procedural complications occurred in 12 (7.4%) of 163, 8 of which were considered serious and 5 of which required open surgery. Median follow-up was 28.4 months. During follow-up, 4 (2.6%) of 155 patients died, and an additional 5 (3.2%) developed infective endocarditis. At 12-month follow-up, more than 90% of patients had absent or mild valve dysfunction as measured by echocardiography.

Eicken et al reported on 102 consecutive patients (mean age, 21.5 years) undergoing TPVI at 2 centers in Germany. Eligibility for the procedure included RVOT dysfunction with evidence of RV compromise or increased RV pressure. One (1.0%) death occurred as a result of compression of the left coronary artery. Two (2.0%) patients had evidence of stent fracture immediately postprocedure and 1 (1.0%) other patient developed infective endocarditis at 6-month follow-up. At a median follow-up of 357 days, there was a significant decrease in the RVOT gradient from a median of 36 to 15 mm Hg (p<0.001). However, there was no significant change in exercise capacity as measured by maximal oxygen uptake.

Other case series reported on smaller numbers of patients, with a range of 7 to 64 patients. These series generally reported similar results as the larger series, with high procedural success and relatively low rates of serious complications. The longest follow-up was reported by Borik et al, who evaluated 51 patients who
underwent TPVI with the Melody valve at a single institution. Over a mean follow-up of 4.5 years (range, 0.9-6.9 years), freedom from any reintervention was 87% and 68% at 3 and 5 years, respectively, and freedom from surgery was 90% at 5 years. Overall, RV functional parameters did not change with longer follow-up.

Section Summary: Studies Using Valves Approved by the U.S. Food and Drug Administration
The evidence for the use of TPVI with the Melody valve consists of the prospective, interventional, noncomparative pivotal study on which the device's FDA approval was based, along with a postapproval registry study and a number of additional case series. Overall, the evidence suggests that TPVI is associated with high rates of short-term technical success and improvements in heart failure-related symptoms and hemodynamic parameters. Studies with follow-up extending to a maximum of 7 years postprocedure have suggested that the functional and hemodynamic improvements are durable, with a number (20%-30%) requiring reintervention on the pulmonary valve.

Non-FDA-Approved Uses of TPVI
A variety of potential off-label uses of TPVI have been reported in the literature. They include use of devices that are not FDA-approved, and use of approved devices for non-FDA-approved indications.

Non-FDA-Approved Devices
A small number of retrospective, comparative studies have compared outcomes of the Edwards Sapien and the Melody valves. Boshoff et al described the off-label uses in 21 patients treated with the Melody valve and 2 patients treated with the Edwards Sapien pulmonic valve. Use has included native RVOT obstruction, in conduits smaller than the FDA-labeled indications, and large RVOT with a dynamic outflow aneurysm. No deaths or major procedural complications were reported for these patients. Clinical outcomes data were lacking or very limited in this publication.

Faza et al reported on 20 patients who underwent successful implantation of the Edwards Sapien pulmonic valve at 1 clinical center. There were no periprocedural deaths, and all but 1 patient had no or trivial pulmonic regurgitation on latest follow-up. A comparison of hemodynamic parameters in these 20 patients was made with 13 patients treated with the Melody valve. Immediately postprocedure, transvalvular gradients were similar between groups. At last follow-up, mean residual transvalvular gradient was higher for patients receiving the Sapien valve (18.4 mm Hg vs 11.2 mm Hg, p=0.016), but this difference was disappeared when patients were matched for length of follow-up.

A few other small case series reporting on the use of the Edwards Sapien pulmonic valve for RVOT obstruction have been published. For example, Kenny et al reported on a phase 1 multicenter study of the Sapien valve in 36 patients from 4 clinical centers. Procedural success was reported in 97% of patients. Procedural complications occurred in 19% (7/36) of patients, including valve migration (n=3), pulmonary hemorrhage (n=2), ventricular fibrillation (n=1), and stent migration (n=1). At 6-month follow-up, there were no deaths and 75% (27/36) of patients were in NYHA class I, compared with 14% at baseline. Freedom from reintervention at 6 months was 97%.
Non-FDA-Approved Indications

Analysis of data from the Valve-in-Valve International Database (VIVID) multicenter registry evaluated the off-label use of transcatheter aortic and TPVI prostheses for tricuspid valve-in-valve implantation (TVIV). One hundred fifty of 156 patients in the registry had successful TVIV with a Melody (n=93) or a Sapien (n=57) valve. During a median 13.3-month follow-up, 22 (15%) patients died, all with NYHA class III or IV. There were 10 (6.6%) tricuspid valve reinterventions and 3 (2%) other patients who had significant recurrent dysfunction of the valve. Preintervention, 71% of patients were NYHA class III or IV; at follow-up, 77% of surviving patients were NYHA class I or II (p<0.001).

A few case series have been reported on use of the Melody valve in patients with clinical characteristics that do not correspond to FDA-approved indications. These indications have included use of valves in positions other than pulmonic, patients with conduit sizes not corresponding to the FDA indications, and patients with prior congenital heart repair surgery not involving construction of a RVOT conduit. In general, these case series have reported high rates of procedural success with low rates of periprocedural complications, but evidence on longer term outcomes is lacking.

Although most studies have evaluated the use of TPVI in patients with a constructed RVOT conduit, a few have evaluated TPVI with either the Melody valve or the Edwards Sapien Transcatheter Heart Valve in a native RVOT or RVOT without a circumferential conduit. Meadows et al reported results from a retrospective, 5-center review of patients who underwent TPV placement in a nonconduit RVOT, with native tissue comprising at least part of the circumference. Thirty-one patients were included, with indications for RVOT intervention including primarily valvular insufficiency in 14 (45%), obstruction in 3 (10%), and mixed obstruction and insufficiency in 14 (45%). TPVI was successful in all patients, but serious complications occurred in 2 (6%). At a median follow-up of 15 months (range, 1 month to 3.8 years), all patients were alive, and none had greater than mild pulmonary regurgitation. Among the 19 patients with adequate imaging at follow-up, 6 (32%) had evidence of stent fracture. Three patients were treated for endocarditis or bloodstream infection. Malekzadeh-Milani reported outcomes for 34 patients with a native or patched noncircular RVOT who underwent Melody TPV insertion at a single center. The procedure was technically successful in all patients, although early complications occurred in 8.8%. At a mean follow-up of 2.6 years, no patients had stent fracture or migration, and 32 (94.1%) of 34 had no or trivial pulmonary regurgitation.

Several other small case series by Demkow et al (N=10) and Odemis et al (N=7) have reported on the use of the Edwards Sapien pulmonary valve for noncircular and large-diameter conduits, respectively. The authors reported high rates of successful valve implantation, but no long-term follow-up.

Adverse Events

In addition to the AEs reported in the case series, several publications have focused on AEs following TPVI. FDA reviewed results from the U.S. Melody TPV trial as part of its approval process and reported data on complications from the procedure. At that time, data were available for 99 patients enrolled between January 2007 and December 2008. Ninety patients were deemed suitable for implantation following catheterization, and 87 of them had successful implantation. There was 1 (1.1%) procedure-related death. Table 1 is adapted from the FDA summary of safety and probable benefit.
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Table 1. Device-Related Adverse Events (N=89 Subjects)

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>Subjects With Event, n (%)</th>
<th>Freedom From Event at 12 Months (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent fracture (all)</td>
<td>16 (18%)</td>
<td>77.1% (7.5%)</td>
</tr>
<tr>
<td>Minor&lt;sup&gt;a&lt;/sup&gt;</td>
<td>11 (12%)</td>
<td>84.1% (6.7%)</td>
</tr>
<tr>
<td>Major&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5 (6%)</td>
<td>90.6% (5.2%)</td>
</tr>
<tr>
<td>Valve stenosis</td>
<td>6 (7%)</td>
<td>90.5% (4.8%)</td>
</tr>
<tr>
<td>Worsening tricuspid regurgitation</td>
<td>1 (1%)</td>
<td>100% (‒)</td>
</tr>
<tr>
<td>Reintervention&lt;sup&gt;b&lt;/sup&gt;</td>
<td>6 (7%)</td>
<td>93.5% (4.3%)</td>
</tr>
<tr>
<td>Reoperation</td>
<td>1 (1%)</td>
<td>98.6% (2.2%)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Stent fractures that did not require intervention were defined as minor; those that required reintervention were defined as major.

<sup>b</sup> Reinterventions were balloon angioplasty in 1 patient; repeat implantation of a second transcatheter pulmonary valve in 5 patients.

Sixty-four patients in the FDA analysis reached the 6-month follow-up. Of them, 56 (87.5%) had acceptable hemodynamic valve function by Doppler echocardiography. At 6 months, approximately 75% of patients were in NYHA class I and 25% were in NYHA class II. Pulmonary regurgitation that was mild or worse was present in 6.2% of patients.

Another publication focusing on AEs from the U.S. Melody TPV trial was published in 2011. This report assessed AEs at a median follow-up of 30 months in 150 patients. Stent fracture occurred in 26% (39/150) of patients. The estimated freedom from stent fracture was 77% at 14 months and 60% at 39 months. Freedom from reinterventions for all patients was estimated to be 86% at 27 months, and freedom from reinterventions for patients with stent fracture was estimated at 49% at 2 years.

McElhinney et al reported rates of infective endocarditis from 3 prospective case series enrolling 311 patients followed for a median of 2.5 years. Sixteen (5.1%) patients were diagnosed with endocarditis at any location and 6 (1.9%) patients had endocarditis at the pulmonic valve location. This corresponded to an annualized rate of pulmonic valve endocarditis of 0.88% per patient-year. Malekzadeh-Milani et al evaluated patients with right-sided infective endocarditis at a single center to compare endocarditis rates in patients who had TPVs with those who had surgically paced pulmonary valves. Thirty-one patients with right-sided endocarditis and pulmonary valve implantation for congenital heart disease were included. Rates of endocarditis were 1.2 and 3.9 cases/100 person-years in patients with surgically implanted valves and TPVs, respectively (p=0.03).

Boudjemline et al conducted a prospective observational study to evaluate predictors of conduit rupture during the preparation of the RVOT for TPVI in a cohort of patients older than age 5 years with RVOT obstruction, pulmonary regurgitation, or mixed lesions, who underwent transcatheter therapies, including balloon dilatation, bare metal stent placement, or TPV placement. Ninety-nine patients were included, 56 of whom were adults. Of the total cohort, 83.8% underwent Melody TPVI. Conduit rupture occurred in 9 (9.09%) patients. In 2 of the 9 patients, conduit rupture was angiographically obvious and severe with extension, causing hemodynamic instability. All conduit ruptures occurred during balloon dilatation and...
occurred in patients with RVOT obstruction. Heavy calcification and the presence of a homograft were associated with conduit rupture risk.

Coronary artery compression during balloon angioplasty or stent placement in the RVOT conduit is considered a relative contraindication to TPV placement. Several studies have evaluated the incidence of coronary artery compression. Morray et al reported the incidence of coronary artery compression in a 4-center series of 404 patients who underwent attempted TPVI. Three hundred forty-three (85%) patients underwent TPVI, and 21 (5%) patients had evidence of coronary artery compression. Most (n=19) patients with coronary artery compression did not undergo TPV placement. Using the same cohort reported in the Boudjemline study, Fraisse et al reported the incidence, diagnosis, and outcome of coronary compression among patients treated with transcatheter RVOT interventions for RVOT obstruction, pulmonary regurgitation, or mixed lesions. All patients underwent balloon dilatation and coronary assessment with angiography, which was followed by TPV placement if RVOT dysfunction was ongoing. Of 100 patients evaluated, 83% had implantation of a Melody TPV. Coronary artery compression occurred in 6 cases, all of which could be diagnosed by selective coronary angiogram and/or aortic root angiogram during balloon dilation of the RVOT. No specific risk factors for coronary artery compression were identified.

Van Dijck et al compared rates of infective endocarditis between transcatheter pulmonary valves and surgically implanted pulmonary valves in a retrospective, single-center study that included 677 patients (738 conduits). Patients who underwent procedures from 1989 to 2013 were included. A total of 107 Melody conduits were implanted in 107 patients. A total of 577 pulmonary valve cryopreserved homografts were implanted in 517 patients, and 54 Contegra grafts were implanted in 53 patients. Freedom from infective endocarditis at 5 years by Kaplan-Meier analysis was 85%, 88%, and 99% for patients with Melody conduits, Contegra grafts, or cryopreserved homografts, respectively.

Malekzadeh-Milani et al reported on the incidence of infective endocarditis among 86 prospectively enrolled consecutive patients who underwent TPVI with the Melody valve. Over a mean follow-up of 23.6 months (range, 2.6-28.3 months) after Melody implantation, 5 patients developed infective endocarditis (5.8%; 95% confidence interval [CI], 0.9% to 10.7%). Factors related to demographics, conduit type, procedural success, residual gradient, and duration of Melody valve implantation did not differ significantly between patients who did or did not develop infective endocarditis. Patients with infective endocarditis were more likely to have undergone invasive procedures after TPVI without antibiotic prophylaxis (odds ratio, 13.69; 95% CI, 1.98 to 94.52; p=0.014), and aspirin use was preventive for infective endocarditis (relative risk, 20.1; 95% CI, 3.34 to 120.9; p=0.001), although confidence intervals around risk estimates for both factors were wide.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 2.

Table 2. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
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Ongoing

| NCT: national clinical trial. | Denotes industry-sponsored or cosponsored trial. |

<table>
<thead>
<tr>
<th>NCT</th>
<th>Title</th>
<th>Enrollment</th>
<th>Follow-Up</th>
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<tr>
<td>00676689</td>
<td>Implantation of the SAPIEN Transcatheter Heart Valve (THV) in the Pulmonic Position</td>
<td>70</td>
<td>Nov 2019</td>
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<tr>
<td>00740870</td>
<td>Implantation of the Medtronic Melody Transcatheter Pulmonary Valve in Patients With Dysfunctional RVOT Conduits: A Feasibility Study</td>
<td>150</td>
<td>Jan 2020</td>
</tr>
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Summary of Evidence

For individuals who have a history of congenital heart disease (CHD) and current RVOT obstruction who receive TPVI with an FDA-approved device and indication, the evidence includes 1 prospective, interventional, noncomparative study and multiple prospective and retrospective case series. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity and mortality. Results of the case series indicate that there is a high rate of procedural success and low procedural mortality, although the rates of serious procedural adverse events reported ranges from 3.0% to 7.4%. Most valves demonstrate competent functioning by Doppler echocardiography at 6- to 12-month follow-up, but complications (eg, stent fractures, need for reinterventions) were reported in an FDA analysis to occur at rates of 18% and 7%, respectively. Other publications with longer follow-up have reported stent fractures in up to 26% of patients; however, most stent fractures have not required re-intervention. Studies with follow-up extending to a maximum of 7 years postprocedure have suggested that the functional and hemodynamic improvements are durable, but a relatively high proportion of patients (20%-30%) require reintervention on the pulmonary valve. No comparative studies were identified, and there is no direct evidence that TPVI leads to a reduction in future open heart procedures. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have a history of CHD and current RVOT obstruction who receive TPVI with a non-FDA-approved device or indication, the evidence includes case series. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity and mortality. There is currently limited published evidence on the off-label use of TPVI, including implantation of a non-FDA-approved valve, or use of an approved valve for a non-FDA-approved indication. The published relatively small case series are heterogeneous in terms of the device used and the indications for TPVI. The evidence is insufficient to determine the effects of the technology on health outcomes.

In patients who are not candidates for open surgery or are at high risk for surgery due to other medical comorbidities, alternative treatment options are limited. Clinical vetting in 2011 indicated near uniform support for use of TPVI in patients who were not candidates for open repair or who were at high risk for open surgery. Based on this clinical vetting and evidence on short-term success, TPVI can be considered medically necessary for patients who are not candidates for open repair or who are at high risk for open repair.

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Original Effective Date: 10/18/2017

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Transcatheter Pulmonary Valve Implantation

Policy # 00576
Original Effective Date: 10/18/2017
Current Effective Date: 10/18/2017

Current Effective Date: 10/18/2017
10/05/2017 Medical Policy Committee review
10/18/2017 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 10/2018

Coding
The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®), copyright 2016 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

<table>
<thead>
<tr>
<th>Code Type</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>33477</td>
</tr>
<tr>
<td>HCPCS</td>
<td>No codes</td>
</tr>
<tr>
<td>ICD-10 Diagnosis</td>
<td>I97.0, I97.110, I97.130, I97.190, Q20.5, Q21.3, Q22.0-Q22.3, T82.01XA-T82.09XS, T82.221A-T82.228S, Z95.2-Z95.4</td>
</tr>
</tbody>
</table>

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

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**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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