Transcatheter Pulmonary Valve Implantation

Policy # 00576
Original Effective Date: 10/18/2017
Current Effective Date: 08/15/2018

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 for patients with congenital heart disease and current right ventricular outflow tract obstruction (RVOT) or regurgitation including the following indications to be **eligible for coverage:**

- Individuals with right ventricle-to-pulmonary artery conduit with or without bioprosthetic valve with at least moderate pulmonic regurgitation;
- Individuals with native or patched RVOT with at least moderate pulmonic regurgitation;
- Individuals with right ventricle-to-pulmonary artery conduit with or without bioprosthetic valve with pulmonic stenosis (mean RVOT gradient at least 35 mm Hg); or
- Individuals with native or patched RVOT with pulmonic stenosis (mean RVOT gradient at least 35 mm Hg).

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

CONGENITAL HEART 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 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.

Treatment
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 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.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Devices for transcatheter pulmonary valve implantation were initially cleared from marketing by the U.S. FDA through the humanitarian device exemption (HDE) process or used off-label until approved by FDA through the premarket approval (PMA) process between 2015 and 2016 (see Table 1).

Table 1. Regulatory Status of Transcatheter Pulmonary Valve Implantation Devices

Device	Manufacturer	Date Approved	PMA No.	Indications
Melody Transcatheter Pulmonary Valve (TPV)	Medtronic	Jan 2010	H080002 (HDE)	Pulmonary valve replacement for pediatric and adult patients with a dysfunctional, noncompliant RVOT conduit
Melody TPV	Medtronic	Jan 2015	P140017	Pulmonary valve replacement for pediatric and adult patients with a dysfunctional, noncompliant RVOT conduit
Melody TPV	Medtronic	Feb 2017	P140017/S005	Valve-in-valve for patients with a dysfunctional surgical bioprosthetic pulmonary valve
SAPIEN XT Transcatheter Heart Valve (pulmonic)	Edwards Lifesciences	Feb 2016	P130009/S037	Pulmonary valve replacement for pediatric and adult patients with a dysfunctional, noncompliant RVOT conduit

HDE: humanitarian device exemption; PMA: premarket approval; RVOT: right ventricular outflow tract.

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 are 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 a beating heart without the 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.

In January 2010, the Melody TPV and the Ensemble Transcatheter Valve Delivery System (Medtronic) were approved by FDA under the HDE 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.

On January 27, 2015, approval of the Melody system was amended to a 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 and the Melody TPV New Enrollment Post Approval Study.

On February 24, 2017, approval of the Melody system was expanded to include patients with a dysfunctional surgical bioprosthetic valve (valve-in-valve).

The Edwards SAPIEN XT™‡ Transcatheter Heart Valve (Pulmonic) (Edwards Lifesciences) is composed of a stainless steel frame with bovine pericardial tissue leaflets and available in 23- and 26-mm sizes. It includes a delivery accessories system. On February 29, 2016, it was approved by FDA as a supplement "for use in pediatric and adult patients with a dysfunctional, noncompliant RVOT conduit with a clinical indication for intervention and:

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

The approval for the pulmonic valve indication is a supplement to the 2014 PMA for use of the Edwards SAPIEN XT Transcatheter Heart Valve System for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis and who are judged by a heart team, including a cardiac surgeon, to be at high or greater risk for open surgical therapy (ie, Society of Thoracic Surgeons operative risk score ≥8% or at a ≥15% risk of mortality at 30 days).

FDA product code: NPV.

Centers for Medicare and Medicaid Services (CMS)
State or federal mandates (eg, Federal Employee Program) may dictate that certain U.S. FDA approved devices, drugs, or biologics may not be considered investigational, and thus these devices may be assessed only by their medical necessity.

Rationale/Source

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

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

The published literature on transcatheter pulmonary valve implantation (TPVI) consists of the registration trials for FDA approval, small case series, and cohort studies.

TPVI DEVICES AND USES APPROVED BY FDA

Melody Transcatheter Pulmonary Valve

The multicenter U.S. Melody TPV trial was a prospective uncontrolled trial designed to assess the safety, procedural success, and short-term effectiveness of the Melody TPV. The Summary of Safety and Probable Benefit (SSPB) to support the approval of a humanitarian device exemption to market the Melody TPV was based on clinical data from 99 subjects who were catheterized for potential implantation with the TPV from January 2007, through December 2008, with expected follow-up and adverse event data on these subjects current through March 2009. Approved indications included RVOT dysfunction, defined as pulmonic regurgitation (moderate or greater) or pulmonic stenosis (mean gradient, ≥35 mm Hg). Also, a circumferential RVOT conduit should exist that is 16 mm or greater in diameter when originally implanted.

The investigators planned to follow 150 patients over 5 years. 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; 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 are indications for pulmonary valve replacement. The primary outcomes were defined as procedural success, adverse events 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 (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 adverse events occurred in 8 (6%) of 136 patients. Adverse events 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 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 (2015) 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 (2012) 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 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 CO_2 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 spirometric measures of pulmonary function. This trial reported modest benefits in exercise parameters for patients treated with TPVI. The results were limited by the lack of a control group and by a large number of patients who did not have completed exercise results available (approximately one-third of total).

The 2015 PMA of the Melody TPV was based on the interim analysis and a retrospective pooling analysis of the 2 postapproval studies conditioned by the prior humanitarian device exemption. An additional supplemental dataset from the Melody TPV European and Canadian Post-Market Surveillance Study (PMSS) was included in the PMA.

Armstrong et al (2014) published 1-year follow-up results of the Melody TPV Long-term Follow-up Post Approval Study (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 adverse events 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 adverse events occurred in 8%, most commonly endocarditis (n=3 patients).

Gillespie et al (2015) 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 PMSS 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.

The Melody TPV New Enrollment Study was intended to roll in the new patient enrollment study specified as a condition of approval for the Melody TPV HDE on January 25, 2010. This study used the protocol dated September 24, 2013, Version 2, included in H080002/S015. The study is a prospective, nonrandomized, multicenter, historically controlled clinical trial, designed to assess the postmarket

performance of the Melody TPV in a representative population of providers and patients, with 5-year follow-up. The primary endpoint is freedom from TPV dysfunction, with a performance goal of 75% or greater at 6 months. Secondary end points include procedural success, serious procedural- and device-related adverse events, stent fracture, reintervention on the TPV, surgical replacement of the RVOT conduit, death (all-cause, procedure-related, and device-related), and NYHA classification.

The February 2017 approval of the Melody system expanded to include patients with a dysfunctional surgical bioprosthetic valve (valve-in-valve) is based on data pooled from 3 sources:

- Melody TPV Long-term Follow-up PAS: 8 patients
- Melody TPV New Enrollment PAS: 17 patients
- Real-World Data: 100 patients.

Of 125 patients pooled from the 3 studies listed above, 56.8% (71) patients were available for analysis at study completion, the 1-year postimplant visit. Baseline pooled subject median age was 22.0 years (range, 5.0-79 years), with 45.6% female and 54.4% male. Tetralogy of Fallot was the most common congenital heart disease diagnosis recorded in 72.8% of subjects, 66.4% of whom had pulmonary stenosis or atresia. There was no mortality for any cause, major stent fracture, occurrence of endocarditis, RVOT reoperation, or catheter reintervention among available patients at 1 year. Procedural failure as defined by more than trivial pulmonary regurgitation by angiography postimplant occurred in 10.1% (12/119) subjects. There were no device explants within 24 hours of implantation. The mean RVOT gradient was reduced from 29.5 mm Hg at baseline to 14.3 mm Hg at 1 year postimplantation. In this PMA, existing clinical data were not leveraged to support approval of a pediatric patient population. This submission included pediatric data to support the pediatric indication and no extrapolation was necessary.

Additional Noncomparative Studies
A number of publications have reported on series of patients treated with TPVI. Some of the larger series are detailed next.

Lurz et al (2008) 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 (2011) 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 measures by maximal oxygen uptake.

Other case series have reported on smaller numbers of patients, ranging from 7 to 64 patients. These series have generally reported similar results as the larger series, with high procedural success and relatively low rates of serious complications. The longest follow-up, reported by Borik et al (2015), 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.

An Australian prospective observational registry (2017) reported information accumulated on 17 patients implanted with Melody device between 2009 and 2016. Mixed valvular dysfunction was present in 7 (41%) patients and 11 (59%) had corrected tetralogy of Fallot. Device implantation was successful in all patients. Peak RVOT gradient was significantly reduced, and there was no significant regurgitation postprocedure. There was 1 (6%) major procedural adverse event and 2 (12%) major adverse events at last recorded follow-up. There were no patient deaths. Follow-up cardiac magnetic resonance imaging revealed a significant reduction in indexed RV end diastolic volume.

Edwards Sapien XT Transcatheter Heart Valve (Pulmonic)
Edwards Lifesciences, manufacturer of the SAPIEN THV, performed a clinical study to establish the safety and efficacy of its pulmonic implantation in patients with dysfunctional RVOT conduits in the United States under IDE G060242 (the COngenital Multicenter trial of Pulmonic vAlve regurgitation Studying the SAPIEN InterventIONal THV, COMPASSION trial). Data from this clinical study were the basis for the PMA decision for the pulmonary valve implantation indication.

Patients were treated between April 2008 and November 2014. The database supplement reflects data collected through March 2015 and includes 81 patients. There were 7 investigational sites.

This prospective, nonrandomized, multicenter clinical study assessed the safety and effectiveness of pulmonic implantation of the SAPIEN THV in patients with dysfunctional RVOT conduits requiring treatment for moderate or severe pulmonary regurgitation by transthoracic echocardiography (TTE) and/or RVOT conduit obstruction with a mean gradient of 35 mm Hg or higher by TTE. The SAPIEN THV, the first-generation valve of the SAPIEN device line, is no longer available for distribution. The valve sizes used in the COMPASSION trial included the 23- and 26-mm sizes, which were the only sizes available for the SAPIEN THV. The 29-mm valve size was not evaluated in the COMPASSION trial. Most data derived from patients who received the 23-mm THV size. Aortic experience with the 29-mm SAPIEN XT THV showed no significant difference in the long-term performance compared with the 23- and 26-mm sizes. Furthermore, no observed results suggested that the 29-mm valve size would perform worse than other available sizes in the pulmonic location.

Enrollment in the COMPASSION study was limited to patients who met the following inclusion criteria:

- Weight ≥35 kg.
- In situ conduit size of 20 to 26 mm in diameter.
- Moderate or severe pulmonary regurgitation defined as ≥3+ pulmonary regurgitation by TTE or
- RVOT conduit obstruction with a mean gradient of ≥35 mm Hg by TTE.
- Symptomatic as evidenced by cardiopulmonary exercise testing.
- Catheterization was determined to be feasible by the treating physician.

All patients were scheduled to return for follow-ups at day 1 postprocedure, discharge, 30 days, 6 months, 12 months, and annually after that for 5 years postoperatively. Baseline evaluation included TTE, x-ray, magnetic resonance imaging, or computed tomography, angiogram, and electroencephalograph. Assessment of NYHA class, magnetic resonance imaging or computed tomography, and angiogram were part of the 6-month evaluation.

The primary end point was freedom from the device- or procedure-related death and/or reintervention at 1 year. The secondary end points were:

- Freedom from major adverse cardiac and cerebrovascular events at 6 months. Major adverse cardiac and cerebrovascular events was defined as all-cause mortality, myocardial infarction, reintervention, vascular injury resulting in the need for an unplanned vascular intervention, stroke, and pulmonary embolism.
- Functional improvement at 6 months as defined by:
    - Improved valve hemodynamics as demonstrated via TTE:
        - Decrease in pulmonary regurgitation to mild or less for regurgitant lesions
        - Decrease in the mean pulmonary gradient to less than 30 mm Hg for stenotic lesions
        - Improvement in both pulmonary regurgitation and gradient (above) for mixed lesions.
    - Improvement of 1 or more NYHA functional classes from baseline for patients in NYHA functional classes $\geq$ 2 at baseline.
    - Freedom from recurrent pulmonary stenosis.

Of 81 patients enrolled in the PMA study, 2 patients were screening failures, 9 patients did not receive the valve, another received the valve in a nontarget location. Therefore, 69 patients were available for analysis in the valve implant population at study completion.

The median duration of follow-up for the safety population was 3.04 years (range, 0-5.31 years). Males were 65.8% of the population, and 63.3% were at least 22 years of age. The primary indications for valve implantation were pulmonary stenosis (8.9%), pulmonary regurgitation (12.7%), and both stenosis and regurgitation (78.5%). The primary etiology requiring reconstruction of the RVOT and placement of a pulmonary conduit for the safety population was tetralogy of Fallot (42%).

The prespecified performance goal for the primary end point was 75%. The primary outcome was met by 100% of patients; there were 3 reintervention events. At 5 years, the primary outcome using a Kaplan-Meier estimate was 77.1%. Because there was no device- or procedure-related patient deaths at 5 years, the incidence of reinterventions solely contributed to the estimate.

Freedom from reintervention to 5 years for the valve implant population using a Kaplan-Meier estimate was reported by type of reintervention: (a) freedom from surgical pulmonic valve repair was 98.3% at 1 year and 91.8% at 5 years; (b) freedom from TPVI was 97.1% at 1 year and 85.8% at 5 years; (c) freedom from balloon valvuloplasty was 100% at 1 year and 93.7% at 5 years; and (d) freedom from other types of reintervention was 100% at 1 year and 97.9% at 5 years.

For secondary outcomes, freedom from major adverse cardiac and cerebrovascular events at 6 months in the valve implant population was 94.1%. Because 2 (2.5%) of 79 patients experienced a device migration early in the trial, the instructions for use were modified. No other device migrations subsequently occurred in the trial. Serious adverse events for RVOT conduit ruptures occurred in 5 (6.3%) of 79 patients. These 5 ruptures were related to balloon valvuloplasty or placement of a prestent; no ruptures occurred during placement of the SAPIEN THV. There was 1 neurologic event (not stroke), 1 thromboembolism, and 4 endocarditis events at the 1-year follow-up.

Adjunctive analyses of safety and effectiveness stratified by patients ages 21 years or younger at baseline vs patients ages 22 years or older at baseline were conducted. The COMPASSION study was not designed to investigate the differences in outcomes between age groups and, therefore, no statistical inferences can be made. The analysis of functional improvement outcomes by age group is summarized in Table 2.

Table 2. Edwards Sapien XT Transcatheter Heart Valve (Pulmonic) PMA Approval Study: Overall Functional Improvement by Age Group for Valve Implanted Population

End Points	Age 21 or Younger (n=27)		Age 22 or Older (n=42)	
	Outcome Rate, n/N (%)		Outcome Rate, n/N (%)	
	1 Year	5 Year	1 Year	5 Year
Overall functional improvement	18/22 (85.7)	3/7 (42.9)	29/33 (87.9)	5/8 (62.5)
Improved valve function	19/19 (100.0)	5/5 (100.0)	28/30 (93.3)	6/6 (100.0)
Functional improvement in NYHA class	13/14 (92.9)	4/4 (100.0)	32/33 (97.0)	8/8 (100.0)
Freedom from recurrent pulmonary stenosis	18/19 (94.7)	5/9 (55.6)	31/31 (100.0)	7/10 (70.0)
Improved gradient	7/8 (87.5)	3/3 (100.0)	7/8 (87.5)	2/2 (100.0)

NYHA: New York Heart Association.

As listed in Table 2, overall functional improvement was defined by the following 4 categories: (a) improved valve function demonstrated by a decrease in pulmonary regurgitation to mild or less per TTE at visit for patients with moderate or more (>2) pulmonary regurgitation at baseline, (b) functional improvement from baseline of 1 or more NYHA functional classes at visit for patients with baseline NYHA functional class of 2 or higher, (c) freedom from recurrent pulmonary stenosis at visit, and (d) improved valve function demonstrated by a decrease in pulmonary stenosis mean gradient to less than 30 mm Hg for patients with

pulmonary stenosis mean gradient greater than 30 mm Hg at baseline. Patients with mild or less (≤2+) pulmonary regurgitation at baseline only use categories b, c, and d to determine overall functional improvement. Patients with an NYHA functional class of less than 2 at baseline only use categories a, c, and d to determine overall functional improvement. Patients treated for indications other than pulmonary stenosis only use categories a, b, and d for overall functional improvement. Patients with pulmonary stenosis mean gradient less than 30 mm Hg at baseline only use categories a, b, and c for overall functional improvement.

A small number of retrospective, comparative studies have compared outcomes of the Edwards SAPIEN and the Melody valves. Boshoff et al (2013) 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 (2013) reported on 20 patients who underwent successful implantation of the Edwards SAPIEN pulmonic valve at a single 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 disappeared when patients were matched for length of follow-up.

A few other small case series has assessed on the use of the Edwards SAPIEN pulmonic valve for RVOT obstruction. For example, Kenny et al (2011) reported on a phase 1 multicenter study of the SAPEIN 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%.

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

NON-FDA-APPROVED TPVI DEVICES AND USES

A variety of potential off-label uses of TPVI have been reported in the literature, including the use of approved devices for non-FDA-approved indications.

Data from the Valve-in-Valve International Database multicenter registry have been evaluated for the off-label use of transcatheter aortic and TPVI prostheses for tricuspid valve-in-valve implantation. One hundred fifty of 156 patients in the registry had successful tricuspid valve-in-valve 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 in NYHA class III or IV; at follow-up, 77% of surviving patients were in NYHA class I or II ($p<0.001$).

A few case series have been on use of the Melody valve in patients with clinical characteristics not corresponding to FDA-approved indications. These indications have included the use of valves in positions other than pulmonic, patients with conduit sizes inconsistent with FDA indications, and patients with prior congenital heart repair surgery not involving the construction of an RVOT conduit. In general, these case series have reported high rates of procedural success with low rates of periprocedural complications, but longer term outcomes are 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 THV in a native RVOT or RVOT without a circumferential conduit. Meadows et al (2014) reported on results from a retrospective, 5-center review of patients who underwent TPV placement in a nonconduit RVOT, with the 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, with serious complications in 2 (6%). At a median follow-up of 15 months (range, 1 month to 3.8 years), all patients were alive, and none reporting 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 (2014) reported on 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, with early complications occurring 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 (2014; N=10) and Odemis et al (2013; N=7), have reported on the use of the Edwards SAPIEN pulmonary valve for noncircumferential RVOT patch 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 adverse events reported in the case series, several publications have focused on adverse events 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 3 is adapted from the FDA summary of safety and probable benefit.

Table 3. Device-Related Adverse Events (N=89 Subjects implanted > 24 hours)

Adverse Events	Subjects With Event, n (%)	Freedom From Event at 12 Months (SE), %
Stent fracture (all)	16 (18)	77.1 (7.5)
Minor[a]	11 (12)	84.1 (6.7)
Major[a]	5 (6)	90.6 (5.2)
Valve stenosis	6 (7)	90.5 (4.8)
Worsening tricuspid regurgitation	1 (1)	100 (–)
Reintervention[b]	6 (7)	93.5 (4.3)
Reoperation	1 (1)	98.6 (2.2)

[a] Stent fractures that did not require intervention were defined as minor; those that required reintervention were defined as major.
[b] 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 adverse events from the U.S. Melody TPV trial was published in 2011. This report assessed adverse events 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 (2013) reported on 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 (2014) 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 (2016) 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 two of the nine 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 (2013) reported on 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 (2014) reported on 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 six 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 (2015) compared rates of infective endocarditis between TPVs 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 valves cryopreserved homografts were implanted in 517 patients, and 54 Contegra grafts were implanted in 53 patients. Freedom from infective endocarditis at 5 years using Kaplan-Meier analysis was 85%, 88%, and 99% for patients with Melody conduits, Contegra grafts, or cryopreserved homografts, respectively.

Malekzadeh-Milani et al (2015) 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, 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% confidence interval, 1.98 to 94.52; p=0.014), and aspirin use was preventive for infective endocarditis (relative risk, 20.1; 95% confidence interval, 3.34 to 120.9; p=0.001), although confidence intervals around risk estimates for both factors were wide.

A 2017 retrospective review of 25 patients undergoing Melody TPVI and 178 surgical pulmonic valve surgeries (bioprostheses and homografts) was reported from New Zealand from October 2009 to May 2015. Four (16%) implant patients experienced endocarditis. Two patients presented with life-threatening endocarditis and obstructive vegetation at 14 and 26 months postimplant, respectively. Two additional patients presented with subacute endocarditis at 5.5 years postimplant. At a median follow-up of 2.9 years, 4 (2%) patients had developed endocarditis in the surgical group.

SUMMARY OF EVIDENCE

For individuals who have a history of CHD and current RVOT obstruction who receive TPVI with an FDA-approved device and indication, the evidence includes prospective, interventional, noncomparative studies, and multiple prospective and retrospective case or cohort series. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related mortality and morbidity. Results of the case series have indicated that there is a high rate of procedural success and low procedural mortality, although the rates of serious procedural adverse events reported ranged from 3.0% to 7.4%. Most valves have demonstrated competent functioning by Doppler echocardiography at 6- to 12-month follow-ups, but complications (eg, stent fractures, need for reinterventions) were reported in an FDA analysis 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 did not require reintervention. 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%) have required reintervention on the pulmonary valve. No comparative studies were identified, and there is no direct evidence that TPVI reduces 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 mortality and morbidity. There is limited evidence on the off-label use of TPVI including the use of a non-FDA-approved valve or use of an approved valve for a non-FDA-approved indication. The published case series enrolled relatively few patients and are heterogeneous regarding devices used and indications for TPVI. The evidence is insufficient to determine the effects of the technology on health outcomes.

Clinical input obtained in 2018 supports that the following indications provide a clinically meaningful improvement in net health outcome and are consistent with generally accepted medical practice.

- Use of TPVI for individuals with right ventricle-to-pulmonary artery conduit with or without bioprosthetic valve with at least moderate pulmonic regurgitation;
- Use of TPVI for individuals with native or patched RVOT with at least moderate pulmonic regurgitation;
- Use of TPVI for individuals with right ventricle-to-pulmonary artery conduit with or without bioprosthetic valve with pulmonic stenosis (mean RVOT gradient at least 35 mm Hg); or

- Use of TPVI for individuals with native or patched RVOT with pulmonic stenosis (mean RVOT gradient at least 35 mm Hg).

Thus, the above indications may be considered medically necessary considering the suggestive evidence and clinical input support.

References

1. Blue Cross and Blue Shield Association, Medical Policy Reference Manual, "Transcatheter Pulmonary Valve Implantation", 7.01.131, 5:2018.
2. Khambadkone S, Nordmeyer J, Bonhoeffer P. Percutaneous implantation of the pulmonary and aortic valves: indications and limitations. J Cardiovasc Med (Hagerstown). Jan 2007;8(1):57-61. PMID 17255818
3. McElhinney DB, Hellenbrand WE, Zahn EM, et al. Short- and medium-term outcomes after transcatheter pulmonary valve placement in the expanded multicenter US Melody Valve trial. Circulation. Aug 3 2010;122(5):507-516. PMID 20644013
4. Food and Drug Administration. Summary of Safety and Effectiveness Data: Melody™ Transcatheter Pulmonary Valve. 2015; http://www.accessdata.fda.gov/cdrh_docs/pdf14/p140017b.pdf. Accessed October 23, 2015.
5. Zahn EM, Hellenbrand WE, Lock JE, et al. Implantation of the Melody transcatheter pulmonary valve in patients with a dysfunctional right ventricular outflow tract conduit early results from the U.S. clinical trial. J Am Coll Cardiol. Oct 27 2009;54(18):1722-1729. PMID 19850214
6. Cheatham JP, Hellenbrand WE, Zahn EM, et al. Clinical and hemodynamic outcomes up to 7 years after transcatheter pulmonary valve replacement in the US Melody valve investigational device exemption trial. Circulation. Jun 2 2015;131(22):1960-1970. PMID 25944758
7. Batra AS, McElhinney DB, Wang W, et al. Cardiopulmonary exercise function among patients undergoing transcatheter pulmonary valve implantation in the US Melody valve investigational trial. Am Heart J. Feb 2012;163(2):280-287. PMID 22305848
8. Armstrong AK, Balzer DT, Cabalka AK, et al. One-year follow-up of the Melody transcatheter pulmonary valve multicenter post-approval study. JACC Cardiovasc Interv. Nov 2014;7(11):1254-1262. PMID 25459038
9. Gillespie MJ, McElhinney DB, Kreutzer J, et al. Transcatheter pulmonary valve replacement for right ventricular outflow tract conduit dysfunction after the Ross procedure. Ann Thorac Surg. Sep 2015;100(3):996-1003. PMID 26190388
10. Lurz P, Coats L, Khambadkone S, et al. Percutaneous pulmonary valve implantation: impact of evolving technology and learning curve on clinical outcome. Circulation. Apr 15 2008;117(15):1964-1972. PMID 18391109
11. Eicken A, Ewert P, Hager A, et al. Percutaneous pulmonary valve implantation: two-centre experience with more than 100 patients. Eur Heart J. May 2011;32(10):1260-1265. PMID 21273201
12. Khambadkone S, Coats L, Taylor A, et al. Percutaneous pulmonary valve implantation in humans: results in 59 consecutive patients. Circulation. Aug 23 2005;112(8):1189-1197. PMID 16103239
13. Momenah TS, El Oakley R, Al Najashi K, et al. Extended application of percutaneous pulmonary valve implantation. J Am Coll Cardiol. May 19 2009;53(20):1859-1863. PMID 19442885
14. Nordmeyer J, Coats L, Bonhoeffer P. Current experience with percutaneous pulmonary valve implantation. Semin Thorac Cardiovasc Surg. Summer 2006;18(2):122-125. PMID 17157232
15. Nordmeyer J, Coats L, Lurz P, et al. Percutaneous pulmonary valve-in-valve implantation: a successful treatment concept for early device failure. Eur Heart J. Mar 2008;29(6):810-815. PMID 18316357
16. Vezmar M, Chaturvedi R, Lee KJ, et al. Percutaneous pulmonary valve implantation in the young 2-year follow-up. JACC Cardiovasc Interv. Apr 2010;3(4):439-448. PMID 20398873
17. Muller J, Engelhardt A, Fratz S, et al. Improved exercise performance and quality of life after percutaneous pulmonary valve implantation. Int J Cardiol. May 15 2014;173(3):388-392. PMID 24713459
18. Butera G, Milanesi O, Spadoni I, et al. Melody transcatheter pulmonary valve implantation. Results from the registry of the Italian Society of Pediatric Cardiology. Catheter Cardiovasc Interv. Feb 2013;81(2):310-316. PMID 22718682
19. Fraisse A, Aldebert P, Malekzadeh-Milani S, et al. Melody (R) transcatheter pulmonary valve implantation: results from a French registry. Arch Cardiovasc Dis. Nov 2014;107(11):607-614. PMID 25453718
20. Borik S, Crean A, Horlick E, et al. Percutaneous pulmonary valve implantation: 5 years of follow-up: does age influence outcomes? Circ Cardiovasc Interv. Feb 2015;8(2):e001745. PMID 25652317

21. Boshoff DE, Cools BL, Heying R, et al. Off-label use of percutaneous pulmonary valved stents in the right ventricular outflow tract: time to rewrite the label? Catheter Cardiovasc Interv. May 2013;81(6):987-995. PMID 22887796
22. Faza N, Kenny D, Kavinsky C, et al. Single-center comparative outcomes of the Edwards SAPIEN and Medtronic Melody transcatheter heart valves in the pulmonary position. Catheter Cardiovasc Interv. Oct 1 2013;82(4):E535-541. PMID 23008193
23. Haas NA, Moysich A, Neudorf U, et al. Percutaneous implantation of the Edwards SAPIEN(TM) pulmonic valve: initial results in the first 22 patients. Clin Res Cardiol. Feb 2013;102(2):119-128. PMID 22932954
24. Kenny D, Hijazi ZM, Kar S, et al. Percutaneous implantation of the Edwards SAPIEN transcatheter heart valve for conduit failure in the pulmonary position: early phase 1 results from an international multicenter clinical trial. J Am Coll Cardiol. Nov 15 2011;58(21):2248-2256. PMID 22078433
25. Odemis E, Guzeltas A, Saygi M, et al. Percutaneous Pulmonary Valve Implantation Using Edwards SAPIEN Transcatheter Heart Valve in Different Types of Conduits: Initial Results of a Single Center Experience. Congenit Heart Dis. Sep 2013;8(5):411-417. PMID 23448542
26. Demkow M, Ruzyllo W, Biernacka EK, et al. Percutaneous Edwards SAPIEN(TM) valve implantation for significant pulmonary regurgitation after previous surgical repair with a right ventricular outflow patch. Catheter Cardiovasc Interv. Feb 15 2014;83(3):474-481. PMID 23804542
27. McElhinney DB, Cabalka AK, Aboulhosn JA, et al. Transcatheter tricuspid valve-in-valve implantation for the treatment of dysfunctional surgical bioprosthetic valves: an international multicenter registry study. Circulation. Apr 19 2016;133(16):1582-1593. PMID 26994123
28. Cheatham SL, Holzer RJ, Chisolm JL, et al. The Medtronic Melody(R) transcatheter pulmonary valve implanted at 24-mm diameter--it works. Catheter Cardiovasc Interv. Nov 1 2013;82(5):816-823. PMID 23359563
29. Meadows JJ, Moore PM, Berman DP, et al. Use and performance of the Melody Transcatheter Pulmonary Valve in native and postsurgical, nonconduit right ventricular outflow tracts. Circ Cardiovasc Interv. Jun 2014;7(3):374-380. PMID 24867892
30. Malekzadeh-Milani S, Ladouceur M, Cohen S, et al. Results of transcatheter pulmonary valvulation in native or patched right ventricular outflow tracts. Arch Cardiovasc Dis. Nov 2014;107(11):592-598. PMID 25218009
31. FDA summary of Safety and Probable Benefit. Melody® Transcatheter Pulmonary Valve and Ensemble® Transcatheter Valve Delivery System. http://www.accessdata.fda.gov/cdrh_docs/pdf8/H080002b.pdf. Accessed June, 2011.
32. McElhinney DB, Cheatham JP, Jones TK, et al. Stent fracture, valve dysfunction, and right ventricular outflow tract reintervention after transcatheter pulmonary valve implantation: patient-related and procedural risk factors in the US Melody Valve Trial. Circ Cardiovasc Interv. Dec 1 2011;4(6):602-614. PMID 22075927
33. McElhinney DB, Benson LN, Eicken A, et al. Infective endocarditis after transcatheter pulmonary valve replacement using the Melody valve: combined results of 3 prospective North American and European studies. Circ Cardiovasc Interv. Jun 1 2013;6(3):292-300. PMID 23735475
34. Malekzadeh-Milani S, Ladouceur M, Iserin L, et al. Incidence and outcomes of right-sided endocarditis in patients with congenital heart disease after surgical or transcatheter pulmonary valve implantation. J Thorac Cardiovasc Surg. Nov 2014;148(5):2253-2259. PMID 25218536
35. Boudjemline Y, Malekzadeh-Milani S, Patel M, et al. Predictors and outcomes of right ventricular outflow tract conduit rupture during percutaneous pulmonary valve implantation: a multicentre study. EuroIntervention. Jan 22 2016;11(9):1053-1062. PMID 25244126
36. Morray BH, McElhinney DB, Cheatham JP, et al. Risk of coronary artery compression among patients referred for transcatheter pulmonary valve implantation: a multicenter experience. Circ Cardiovasc Interv. Oct 1 2013;6(5):535-542. PMID 24065444
37. Fraisse A, Assaidi A, Mauri L, et al. Coronary artery compression during intention to treat right ventricle outflow with percutaneous pulmonary valve implantation: incidence, diagnosis, and outcome. Catheter Cardiovasc Interv. Jun 1 2014;83(7):E260-268. PMID 24619978
38. Van Dijck I, Budts W, Cools B, et al. Infective endocarditis of a transcatheter pulmonary valve in comparison with surgical implants. Heart. May 15 2015;101(10):788-793. PMID 25539944
39. Malekzadeh-Milani S, Ladouceur M, Patel M, et al. Incidence and predictors of Melody(R) valve endocarditis: a prospective study. Arch Cardiovasc Dis. Feb 2015;108(2):97-106. PMID 25445752
40. Hijazi ZM, Ruiz CE, Zahn E, et al. SCAI/AATS/ACC/STS Operator and institutional requirements for transcatheter valve repair and replacement, Part III: Pulmonic valve. J Am Coll Cardiol. Jun 16 2015;65(23):2556-2563. PMID 25819263

41. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. Jun 10 2014;63(22):e57-185. PMID 24603191
42. Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines on the Management of Adults With Congenital Heart Disease). Developed in Collaboration With the American Society of Echocardiography, Heart Rhythm Society, International Society for Adult Congenital Heart Disease, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. Dec 2 2008;52(23):e143-263. PMID 19038677
43. Food and Drug Administration. Conditions for Approval for an HDE: Medtronic Melody® Transcatheter Pulmonary Valve (Model PB 10) and Medtronic Ensemble® Transcatheter Valve Delivery System (NU10) (H080002). 2010; https://www.accessdata.fda.gov/cdrh_docs/pdf8/H080002A.pdf. Accessed May 17, 2018.
44. Markham R, Challa A, Kyranis S, et al. Outcomes following Melody transcatheter pulmonary valve implantation for right ventricular outflow tract dysfunction in repaired congenital heart disease: first reported Australian single centre experience. *Heart Lung Circ.* Oct 2017;26(10):1085-1093. PMID 28185817
45. O'Donnell C, Holloway R, Tilton E, et al. Infective endocarditis following Melody valve implantation: comparison with a surgical cohort. *Cardiol Young.* Mar 2017;27(2):294-301. PMID 27161361

Policy History

Original Effective Date: 10/18/2017
Current Effective Date: 08/15/2018

10/05/2017	Medical Policy Committee review
10/18/2017	Medical Policy Implementation Committee approval. New policy.
08/09/2018	Medical Policy Committee review
08/15/2018	Medical Policy Implementation Committee approval. Clinical input was obtained and the first policy statement changed to: Transcatheter pulmonary valve implantation is considered medically necessary for patients with congenital heart disease and current right ventricular outflow tract obstruction or regurgitation including the specified indications.

Next Scheduled Review Date: 08/2019

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 2017 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.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

Transcatheter Pulmonary Valve Implantation

Policy # 00576
Original Effective Date: 10/18/2017
Current Effective Date: 08/15/2018

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:

Code Type	Code
CPT	33477
HCPCS	No codes
ICD-10 Diagnosis	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

*****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.

**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.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.