I. Description

Transcatheter pulmonary valve implantation (TPVI) received approval from the U.S. Food and Drug Administration (FDA) under the Humanitarian Device Exception program in January 2010 for patients with previous repair of congenital heart disease (CHD) and right ventricular outflow tract (RVOT) obstruction. Patients with prior CHD repair are at risk of needing repeated reconstruction procedures. TPVI has been proposed as a less invasive alternative to open surgical pulmonary valve replacement or reconstruction for RVOT obstruction.

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 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. The 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 in these series ranges from 3.0% to 7.4%. most valves demonstrate competent functioning by Doppler echocardiography at 6- to 12-month follow-up, but complications at 6-month follow-up (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 reintervention. Studies with follow-up extending to a maximum of 7 years postprocedure suggest 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 is case series. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related
Transcatheter Pulmonary Valve Implantation

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 evidence consists of relatively small case series that 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 who are at high risk for surgery due to other medical comorbidities, alternative treatment options are limited. Clinical vetting received 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 the 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.

Background

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.

As individuals with surgically corrected congenital heart disease repair are living longer into adulthood, the problem of 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 in 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.

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
Transcatheter Pulmonary Valve Implantation

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 up the artificial valve, and then the outer balloon is inflated to position the valve into place.

**Regulatory Status**

On January 25, 2010, the Melody® Transcatheter Pulmonary Valve (TPV) and the Ensemble® Transcatheter Valve Delivery System (Medtronic, Minneapolis, MN) were approved by the U.S. Food and Drug Administration (FDA) under the Humanitarian Device Exemption Program. Approval was for use as an adjunct to surgery in the management of pediatric and adult patients with the following clinical conditions:

A. Existence of a full (circumferential) right ventricular outflow tract RVOT conduit that was equal to or greater than 16 mm in diameter when originally implanted, and

B. Dysfunctional RVOT conduits with clinical indication for intervention, and either:
   1. Regurgitation: >moderate regurgitation, or
   2. 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 represents 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 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 Right Ventricular Outflow Tract (RVOT) conduit with a clinical indication for intervention and:

- pulmonary regurgitation ≥ moderate and/or
- mean RVOT gradient ≥ 35 mmHg.”

FDA product code: NPV.

**II. Criteria/Guidelines**

Transcatheter pulmonary valve implantation, when performed according to Food and Drug Administration approved indications, is covered (subject to Administrative Guidelines) for patients with prior repair of congenital heart disease and right ventricular outflow tract (RVOT) dysfunction, who are not good candidates for open repair due to one or more of the following conditions:
A. High-risk for surgery due to concomitant medical comorbidities; or
B. Poor surgical candidate due to multiple prior thoracotomies for open heart surgery.

III. Limitations

A. Transcatheter pulmonary valve implantation is not covered for all other indications because it has not been shown to improve health outcomes.
B. Procedures done with non-FDA approved devices will not be covered.

IV. Administrative Guidelines

A. Precertification is required. To precertify, complete HMSA's Precertification Request and mail or fax the form, or use iExchange as indicated along with the following documentation:
   1. Clinical notes including documentation of the severity of the RVOT dysfunction
   2. Documentation from at least two cardiac or cardiovascular specialists that the patient is a high or unacceptable risk for open surgical treatment
B. HMSA reserves the right to perform retrospective review using the above criteria to validate if services rendered met payment determination criteria.
C. Applicable codes:

Effective in 2016, there is a category I CPT code for this procedure:

- 33477: Transcatheter pulmonary valve implantation, percutaneous approach, including pre-stenting of the valve delivery site, when performed

Prior to 2016, there was a category III CPT code for this procedure:

- 0262T: Implantation of catheter-delivered prosthetic pulmonary valve, endovascular approach.

<table>
<thead>
<tr>
<th>CPT Codes</th>
<th>Description</th>
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<td>33477</td>
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<tr>
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<tr>
<td>02RH3JZ, 02RH4JZ</td>
<td>Surgery, heart and great vessels, replacement, pulmonary valve, synthetic substitute, percutaneous or percutaneous endoscopic</td>
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<td>Q20.5</td>
<td>Corrected transposition of great vessels</td>
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V. Scientific Background

This evidence review was created in November 2011 and has been updated periodically with literature reviews. The most recent update with literature review covers the period through April 28, 2016. The published literature on transcatheter pulmonary valve implantation (TPVI) consists of small case series, which generally report on short-term outcomes. Some of the larger, representative publications are discussed in this literature review.

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

US Melody TPV trial
The multicenter US Melody TPV trial is a prospective uncontrolled trial from 5 clinical sites that was designed to study the safety, procedural success, and short-term effectiveness of the Melody transcatheter pulmonary valve. This was the pivotal trial on which FDA approval for the Melody valve was based. The study was designed to follow 150 patients over a 5-year period. Eligibility criteria included a dysfunctional right ventricular outflow tract (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 pulmonic regurgitation was required, and for patients with NYHA class II-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 from the procedure, and effectiveness, as measured by the proportion of patients with acceptable valve function at 6 months.

Results from this trial 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 of 136 patients (91.2%) had successful implantation. In 12 patients, implantation was
not possible due to anatomic or other intraprocedural findings that precluded implantation. One death occurred as a result of the procedure (0.7%), and serious AEs occurred in 8 of 136 patients (6%). AEs included coronary artery dissection, conduit rupture/tear, wide complex tachycardia, respiratory failure, femoral vein thrombosis, and perforation of the pulmonary artery.

A total of 94 patients had successful implantation and 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 greater than 90% of patients. Right ventricular pressure and right ventricular outflow tract gradient improved following the procedure, and 71/94 (75.5%) were in NYHA class I heart failure at 6 months. Over the course of follow-up, stent fractures were diagnosed in 25/124 (20.2%) patients, and 9/124 (7.3%) 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 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 RV outflow tract, 25 of which were transcatheter TPV reinterventions. A total of 11 patients required Melody valve explanation. Among the 113 patients who were alive and free from reintervention a median of 4.5 years after implantation, 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 US Melody TPV trial focused on the change in exercise function following TPVI. Patients completed a standardized cardiopulmonary regimen 2 months prior to TPVI and 6 months following TPVI. Results of pre- and post-exercise parameters were available for 94-114 patients, depending on the specific outcome. There were numerous physiologic outcome measures reported, with some of these showing a statistically significant change between the 2 time points, and others not showing a significant change. 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 study reports 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 Transcatheter Pulmonary Valve Post Approval Study**

Armstrong et al published 1-year follow-up results of the Melody TPVI postapproval study (PAS), a prospective study designed to evaluate the short-term hemodynamic changes following device
implantation. The study used historical controls from the Melody IDE trial (described above) to investigate whether the short-term effectiveness of the device was noninferior to results shown in the IDE trial. The study 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 of 120; 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 Melody TPV trial and postapproval study and an additional European registry, the manufacturer-sponsored Melody TPV Post-Market Surveillance Study which was conducted in Canada and Europe (NCT00688571). In the pooled sample (N=358), 67 (19%) had a prior Ross procedure. A Melody valve was successfully implanted in 56 of 67 (84%) of the Ross patients who underwent catheterization with intent for TPVI. Six patients (9%) 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 who were 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 This publication reported on 163 patients who underwent attempted TPVI from 4 clinical centers in Europe. Eligibility for the procedure included elevated right ventricular (RV) systolic pressure, increased RVOT dimensions, and either symptoms or evidence of severe RV dysfunction. Procedural success was achieved in 155/163 patients (95.1%). Procedural complications occurred in 12/163 (7.4%), 8 of which were considered serious and 5 of which required open surgery. The median follow-up was 28.4 months. Over the course of follow-up, 4/155 patients (2.6%) died, and an additional 5/155 patients (3.2%) developed infective endocarditis. At 12 months’ follow-up, greater than 90% of patients had absent or mild valve dysfunction as measured by echocardiography.

Eicken et al This study reported on 102 consecutive patients (mean age 21.5 years) undergoing transcatheter pulmonary valve implantation at 2 centers in Germany. Eligibility for the procedure included RVOT dysfunction with evidence of RV compromise or increased RV pressure. There was one death (1.0%) that occurred as a result of compression of the left coronary artery. Two patients (2.0%) had evidence of stent fracture immediately post-procedure, and one additional patient (1.0%) 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 mm Hg to 15 mm Hg \((p<0.0001)\). However, there was no significant change in exercise capacity as measures by maximal oxygen uptake.

Other case series reported on smaller numbers of patients, with patient populations ranging from 7-64. These publications reported generally 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 suggest that the functional and hemodynamic improvements are durable, but a relatively high proportion of patients (20%-30%) require reintervention on the pulmonary valve.

**Non-FDA approved uses of TPVI**

There are a variety of potential off-label uses of TPVI that have been reported in the literature. These 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® pulmonic valve with the Melody® pulmonic valve. 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. These included use in native RVOT obstruction, in conduits that were smaller than the FDA-labeled indications, and in large RVOT with a dynamic outflow aneurysm. There were no deaths or major procedural complications reported for these patients. Clinical outcome 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 one clinical center. There were no periprocedural deaths, and all but one 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 who were treated with the Melody valve. Immediately following the procedure, the transvalvular gradient was similar between groups. At last follow-up, the mean residual transvalvular gradient was higher for patients receiving the SAPIEN® valve (18.4 mm Hg versus 11.2 mm Hg, \(p=0.016\)), but this difference was no longer present 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 I multicenter study of the Sapien pulmonic valve in 36 patients from 4 clinical centers. Procedural success was reported in 97% of patients. Procedural complications occurred in 19% of patients (7/36), 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% of patients (27/36) were in NYHA class I, compared to 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 have included use in valves other than the pulmonic position, patients with conduit sizes that do not correspond to the FDA indications, and patients with prior congenital heart repair surgery that did not involve construction of a right ventricular outflow tract (RVOT) conduit. In general, these case series have reported high rates of procedural success with low rates of peri-procedural complications, but evidence on longer term outcomes is lacking.

Although most studies have evaluated the use of TPV implantation in patients with a constructed RVOT conduit, a few studies have evaluated TPV implantation with either the Melody or Edwards SAPIEN pulmonary 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. 22 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%). TPV implantation was successful in all patients, but serious complications occurred in 2 patients (6%). At a median follow-up of 15 months (range, 1 month-3.8 years), all patients were alive, and no patient 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. 23 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 stent migration, and 32/34 (94.1%) had absent or trivial pulmonary regurgitation.
Several other small case series by Demkow et al (N=10 patients) and Odemis et al (N=7 patients) report on the use of the Edwards Sapien pulmonary valve for noncircumferential RVOT patch and large-diameter conduits, respectively. The authors report high rates of successful valve implantation, but 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. The FDA reviewed results from the US Melody TPV trial as part of the FDA approval process and reported detailed data on complications from the procedure. At that time, data were available for 99 patients enrolled between January 2007 and December 2008. A total of 90 patients were deemed suitable for implantation following catheterization, and 87/90 patients had successful implantation. There was one procedural-related death (1.1%). Table 1 is adapted from the FDA summary of safety and probable benefit.

**Table 1. Device-related adverse effects** (N=89 subjects)

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<th>Event</th>
<th>Subjects with Event</th>
<th>Freedom from event at 12 month (SE)</th>
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<tbody>
<tr>
<td>Stent fracture (all)</td>
<td>16 (18%)</td>
<td>77.1% (7.5)</td>
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<tr>
<td>Minor(^1)</td>
<td>11 (12%)</td>
<td>84.1% (6.7)</td>
</tr>
<tr>
<td>Major(^2)</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>
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<tr>
<td>Reintervention(^2)</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>

\(^1\) Stent fractures that did not require intervention were defined as minor; those that required reintervention were defined as major.

\(^2\) Reinterventions were balloon angioplasty in one patient; repeat implantation of a second TPV in 5 patients.

There were 64 patients in the FDA analysis who reached 6 months of follow-up. Of these, 56 (87.5%) had acceptable hemodynamic function of the valve 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 in the US Melody TPV trial was published in 2011. This publication reported on 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 re-interventions for all patients was estimated to be 86% at 27 months, and freedom from re-interventions for patients with stent fracture was estimated at 49% at 2 years.
McElhinney et al reported rates of infective endocarditis from 3 prospective cases series enrolling a total of 311 patients followed for a median of 2.5 years. There were a total of 16 patients (5.1%) diagnosed with endocarditis at any location and 6 patients (1.9%) who had endocarditis at the pulmonic valve location. This corresponded to an annualized rate of pulmonic valve endocarditis of 0.88%/patient-year. Malekzadeh-Milani et al evaluated patients with right-sided infective endocarditis at a single center to evaluate endocarditis rates in patients with TPVs compared with surgically-paced pulmonary valves. 32 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. 33 Ninety-nine patients were included, 56 of whom were adults. Of the total cohort, 83.8% underwent Melody TPV implantation. Conduit rupture occurred in 9 patients (9.09%). 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 all 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 TPV implantation. 34 Three hundred forty-three patients (85% of total) underwent TPV implantation, and 21 patients (5% of total) had evidence of coronary artery compression. Most patients (n=19) with coronary artery compression did not undergo TPV placement. Using the same cohort reported in the Boudjemline et al 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. 35 All patients underwent balloon dilatation and coronary assessment with angiography, which was followed by TPV placement if there was ongoing RVOT dysfunction. 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 which included 677 patients (738 conduits). 36 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 84.9%, 87.8%, and 98.7% 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 the table below.

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<th>NCT No. Ongoing</th>
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<td>Nov 2019</td>
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<td>NCT00740870a</td>
<td>Implantation of the Medtronic Melody Transcatheter Pulmonary Valve in Patients With Dysfunctional RVOT Conduits: A Feasibility Study</td>
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NCT: National Clinical Trial
a Denotes industry-sponsored or cosponsored trial

Summary of Evidence
The evidence for TPVI with an FDA-approved device according to FDA indications in patients who have a history of CHD and current RVOT 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. The results of the case series indicate that there is a high rate of procedural success and low procedural mortality. The rate of serious procedural adverse events reported in these series ranges from 3.0% to 7.4%. At 6- to 12-month follow-up, there is evidence that most valves demonstrate competent functioning by Doppler echocardiography, with most patients in New York Heart Association functional class I or II. Complications at 6-month follow-up (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 reintervention. Studies
with follow-up extending to a maximum of 7 years postprocedure suggest 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 patients 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 evidence consists of relatively small case series that 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.

SUPPLEMENTAL INFORMATION

Clinical Input Received through Physician Specialty Societies and Academic Medical Centers
While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

Overall response to whether TPVI was investigational was mixed, with 2 of 5 reviewers indicating they agree with the investigational status, and 3 reviewers who indicated it was a split decision. The majority of reviewers (4/5) indicated in their written response that there was a subpopulation of patients who were high risk for surgery or who were not candidates for surgery, in whom there were no other available options. These reviewers felt that TPVI was a viable alternative that offered potential benefit for these patients.

Practice Guidelines and Position Statements

Society for Cardiovascular Angiography and Interventions et al
In 2015, the Society for Cardiovascular Angiography and Interventions, American Association for Thoracic Surgery, American College of Cardiology (ACC) and the Society of Thoracic Surgeons published a consensus-based report on operator and institutional requirements for TPVI.39 Recommendations to qualify for a TPVI program included 150 catheterizations/year, association with a surgical program, submission of all cases to a national registry, and, for patients, 80% freedom from re-intervention at 1 year.

American Heart Association and American College of Cardiology
In 2014, American Heart Association (AHA) and American College of Cardiology (ACC) issued guidelines for the management of patients with valvular disease. These guidelines do not make specific recommendations regarding the treatment of primary pulmonary valve disease (stenosis or
regurgitation), but instead refer to the 2008 guidelines for the management of adults with congenital heart disease.

In 2008, the AHA and ACC issued guidelines for the management of adults with congenital heart disease. For patients with isolated valvular pulmonary stenosis, the guidelines make recommendations regarding balloon valvulotomy or surgical; however, TPVI is not addressed.

**Medicare National Coverage**

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

**VI. Important Reminder**

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

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

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

**VII. References**


