Clinical Policy Bulletin:
Transcatheter Pulmonary Valve Implantation

Number: 0821

Policy
*Please see amendment for Pennsylvania Medicaid at the end of this CPB.*

Aetna considers transcatheter pulmonary valve implantation using FDA-approved devices (e.g., Melody Transcatheter Pulmonary Valve) medically necessary for the treatment of dysfunctional right ventricular outflow tract (RVOT) conduits whose pulmonary valve has become stenotic (mean RVOT gradient greater than or equal to 35 mm Hg) or regurgitant (moderate or more severe regurgitation), where individuals indicated for the procedure have a full circumferential RVOT conduit greater than or equal to 16 mm in diameter when originally implanted.

Aetna considers transcatheter pulmonary valve implantation for other indications (e.g., individuals with a degenerated bioprosthetic valve (valve-in-valve” implantation)) experimental and investigational because its effectiveness for these indications has not been established.

Background

The pulmonary valve (PV), located between the right ventricle and the pulmonary artery, opens upon contraction of the right ventricle to release oxygen-depleted blood from the right ventricle into the pulmonary artery for delivery to the lungs. Congenital defects cause the great majority of cases of PV insufficiency or stenosis. Patients with severe PV dysfunction require surgical reconstruction of the right ventricular outflow tract (RVOT) between the heart and the pulmonary artery in order to re-establish blood flow to the lungs and mitigate right ventricular strain. In general, RVOT reconstruction entails implantation of a valved conduit through the defective native valve. Most infants with congenital PV defects undergo successful RVOT conduit implantation. However, as RVOT conduits age, valves begin to leak or fail, and adults successfully treated for PV dysfunction as children require surgery to replace failing conduits. Although uncommon, some patients may develop PV dysfunction as adults. Surgical implantation of RVOT conduits for acquired stenosis or insufficiency is rare.

Percutaneous pulmonary valve implantation (PPVI) is a new treatment option in patients with RVOT conduit regurgitation or stenosis. The objective of PPVI is to prolong the lifespan of right ventricle to pulmonary artery conduits; thus postponing open-heart surgery. Percutaneous pulmonary valve implantation (PPVI) devices are used to prolong the life span of failing prosthetic pulmonary conduits in individuals with congenital heart defects. The PPVI is not expected to replace the initial open heart surgery for placement of a pulmonary conduit, but it is expected to reduce the total number of open heart right ventricular outflow tract (RVOT) procedures over an individual’s lifetime. The Melody transcatheter pulmonary valve (TPV) is an example of an FDA approved device.

Early results following PPVI had shown a significant reduction in right ventricular pressure and RVOT
The most common complication during follow-up is stent fractures. Although clinically silent in the majority of cases, stent fractures led to re-intervention in the form of implantation of a second device (valve-in-valve). Significant pulmonary regurgitation (PR) was only seen in the context of endocarditis. Percutaneous pulmonary valve implantation has the potential to become the standard procedure in the treatment of dysfunctional conduits.

Neyt and associates (2009) evaluated current evidence supporting the use of percutaneous heart valves in degenerative aortic valve and congenital pulmonary outflow tract disease, as compared to conservative medical therapy or traditional surgical valve replacement. A systematic review of the literature on percutaneous heart valve was performed. No randomized controlled trials on percutaneous heart valves have been published so far. Only observational data from series and data presented at cardiology meetings are available. Both percutaneous aortic valve as well as percutaneous pulmonary valve seem feasible in the hands of an experienced team. The authors concluded that PPVI appears to be a safe and promising technology for which reimbursement under strict conditions may be recommended.

Oosterhof et al (2009) stated that PR is the most important residual lesion after initial surgical correction for pulmonary sub-valvular stenosis in the early life of patients with tetralogy of Fallot or isolated pulmonary stenosis. Symptomatic or asymptomatic patients with severe right ventricular dilatation due to pulmonary regurgitation may benefit from pulmonary valve replacement. Surgery is ideally performed before the right ventricle becomes irreversibly damaged as a result of long-standing volume overload. However, the beneficial effects must be weighed up against the problems associated with degradation of the allograft, which often result in re-operations. Owing to the higher risk of thrombo-embolic events in mechanical prosthesis and the lifetime need for anti-coagulation, allografts are the most widely used prosthesis. Degradation of the allograft often leads to re-operation, mostly 10 to 20 years after initial implantation. For a patient receiving his first allograft at 20 years of age, several re-operations will have to be performed later in life. In this regard, PPVI has the potential to decrease the number of surgical re-operations.

Zahn and co-workers (2009) assessed the safety, procedural success, and short-term effectiveness of the Melody/Ensemble transcatheter pulmonary valve (Medtronic, Inc., Minneapolis, MN) in patients with dysfunctional RVOT conduits. The Melody/Ensemble transcatheter pulmonary valve system is a novel, minimally invasive alternative to surgical pulmonary valve replacement in children and adults with significant RVOT conduit regurgitation or stenosis. Standardized entry criteria, implantation, and follow-up protocols were used. Non-implanting core laboratories were used to evaluate results. Between January 2007 and September 2007, a total of 34 patients underwent catheterization for intended Melody valve implantation at 3 centers. Mean age was 19.4 +/- 7.7 years. Initial conduit Doppler mean gradient was 28.8 +/- 10.1 mm Hg, and 94 % of patients had moderate or severe PR. Implantation was successful in 29 of 30 attempts and not attempted in 4 patients. Procedural complications included conduit rupture requiring urgent surgery and device removal (n = 1), wide-complex tachycardia (n = 1), and distal pulmonary artery guide-wire perforation (n = 1). Peak systolic conduit gradient fell acutely from 37.2 +/- 16.3 mm Hg to 17.3 +/- 7.3 mm Hg, and no patient had more than mild PR. There were no deaths or further device explants. At 6-month follow-up, conduit Doppler mean gradient was 22.4 +/- 8.1 mm Hg, and PR fraction by magnetic resonance imaging was significantly improved (3.3 +/- 3.6 % versus 27.6 +/- 13.3 %, p < 0.0001). Stent fracture occurred in 8 of 29 implants; 3 of these were treated with a second Melody valve for recurrent stenosis later in follow-up. The authors concluded that implantation of the Melody valve for RVOT conduit dysfunction can be performed by experienced operators at multiple centers, appears safe, and has encouraging acute and short-term outcomes.

Vezmar et al (2010) examined physiological and clinical consequences of PPVI in patients with chronic RVOT obstruction and volume overload. A total of 28 adolescents (median age of 14.9 years; age range of 10.9 to 19 years) underwent PPVI due to RVOT stenosis and/or PR. Before and after PPVI, echocardiography and magnetic resonance imaging, cardiopulmonary exercise tests were obtained. The RVOT gradient (p < 0.001) and right ventricular systolic pressure decreased (p < 0.001), acutely.
Magnetic resonance imaging (median of 6 months) documented reduction in right ventricular end-diastolic (RVED) (149 +/- 49 ml/m² versus 114 +/- 35 ml/m², p < 0.005) volume, increases in left ventricular end-diastolic (LVED) (p < 0.007) volume and cardiac output (RVED volume: p < 0.04 and LVED volume: p < 0.02), and reduced PR fraction (24 +/- 10 % to 7 +/- 7 %, p < 0.0001). Symptoms, aerobic exercise performance (maximal oxygen consumption: p < 0.0001) and ventilatory response to carbon dioxide production (p < 0.0001) improved. After 24 months, echocardiography demonstrated the right ventricle/systemic-pressure ratio, and RVOT peak pressure gradient reductions persisted, and PR was absent in 93 % (n = 12 of 13) of the cohort. Freedom from surgery was 91 %, 83 %, and 83 %, and freedom from transcatheter re-intervention was 91 %, 80 %, and 80 %, at 12, 24, and 36 months, respectively. There were no acute device-related complications, with stent fractures noted in 10.8 %. The authors concluded that PPVI is feasible and safe in the young with dysfunctional RVOT conduits. An improvement in symptoms, hemodynamic status, and objective findings of exercise performance occurs. Early follow-up demonstrates persistent improvement in ventricular parameters, PR, and objective exercise capacity.

McElhinney et al (2010) reported the short-term (6 months to 1 year) and medium-term (2 years) outcomes after PPVI in the expanded multi-center United States (U.S.) Melody valve trial. From 1/07 to 8/09, 136 patients (median age of 19 years) underwent catheterization for intended Melody valve implant at 5 centers. Implant was attempted in 124 patients; in the other 12, PPVI was not attempted due to risk of coronary artery compression (n = 6) or other clinical or protocol contraindications. There was 1 death from intra-cranial hemorrhage following coronary artery dissection, and 1 valve was explanted after conduit rupture. The median peak RVOT gradient was 37 mm Hg pre-implant and 12 mm Hg acutely post-implant. Prior to implant, PR was moderate or severe in 92 patients (81 % with data); no patient had more than mild PR early after implant or during follow-up (greater than or equal to 1 year in 65 patients). Freedom from diagnosis of stent fracture was 77.8 +/- 4.3 % at 14 months. Freedom from Melody valve dysfunction or re-intervention was 93.5 +/- 2.4 % at 1 year. A higher RVOT gradient at discharge (p = 0.003) and younger age (p = 0.01) were associated with shorter freedom from dysfunction. The authors concluded that this updated report from the multi-center U.S. Melody valve trial demonstrated an ongoing high rate of procedural success and encouraging short-term valve function. All re-interventions in this series were for RVOT obstruction, high-lighting the importance of patient selection, adequate relief of obstruction, and measures to prevent and manage stent fracture.

Webb and colleagues (2010) stated that transcatheter heart valve implantation within a failed bioprosthesis, a "valve-in-valve" procedure, may offer a less invasive alternative than repeat cardiac surgery. These investigators reported the findings of valve-in-valve implantations in 24 high-risk patients. Failed valves were aortic (n = 10), mitral (n = 7), pulmonary (n = 6), or tricuspid (n = 1) bioprostheses. Implantation was successful with immediate restoration of satisfactory valve function in all but 1 patient. No patient had more than mild regurgitation after implantation. No patients died during the procedure. Thirty-day mortality was 4.2 %. Mortality was related primarily to learning-curve issues early in this high-risk experience. At baseline, 88 % of patients were in New York Heart Association (NYHA) functional class III or IV; at the last follow-up, 88 % of patients were in NYHA functional class I or II. At a median follow-up of 135 days (inter-quartile range [IQR] of 46 to 254 days) and a maximum follow-up of 1,045 days, 91.7 % of patients remained alive with satisfactory valve function. The authors concluded that transcatheter valve-in-valve implantation is a reproducible option for the management of bioprosthetic valve failure. Aortic, mitral, pulmonary, and tricuspid tissue valves were amenable to this approach.

In January 2010, the Food and Drug Administration (FDA) approved the Medtronic Melody/Ensemble Transcatheter Pulmonary Valve System for the treatment of adults and children with previously implanted, poorly functioning pulmonary valve conduits. The FDA approved the Melody/Ensemble system under the Humanitarian Device Exemption program. It is indicated for the treatment of dysfunctional RVOT conduits whose pulmonary valve has become stenotic or regurgitant (wide open with little or no valve function). Patients indicated for the procedure must have a full circumferential RVOT conduit greater than or equal to 16 mm in diameter when originally implanted. The approval
was based on clinical studies of 99 subjects in the United States and 68 subjects in Europe, which showed that the device improved function of the heart, and the majority of participants have noted improvements in their clinical symptoms. The device showed similar, limited durability compared with existing alternative treatments; 21% of U.S. subjects reported a stent fracture, a rate consistent with stent fractures reported for the bare metal stents presently used to treat congenital heart defects of the pulmonary valve.

As a condition of the FDA's approval, Medtronic will conduct 2 post-approval studies to evaluate long-term risks and benefits as well as the physician specialization needed to perform the implantation procedure. One study will continue to follow 150 subjects from the initial clinical trial for 5 years, and the second study will enroll more than 100 new subjects to be evaluated over 5 years, in order to assess the training program. Safety and benefit assessments will be part of both studies. The FDA also requires that Medtronic maintain a database of Melody/Ensemble recipients.

In January 2015, the Melody Transcatheter Pulmonary Valve (TPV) received Pre-Market Approval (PMA) from the FDA based upon evidence from 3 clinical studies demonstrating the valve's effectiveness in delaying open-heart reoperation. The Melody TPV was originally approved in 2010 under a Humanitarian Device Exemption (HDE), a regulatory approval for treatments intended for fewer than 4,000 U.S. patients per year. HDEs are granted for medical devices that have demonstrated reasonable safety and probable benefit, but do not have evidence of clinical effectiveness. PMA approval has been issued based on the new evidence that supports both safety and effectiveness of the Melody TPV. This device is indicated 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 was equal to or greater than 16 mm in diameter when originally implanted, and
- Dysfunctional RVOT conduit with a clinical indication for intervention, and:
  - Regurgitation: greater than moderate regurgitation, and/or
  - Stenosis: mean RVOT gradient greater than 35 mm Hg.

Melody TPV is intended to prolong the time between open-heart surgeries for patients with a dysfunctional RVOT conduit caused by congenital heart disease (CHD). The PMA approval was based on accumulated data from 3 clinical studies that followed a total of 310 patients implanted with Melody TPV - the Melody U.S. IDE Study, the Melody U.S. Post Approval Study (PAS) and the Melody European and Canadian Post-Market Surveillance Study (PMSS). Approximately 98% of patients were free from conduit re-operation (open-heart surgery) at 1 year post-implant of the Melody TPV. Additionally, 91% of patients in the IDE cohort were free from conduit re-operation at 5 years post-implant.

In a review on transcatheter valve interventions for heart valve diseases, Schaefer and Bertram (2010) stated that PPVI is an interventional treatment for adolescents and young adults with congenital heart disease. After corrective or palliative operation in infancy or early childhood, some patients regularly need re-operations for RVOT reconstruction. In the last decade, PPVI has evolved as an alternative treatment option with much less morbidity compared to repeated surgery.

Lurz et al (2011) evaluated the potential of late positive functional remodeling after PPVI in RVOT dysfunction. A total of 65 patients with sustained hemodynamic effects of PPVI at 1 year were included in this study. Patients were divided into 2 subgroups based on pre-procedural predominant pulmonary stenosis (PS) (n = 35) or predominant PR (n = 30). Data from magnetic resonance imaging and cardiopulmonary exercise testing were compared at 3 time points: (i) before PPVI, (ii) within 1 month (early), and (iii) at 12 months (late) after PPVI. There was a significant decrease in RVED volume early after PPVI in both subgroups of patients. Right ventricle ejection fraction improved early only in the PS group (51 +/- 11 % versus 58 +/- 11 % and 51 +/- 12 % versus 50 +/- 11 %, p < 0.001 for PS, p = 0.13 for PR). Late after intervention, there were no further changes in magnetic resonance
parameters in either group (right ventricle ejection fraction, 58 +/- 11 % in the PS group and 52 +/- 11 % in the PR group, p = 1.00 and p = 0.13, respectively). In the PS group at cardiopulmonary exercise testing, there was a significant improvement in peak oxygen uptake early (24 +/- 8 ml/kg/min versus 27 +/- 9 ml/kg/min, p = 0.008), with no further significant change late (27 +/- 9 ml/kg/min, p = 1.00). In the PR group, no significant changes in peak oxygen uptake from early to late could be demonstrated (25 +/- 8 ml/kg/min versus 25 +/- 8 ml/kg/min versus 26 +/- 9 ml/kg/min, p = 0.48). The authors concluded that in patients with a sustained hemodynamic result 1 year after PPVI, a prolonged phase of maintained cardiac function is observed. However, there is no evidence for further positive functional remodeling beyond the acute effects of PPVI.

Nordmeyer et al (2011) examined the feasibility and safety of pre-stenting with a bare metal stent (BMS) before PPVI, and analyzed if this approach improves hemodynamic outcomes and impacts on the incidence of PPVI stent fractures. A total of 108 consecutive patients with congenital heart disease underwent PPVI (54 with PPVI alone, 54 with BMS pre-stenting before PPVI). There were no significant differences in procedural complication rates. Acutely, there was no difference in hemodynamic outcomes. Serial echocardiography revealed that in the subgroups of "moderate" (26 to 40 mm Hg) and "severe" (> 40 mm Hg) RVOT obstruction, patients with pre-stenting showed a tendency towards lower peak RVOT velocities compared to patients after PPVI alone (p = 0.01 and p = 0.045, respectively). The incidence of PPVI stent fractures was not statistically different between treatment groups at 1 year (PPVI 31 % versus BMS+PPVI 18 %; p = 0.16). However, pre-stenting with BMS was associated with a lower risk of developing PPVI stent fractures (hazard ratio: 0.35; 95 % confidence interval: 0.14 to 0.87, p = 0.024). The probability of freedom from serious adverse follow-up events (death, device explantation, repeat PPVI) was not statistically different at 1 year (PPVI 92 % versus BMS+PPVI 94 %; p = 0.44). The authors concluded that pre-stenting with BMS before PPVI is a feasible and safe modification of the established implantation protocol. Pre-stenting is associated with a reduced risk of developing PPVI stent fractures.

Eicken and associates (2011) reported on the combined 2-center experience with PPVI. A total of 102 patients with RVOT dysfunction (median weight of 63 kg; range of 54.2 to 75.9 kg, median age of 21.5 years; range of 16.2 to 30.1 years) were included in this study. Percutaneous pulmonary valve implantation was performed in all patients. Pre-stenting of the RVOT was done in 97 patients (95 %). The median peak systolic RVOT gradient decreased from 37 mm Hg (29 to 46 mm Hg) to 14 mm Hg (9 to 17 mm Hg, p < 0.001) and the ratio RV pressure/aortic blood pressure decreased from 62 % (53 to 76 %) to 36 % (30 to 42 %, p < 0.0001). The median RVED-volume index (MRI) decreased from 106 ml/m(2) (93 to 133 ml/m(2)) to 90 ml/m(2) (71 to 108 ml/m(2), p = 0.001). Pulmonary regurgitation was significantly reduced in all patients. One patient died due to compression of the left coronary artery. The incidence of stent fractures was 5 of 102 (5 %). During follow-up (median of 352 days; range of 99 to 390 days), 1 percutaneous valve had to be removed surgically 6 months after implantation due to bacterial endocarditis. In 8 of 102 patients, a repeated dilatation of the valve was done due to a significant residual systolic pressure gradient, which resulted in a valve-in-valve procedure in 4. The authors concluded that these findings showed that PPVI is feasible and it improves the hemodynamics in a selected patient collective. Apart from 1 coronary compression, the rate of complications at short-term follow-up was low. They stated that PPVI can be performed by experienced interventionalists with similar results as originally published.

Raikou et al (2011) evaluated the cost of PPVI and the cost of surgical pulmonary valve replacement in patients with RVOT dysfunction using a cohort simulation model applied to the United Kingdom population. The model resulted in an estimate of mean cost per patient of £5,791 when PPVI is unavailable as a treatment option and in an estimate of mean cost per patient of £8,734 when PPVI is available over the 25-year period of analysis. After sensitivity analysis was undertaken the results showed that the mean per patient cost difference in implementing PPVI over 25 years as compared to surgical pulmonary valve replacement lies somewhere between £2,041 and £3,913. The authors noted that given the lack of long-term data on treatment progression, the cost estimates derived here are subject to considerable uncertainty, and extensive sensitivity analysis has been used to counter this. Thus, this study is merely indicative of the levels of cost that can be expected in a cohort of 1,000
patients faced with a choice of treatment with PPVI or surgery. It is not a cost-effectiveness study, but it helps place current knowledge on short-term benefits into context. The authors concluded that as this analysis shows PPVI is associated with a relatively small increase in treatment management costs over a long time period. Whether this inferred increase in long-term cost is worthwhile given the known short-term benefits and any personal judgment formed over long-term benefit is left to the reader.

McElhinney et al (2011) stated that among patients undergoing transcatheter pulmonary valve (TPV) replacement with the Melody valve, risk factors for Melody stent fracture (MSF) and RVOT re-intervention have not been well defined. From 1/2007 to 1/2010, a total of 150 patients (median age of 19 years) underwent TPV implantation in the Melody valve Investigational Device Exemption trial. Existing conduit stents from a prior catheterization were present in 37 patients (25%, fractured in 12); 1 or more new pre-stents were placed at the TPV implant catheterization in 51 patients. During follow-up (median of 30 months), MSF was diagnosed in 39 patients. Freedom from a diagnosis of MSF was 77 ± 4 % at 14 months (after the 1-year evaluation window) and 60 ± 9 % at 39 months (3-year window). On multi-variable analysis, implant within an existing stent, new pre-stent, or bioprosthetic valve (combined variable) was associated with longer freedom from MSF (p < 0.001), whereas TPV compression (p = 0.01) and apposition to the anterior chest wall (p = 0.02) were associated with shorter freedom from MSF. Freedom from RVOT re-intervention was 86 ± 4 % at 27 months. Among patients with a MSF, freedom from RVOT re-intervention after MSF diagnosis was 49 ± 10 % at 2 years. Factors associated with re-intervention were similar to those for MSF. The authors concluded that MSF was common after TPV implant in this multi-center experience and was more likely in patients with severely obstructed RVOT conduits and when the TPV was directly behind the anterior chest wall and/or clearly compressed. A TPV implant site protected by a pre-stent or bioprosthetic valve was associated with lower risk of MSF and re-intervention. Moreover, these investigators stated that assessment of MSF in this study was of limited sensitivity and resolution for a combination of reasons. Radiography was performed at pre-determined intervals, so the precise timing of MSF could not be defined. Bi-plane chest radiography, used for evaluation of MSF at all but the 6-month evaluation, may not profile the stent clearly in both views. Multi-plane fluoroscopy, which they assumed would be more sensitive for detection of MSF, was only performed routinely at the 6-month evaluation. Additional stents in the RVOT conduit may confound the visualization of fractured TPV stent struts because of radiographic interference and reduction of displacement at fracture points. For all of these reasons, it is possible that subtle MSF may have been missed or ascertainment delayed, although the clinical importance of such MSF is likely to be minimal. The grading scale these researchers used for MSF is imprecise, with the distinction between types I and II hinging on “stent integrity”, which is not defined and may be variably interpreted, and there was no core laboratory assessment to ensure consistency. It is likely that many patients with existing pre-stents had an underlying obstructive substrate of conduit dysfunction that was not reflected in baseline data due to the prior stent, which may have confounded assessment of risk factors for MSF. Also, there may have been important factors not assessed or included in the analyses, such as TPV “recoil”. Similarly, due to difficulty distinguishing solid body motion from more complex stent motion, the assessment of the dynamic mechanical environment of the implanted TPV was qualitative and simplistic. Two mid-study protocol modifications allowing implantation within a bioprosthetic valve (BPV) and pre-stenting after the first 70 and 35 patients, respectively, may have confounded the outcome evaluations. Similarly, institutional practice variation regarding pre-dilation, pre-stenting, and post-dilation confounded assessment of the independent importance of these technical factors.

These investigators stated that MSF was common after Melody valve implant in this multi-center experience and was more likely in patients with smaller and more obstructed RVOT conduits, those with homografts rather than BPV, and when the implanted TPV was directly behind the anterior chest wall and/or compressed. Melody valve implant within a protected RVOT, either a BPV with a rigid frame or a pre-stented conduit, was associated with lower risks of MSF, TPV dysfunction, and re-intervention. However, the small number of clinically important outcomes precluded robust multi-variable or subgroup analysis. Aside from those with a BPV, it is not yet possible to define patients who will or will not benefit from pre-stenting, although direct apposition of the conduit to the anterior
Gillespie et al (2012) stated that transcatheter pulmonary valve implantation using the Melody valve has emerged as an important therapy for the treatment of post-operative RVOT dysfunction. Melody-in-bioprosthetic valves (BPV) is currently considered an off-label indication. These investigators reviewed the combined experience with transcatheter pulmonary valve implantation within BPVs from 8 centers in the U.S. and discussed technical aspects of the Melody-in-BPV procedure. A total of 104 patients underwent Melody-in-BPV in the pulmonary position at 8 U.S. centers from April 2007 to January 2012. Ten different types of BPVs were intervened on, with Melody valve implantation at the intended site in all patients. Following Melody valve implant, the peak right ventricle-to-pulmonary artery gradient decreased from 38.7 ± 16.3 to 10.9 ± 6.7 mm Hg (p < 0.001), and the right ventricular systolic pressure fell from 71.6 ± 21.7 to 46.7 ± 15.9 mm Hg (p < 0.001). There was no serious procedural morbidity, and no deaths related to the catheterization or implant. At a median follow-up of 12 months (1 to 46 months), no patients had more than mild regurgitation, and 4 had a mean RVOT gradient of greater than or equal to 30 mm Hg. During follow-up, there were 2 stent fractures, 3 cases of endocarditis (2 managed with surgical explant), and 2 deaths that were unrelated to the Melody valve. The authors concluded that transcatheter pulmonary valve implantation using the Melody valve within BPVs can be accomplished with a high rate of success, low procedure-related morbidity and mortality, and excellent short-term results. Moreover, they state that the findings of this preliminary multi-center experience suggested that the Melody valve is an effective transcatheter treatment option for failed BPVs.

The main drawbacks of this study were its retrospective design, and its largely descriptive nature. The relationship between valve size and balloon waist may reflect selection and procedural bias, as larger balloon waists in 27 and 29 mm valves, for example, would not permit Melody valve implant. These data were intended simply to be descriptive, not prescriptive; and follow-up for stent fracture varied by institution. While all institutions performed fluoroscopy to screen for fractures in valves that became stenotic or regurgitant by echocardiography, not all institutions performed routine fluoroscopy at time points earlier than 12 months, relying instead on echocardiography and chest radiography. Therefore, it is possible that some hemodynamically insignificant fractures were missed. Also, because the duration of follow-up was relatively short in most patients, these researchers cannot comment on the long-term function of the Melody valve after implant within a failed BPV. These investigators stated that more data are needed to ascertain the role of TPVI in the management of patients with post-operative RVOT dysfunction, but the findings of this preliminary multi-center experience with Melody valve-in-BPV therapy are encouraging.

Has et al (2013) noted that PPVI was introduced in 2000 as an interventional procedure for the treatment of RVOT dysfunction. The new Edwards SAPIEN pulmonic valve has reached CE certification at the end of 2010 thus offering an attractive alternative with extended sizes (23 and 26 mm) to the conventional Melody valve (sizes 18, 20 and 22 mm). Over a 1-year period, PPVI using the Edwards SAPIEN pulmonic valve was performed in 22 patients using a standardized procedure. Primary diagnosis was tetralogy of Fallot (n = 11), pulmonary atresia (n = 2), Truncus arteriosus (n = 3), TGA/PS-Rastelli (n = 1), Ross surgery (n = 2), double outlet right ventricle (n = 2) and absent pulmonary valve syndrome (n = 1). The character of the RVOT for PPVI was transannular patch (n = 4), bioprosthesis (n = 2), homograft (n = 5), and Contegra conduit (n = 11). The leading hemodynamic problem consisted of a pulmonary stenosis (PS) (n = 2), pulmonary regurgitation (PR) (n = 11), and a combined PS/PR lesion (n = 9). In 21 of the 22 patients, PPVI was performed successfully (10 × 23 and 11 × 26 mm). There were 9 female and 13 male patients; the mean age was 21.7 years (range of 6 to 83 years), the mean length was 162 cm (range of 111 to 181 cm) and the weight 56.5 kg (range of 20 to 91 kg). Invasive data showed a decrease of RV-systolic pressure from 61.2 mmHg (± 23.1) to 41.2 mmHg (± 8.6) and reduction of RV-PA gradient from 37.3 mmHg (± 23.2) to 6.9 mmHg (± 5.3).
The PA-systolic pressure increased from 25.8 mmHg (± 8.6) to 33.9 mmHg (± 9.3) as did the PA diastolic pressure (from 6.0 mmHg (± 5.6) to 14.6 mmHg (± 4.3). There was a substantial reduction of pulmonary regurgitation from before (none/trivial n = 0, mild n = 2, mode rate n = 9, severe n = 11) to after PPVI (none/trivial n = 20, mild n = 1). During the short-term follow-up of 5.7 months there was no change in the immediate results. The authors concluded that PPVI using the Edwards SAPIEN pulmonic valve can be performed safely in a wide range of patients with various diagnoses and underlying pathology of the RVOT and enables the restoration of an adult-size RVOT diameter. Moreover, they stated that although the immediate and short-term results seem promising, the long-term effects and safety have to be assessed in further clinical follow-up studies.

Odemis et al (2013) noted that percutaneous PV implantation is frequently used as a less invasive method in patients with conduit dysfunction. The common valve type cannot be used in conduits with a diameter larger than 22 mm. There has been limited experience concerning the use of the SAPIEN Transcatheter Heart Valve, produced for use in conduits with a large diameter. These researchers presented hemodynamic and early follow-up results from a single center in Turkey concerning the use of the SAPIEN Transcatheter Heart Valve in different types of conduits and different lesions. Between October 2010 and July 2012, a total of 7 SAPIEN Transcatheter Heart Valve implantations were performed. There was mixed type 2 pure insufficiency with stenosis and insufficiency in 5 patients. Three different conduits were used, and 1 native pulmonary artery process was performed. Patients were followed for hemodynamic findings, functional capacities, valve competence, re-shrinking, and breakage in the stent, and the results were evaluated. Implantations were successfully performed in all patients. Right ventricular pressures and gradients were significantly reduced, and there was no pulmonary regurgitation in any patient. Functional capacities improved in all patients except for 1 with pulmonary hypertension; no major complication was observed. During the mean time of follow-up (7.2 ± 4.7 months), no valve insufficiency or stent breakage was observed. The authors concluded that procedural results and short-term outcomes of the SAPIEN Transcatheter Heart Valve were very promising in the patients included in the study. The SAPIEN Transcatheter Heart Valve can be a good alternative to surgical conduit replacement, particularly in patients with larger and different types of conduits.

Meadows and colleagues (2014) stated that Melody transcatheter PV (TPV) replacement therapy represents an important advance in congenital cardiovascular interventions. The off-label extension of the Melody TPV to patients with non-conduit outflow tracts (RVOT) has the potential to vastly expand the population of patients eligible to benefit from non-surgical restoration of RVOT function. However, knowledge on the performance of the Melody TPV in this setting is limited. These investigators performed a retrospective review of the Melody TPV when placed in non-conduit RVOTs, in which at least a portion of the circumference was composed of native tissue. A total of 5 centers contributed data on 31 patients. The median age at implantation was 24 years (range of 7 to 66). At a median follow-up of 15 months, all patients were alive. No patient had greater than mild TPV insufficiency, and the median maximum instantaneous gradients across the RVOT was 23 mm Hg. Stent fracture occurred in 32%; 8 patients developed more than mild TPV obstruction (6 were associated with identified stent fracture); 3 patients developed blood stream infections. There were 5 re-interventions in 3 patients, including 3 repeat TPV implantations and 2 TPV explantations. The authors concluded that Melody TPV implantation is feasible in selected patients with RVOTs comprised solely or predominantly native tissue and has the potential to expand the population of patients eligible to benefit from non-surgical restoration of RVOT function. In early follow-up, valve competency seems preserved. The dominant mechanism of valve dysfunction seems to be related to stent fracture with recurrent obstruction. They stated that additional data are needed to better understand how to safely expand TPV therapy to this population.

Raval et al (2014) stated that transcatheter aortic valve implantation (TAVI) has become an alternative to open surgery in those deemed high risk. These researchers evaluated the effectiveness and outcomes of this emerging procedure. They have examined available literature to provide an overview of valve-in-valve implantation using transcatheter heart valves (THVs) in aortic, mitral, pulmonary,
tricuspid positions. A systematic search was conducted using MEDLINE, PubMed, EMBASE, Current Contents Connect, Cochrane library, Google Scholar, Science Direct, and Web of Science. Only 61 studies met full criteria and were included the review. This included 31 studies reporting transcatheter aortic valve-in-valve implantation, mitral valve-in-valve implantation (13 studies), tricuspid valve-in-valve implantation (12 studies), and pure native aortic valve regurgitation (9 studies). One of the limitations of this review was that most of the studies included were case reports, together with some case series. The authors concluded that valve-in-valve implantation can be considered as an acceptable alternative to conventional open heart surgery for elderly high-risk surgical patients with bioprosthetic degeneration. Moreover, they stated that long-term follow-up of treated patients will be needed to establish the true role of valve-in-valve implantation for bioprosthetic degeneration. Patients should be evaluated on an individual basis until outcomes are proven in large cohort studies or randomized trials.

Treatment of Failed Bioprosthetic Pulmonary Valves:

Nordmeyer et al (2008) stated that PPVI is now an accepted treatment strategy for RVOT dysfunction in many European heart centers. These investigators analyzed the effectiveness of repeat PPVI as a treatment modality for early device failure. A total of 20 patients underwent repeat PPVI for RVOT obstruction because of early device failure ('Hammock effect', 'Hammock-like effect', stent fracture, residual stenosis). Repeat PPVI was feasible in all patients with no procedural complications. Following implantation of a second device, catheter-measured RVOT gradient and RV systolic pressure fell significantly (RVOT gradient: 46.1 +/- 3.9 to 18.1 +/- 2.4 mmHg, p < 0.001; RVSP: 70.9 +/- 4.8 to 46.1 +/- 2.6 mmHg, p < 0.001), in all but 1 patient (15 years of age, male, common arterial trunk, 11.5 mm homograft). During follow-up, 4 of 20 required re-intervention [3rd PPVI for stent fracture (n = 2), device explantation: external compression by the sternum (n = 1), endocarditis (n = 1)], and 1 of the 20 is awaiting surgical management. In the remainder, 2nd PPVI resulted in a sustained improvement in hemodynamics with a mean follow-up of 10.9 +/- 3.0 months. In this series, the probability of freedom from re-intervention at 2 years was higher after 2nd PPVI when compared with the index procedure (89.4 versus 20.0 %, p < 0.001). The authors concluded that repeat PPVI is an effective treatment for early device failure in defined conditions and leads to improved freedom from re-intervention.

Webb et al (2010) noted that the majority of prosthetic heart valves currently implanted are tissue valves that can be expected to degenerate with time and eventually fail. Repeat cardiac surgery to replace these valves is associated with significant morbidity and mortality. Transcatheter heart valve implantation within a failed bioprosthesis, a "valve-in-valve" procedure, may offer a less invasive alternative. Valve-in-Valve implantations were performed in 24 high-risk patients. Failed valves were aortic (n = 10), mitral (n = 7), pulmonary (n = 6), or tricuspid (n = 1) bioprostheses. Implantation was successful with immediate restoration of satisfactory valve function in all but 1 patient. No patient had more than mild regurgitation after implantation. No patients died during the procedure; 30-day mortality was 4.2 %. Mortality was related primarily to learning-curve issues early in this high-risk experience. At baseline, 88 % of patients were in NYHA functional class III or IV; at the last follow-up, 88 % of patients were in class I or II. At a median follow-up of 135 days (IQR, 46 to 254 days) and a maximum follow-up of 1045 days, 91.7 % of patients remained alive with satisfactory valve function. The authors concluded that transcatheter valve-in-valve implantation is a reproducible option for the management of bioprosthetic valve failure. Aortic, pulmonary, mitral, and tricuspid tissue valves were amenable to this approach.

Eicken et al (2011) reported on their experience with PPVI. A total of 102 patients with RVOT dysfunction (median weight of 63 kg (54.2 to 75.9 kg), median age of 21.5 years (16.2 to 30.1 years), diagnoses: TOF/PA 61, TAC 14, TGA 9, other 10, AoS post-Ross-OP 8) were scheduled for PPVI since December 2006. Percutaneous pulmonary valve implantation was performed in all patients. Pre-stenting of the RVOT was done in 97 patients (95 %). The median peak systolic RVOT gradient decreased from 37 mmHg (29 to 46 mmHg) to 14 mmHg (9 to 17 mmHg, p < 0.001) and the ratio RV pressure/AoP decreased from 62 % (53 to 76 %) to 36 % (30 to 42 %, p < 0.0001). The median end-diastolic RV-volume index (MRI) decreased from 106 ml/m(2) (93 to 133 ml/m(2)) to 90 ml/m(2) (71 to
Pulmonary regurgitation was significantly reduced in all patients. One patient died due to compression of the left coronary artery. The incidence of stent fractures was 5 of 102 (5%). During follow-up (median of 352 days (99 to 390 days)) 1 percutaneous valve had to be removed surgically 6 months after implantation due to bacterial endocarditis. In 8 of 102 patients, a repeated dilatation of the valve was done due to a significant residual systolic pressure gradient, which resulted in a valve-in-valve procedure in 4. The authors concluded that the findings of this study showed that PPVI is feasible and it improved the hemodynamics in selected patients. Apart from 1 coronary compression, the rate of complications at short-term follow-up was low.

Filsoof et al (2014) stated that bioprosthetic heart valves can degenerate and fail over time. Repeat surgery as a means of replacement increases morbidity and mortality rates, and some patients are not candidates for re-operation. A newer treatment, percutaneous transcatheter valve-in-valve implantation, might delay or substitute for invasive procedures. These researchers presented the case of a 51-year old woman, a poor candidate for surgery who had prosthetic tricuspid valve degeneration and stenosis. These investigators successfully performed valve-in-valve placement of a Melody valve, using a procedure originally intended to treat pulmonary valve conduit obstruction or regurgitation. This was among the first case reports to describe the use of the Melody pulmonary valve in transcatheter valve-in-valve replacement for prosthetic tricuspid stenosis that was otherwise not correctable. The authors concluded that additional data and longer follow-up periods are needed to gain an understanding of ideal indications and selection of patients for the percutaneous transcatheter treatment of tricuspid valve stenosis.

Tzifa et al (2014) noted that transcatheter implantation of valved stents (Melody and Edwards valves) for replacement of the pulmonary valve is currently an established procedure. These investigators reviewed their experience on implantation of such valves in the tricuspid valve position. Transcatheter valve implantation in the tricuspid position was attempted in 5 patients: 4 patients had predominantly tricuspid valve regurgitation, 2 of whom also had tricuspid valve stenosis. All patients had severely symptomatic right heart failure. Patient median age and weight were 12 years and 50 kg (range of 6 to 43 years and 13 to 68 kg, respectively). All patients had a bioprosthetic valve already in place. The mean gradient across the tricuspid valve decreased from 12 to 3 mmHg after the procedure. Median procedure time and fluoroscopy time were 100 and 39 minutes (range of 60 to 180 and 30 to 57 minutes, respectively). The patients’ functional class improved from NYHA Class III to II in 3 and from Class III to I in 2 patients during a follow-up period of 15 to 22 months. The authors concluded that transcatheter replacement of malfunctioning bioprosthetic valves in the tricuspid position using valved stents is an attractive alternative to repeat surgery in high-risk or multi-operated patients. Moreover, they stated that longer follow-up and a larger number of patients are needed to establish the long-term benefit of the procedure and freedom from re-interventions.

Milburn et al (2014) stated that transcatheter aortic valve implantation has established itself as an alternative treatment for patients with valvular disease. In the current context of increasing bioprosthetic valve implants and an aging population with growing co-morbidities, a less invasive approach to the treatment of bioprosthetic dysfunction would be an appealing alternative to the standard of care. Transcatheter valve-in-valve implantation could be an alternative for patients who are deemed to be a high surgical risk. The valve-in-valve procedure is a minimally invasive percutaneous procedure where a valve can be implanted directly within a failing bioprosthetic valve. This technique can be applied to dysfunctional aortic bioprosthetic valves and can also be used in the pulmonary and atrio-ventricular valve bioprosthesis.

An UpToDate review on “Percutaneous pulmonic valve implantation” (Fratz, 2015) states that “PPVI [percutaneous pulmonary valve implantation] can also be performed as a repeat intervention after failure of the primary device in the RVOT. The indications and the implantation technique are the same for repeat PPVI as for primary PPVI. Valve-in-valve technology has also been used in other prosthetic valve sites”.

Law et al (2012) stated that the transcatheter valve-in-valve implantation (VIV) is a minimally invasive,
trans-catheter, off-pump, alternative to conventional valve replacement, which uses a failing bioprosthesis to anchor a 2nd trans-catheter-delivered prosthesis. This technique appeared effective for prolonging freedom from re-intervention and treating early device failure. However, it is unknown as to how long re-intervention can be avoided. These investigators presented the pathological findings of a VIV implant explanted after 47 months, as well as the failure modes of these devices. The VIV approach in this case ultimately failed, likely due to the proximity of the host's tissues to the prosthetic device, resulting in a combination of pannus, calcification, and a cusp tear. The authors concluded that additional long-term follow-up of pulmonary VIV implantations is needed in order to determine the life span of VIV implants and what causes them to fail.

Conrad et al (2015) noted that trans-catheter VIV is emerging as a novel treatment option for patients with deteriorated bioprostheses. These investigators reported their cumulative experience using 6 types of THVs in all anatomic positions. A total of 75 consecutive patients (74.1 ± 12.9 years, 50.7 % male (38/75), logEuroSCORE I 26.2 % ± 17.8 %, STS-PROM 8.8 % ± 7.4 %) receiving VIV procedures from 2008 to 2014 were included for analysis. Data were prospectively gathered and retrospectively analyzed. VIV was performed in aortic (72.0 %, 54/75), mitral (22.7 %, 17/75), tricuspid (2.7 %, 2/75), and pulmonary (2.7 %, 2/75) positions. Trans-catheter heart valves used were Edwards SAPIEN (XT)/SAPIEN3 (52.0 %, 39/75), Medtronic Core Valve/Core Valve Evolut(R) (34.7 %, 26/75), St Jude Portico (4.0 %, 3/75), Boston Scientific Lotus (4.0 %, 3/75), Jena Valve (2.7 %, 2/75), and Medtronic Engager (2.7 %, 2/75). Interval from index procedure to VIV was 9.3 ± 4.9 years. Access was trans-apical in 53.3 % (40/75), trans-femoral (trans-arterial or trans-venous) in 42.7 % (32/75), trans-aortic in 2.7 % (2/75), and trans-jugular in 1.3 % (1/75). VIV was successful in 97.3 % (73/75) with 2 patients requiring sequential THV implantation for initial mal-positioning. Overall immediate procedural (less than or equal to 72 hours) and all-cause 30-day mortality were 2.7 % (2/75) and 8.0 % (6/75). Corresponding values after aortic VIV were 1.9 % (1/54) and 5.6 % (3/54). No peri-procedural strokes or cases of coronary obstruction occurred. Para-valvular leakage was less than or equal to mild in all cases. After aortic VIV, gradients were max/mean 34.1 ± 14.2/20.1 ± 7.1 mm Hg and effective orifice area (EOA) was 1.5 ± 1.4 cm(2). Corresponding values after mitral VIV were gradients max/mean 14.2 ± 8.2/4.7 ± 3.1 mm Hg and EOA 2.4 ± 0.9 cm(2). The authors concluded that VIV can be performed in all anatomic positions with acceptable hemodynamic and clinical outcome in high-risk patients; increasing importance of VIV can be anticipated considering growing use of surgical bioprostheses.

The evidence on transcatheter pulmonary valve replacement within a failed bioprosthesis (valve-in-valve procedure) consists mainly of case series and therefore is insufficient to determine whether outcomes are improved compared to alternatives.

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<tr>
<th>CPT Codes / HCPCS Codes / ICD-10 Codes</th>
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<td>Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by &quot;+&quot;:</td>
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**CPT codes covered if selection criteria are met:**

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

**ICD-10 codes covered if selection criteria are met:**

T82.857+ Stenosis of cardiac devices, implants and grafts

T82.897+ Other specified complication of cardiac devices, implants and grafts [regurgitation]

**ICD-10 codes not covered for indications listed in the CPB:**
The above policy is based on the following references:

AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0821 Transcatheter Pulmonary Valve Implantation

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania updated 11/22/2017