Molina Clinical Policy
Transcatheter Pulmonary Valve Replacement: Policy No. 148

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DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Congenital heart disease (CHD) refers to conditions that affect the heart and the proximal vasculature at birth. Some types of CHD may affect the structure and function of the heart. CHD ranges from mild to severe and requires treatment. CHD, which includes tetralogy of Fallot, pulmonary atresia, and transposition of the great arteries, is treated by surgical repair at an early age. Right ventricular outflow tract (RVOT) dysfunction, an issue with the blood flow as it exits the heart and travels to the lungs, is one form of CHD. The repair of RVOT entails reconstructing the RVOT and pulmonary valve by inserting a tube or surgical conduit to facilitate normal blood flow. However, the conduit can become narrowed over time, or a specific valve can leak, necessitating a second valve replacement surgery. This second surgery is typically performed as an open procedure. Interventions for correction of pulmonary stenosis include open heart surgery with valve replacement, balloon dilatation, or percutaneous stenting. Interventions for pulmonary regurgitation are generally surgical, consisting of either RVOT conduit reconstruction or pulmonary valve replacement.

Transcatheter pulmonary valve implantation (TPVI) is a non-surgical option to restore pulmonary valve function in children and adults with CHD. The procedure offers a less invasive alternative to surgical pulmonary valve implantation for patients who would otherwise require open surgical pulmonary valve replacement or reconstruction for RVOT obstruction. This procedure may be also important for non-congenital, destructive lesions of the pulmonary artery valve.

There are ongoing post approval studies to assess long-term clinical performance of the Melody transcatheter pulmonary valve (TPV) and the SAPIEN XT Transcatheter Heart Valve – Pulmonic after transcatheter implantation in participants with dysfunctional RVOT conduits; however, there are no randomized controlled trials (RCTs) to compare the transcatheter approach to open-heart surgical technique.

Regulatory Status

Devices for TPVI were initially cleared from marketing by the FDA through the humanitarian device exemption (HDE) process or used off-label until FDA-approved through the premarket approval (PMA) process. FDA product code: NPV.

Melody. The Melody valve system consists of two components: the Melody TPV (bovine jugular valve with stent) and the Ensemble Transcatheter Valve Delivery System (Medtronic) were originally approved under HDE (H080002) on January 25, 2010. The approval of the Melody device was amended to a PMA due to the determination by the FDA that the device represents a breakthrough technology (FDA 2015). The PMA was based, in part, on two prospective clinical studies: the Melody TPV Long-term Follow-up Post Approval Study and the Melody TPV New Enrollment Post Approval Study. The Melody TPV and Ensemble System received PMA (P140017) on January 27, 2015, 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 conduits with a clinical indication for intervention, and either:
  - Regurgitation: $\geq$ moderate regurgitation, or
  - Stenosis: mean RVOT gradient $\geq$ 35 mmHg.

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

SAPIEN XT. The Edwards SAPIEN XT Transcatheter Heart Valve and accessories (Edwards Lifesciences) received FDA approval for pulmonary valve use through the PMA process on February 29, 2016. The Edwards Sapien XT Transcatheter Heart Valve (Pulmonic) 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. The Edwards SAPIEN was originally approved for aortic valve use in 2011 (FDA 2012). Approval was based on clinical evidence from the Congenital Multicenter trial of Pulmonic valve regurgitation studying the SAPIEN Interventional (COMPASSION) transcatheter heart value (THV) trial (Clinical Trials 2020). According to the PMA approval order, this device is indicated for use in pediatric and adult patients with the following clinical conditions:

- A dysfunctional, non-compliant RVOT conduit with a clinical indication for intervention and either:
    1. Regurgitation: ≥ moderate regurgitation, and/or
    2. Stenosis: mean RVOT gradient ≥ 35 mmHg.

Harmony. The Harmony TPV (Medtronic) received breakthrough technology status in 2019 and PMA in March 2021 (FDA 2021). It is the first non-surgical heart valve to treat pediatric and adult patients with a native or surgically repaired RVOT to stop severe pulmonary valve regurgitation caused by CHD. Harmony TPV is composed of self-expanding nitinol wire struts, a knitted polyester fabric graft, and a porcine pericardial tissue valve. It includes a delivery accessory system and is indicated for use in the management of pediatric and adult patients with severe regurgitation (i.e., severe as determined by echocardiography and/or pulmonary regurgitant fraction > 30% as determined by cardiac magnetic resonance imaging) who have a native or surgically repaired right ventricular outflow tract and are clinically indicated for surgical pulmonary valve replacement.

Refer to 'Supplemental Information' section of policy for the 'Regulatory Status of TPVI Devices' (Table 1).

COVERAGE POLICY

Transcatheter pulmonary valve implantation (TPVI) using an FDA approved valve is considered medically necessary for congenital heart disease and current right ventricular outflow tract obstruction (RVOT) or regurgitation when **ALL** of the following criteria are met:

1. Existence of a full (circumferential) RVOT conduit that was equal to or greater than 16 mm in diameter when originally implanted; **AND**

2. Definitive diagnosis of **ONE** of the following:

    a. Dysfunctional RVOT conduit with a clinical indication for intervention, and **EITHER** of the following:
        - Moderate or greater pulmonic regurgitation; **OR**
        - Pulmonic stenosis with a mean RVOT gradient greater or equal to 35 mmHg.

    OR

    b. Dysfunctional non-conduit, patch repaired RVOT

LIMITATIONS AND EXCLUSIONS

Percutaneous pulmonary valve implantation (PPVI) are **contraindicated and may not be authorized** if **ANY** of the following circumstances are present:

1. History of endocarditis or other active infection within 6 months of PPVI
2. RVOT size is not appropriate for stent valve delivery (size range depends on the valve system)
3. Venous occlusions that do not permit percutaneous femoral or jugular vein access
4. Vessel size and characteristics in which the placement of a 22- to 24-Fr introducer sheath would not be safe
5. Morphology of the RVOT does not permit a percutaneous approach
6. Presence of coronary artery compression
7. Weight < 30 kg
8. Pregnancy

The following are considered **experimental, investigational, and unproven** based on insufficient evidence:

1. Any indications other than those listed above

Exceptions (case-by-case review): There are rare patients without congenital heart disease (CHD) who may have pulmonary valve dysfunction requiring replacement. Native outflow tract pulmonary valve implantation with balloon-expandable valves while considered off-label may be considered appropriate as an alternative to surgery in some cases and may be an exception. There may also be cases where the exclusion criteria are not met but a multidisciplinary cardiology team may determine that TPVI is favorable in exceptional scenarios.

These exceptional cases require the following as deemed appropriate by the Molina clinical reviewer: a peer-to-peer with a Molina Medical Director, consult with multidisciplinary cardiology team, and relevant clinical documentation(s) or supporting evidence to assess whether a TPVI is favorable in an individual member's case.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

Registration trials for FDA approval, short case series, and cohort studies are included in the published literature on transcatheter pulmonary valve implantation (TPVI). The Melody valve is the most extensively researched transcatheter pulmonary value (TPV) with the largest body of clinical evidence.

Melody TPV and the Ensemble® Transcatheter Valve Delivery System are used in conjunction to replace a dysfunctional pulmonary valve percutaneously. A section of bovine jugular vein with an intact native venous valve serves as the Melody valve. A platinum-iridium stent scaffolding is used to suture the valve and surrounding tissue. The transcatheter delivery system is composed of a balloon-in-balloon catheter with a retractable sheath and distal cup into which the valve is positioned. The procedure is performed without the use of cardiopulmonary bypass on a beating heart. First, the Melody valve is crimped to fit the delivery system. It is inserted via the femoral vein, progressed into the right side of the heart, and positioned at the pulmonary valve site. The inner balloon is inflated to open the artificial valve, followed by the outer balloon to secure the valve in place.

US Investigational Device Exemption (IDE) Study

The multicenter US Melody TPV trial is a prospective uncontrolled trial intended to evaluate the safety, procedural success, and short-term efficacy of the Melody valve (McElhinney et al. 2010; Zahn et al. 2009). Beginning in January 2007, Melody TPV was implanted in 150 patients at five sites in the United States for the treatment of RVOT dysfunction according to the IDE approach. In January 2010, enrollment in the U.S. Melody valve IDE trial closed, and the Melody valve was approved for installation in defective RVOT catheters as palliative therapy designed to delay surgical intervention (McElhinney et al. 2011).

Zahn et al. (2009) published data on 30 patients with a success rate of 29 Melody valve implantations in the Melody U.S. Clinical Trial. This study assessed the safety, procedural success, and short-term efficacy of the Melody transcatheter pulmonary valve in patients with defective right ventricular outflow tract conduits. Between January and September 2007, 34 patients had catheterization for Melody valve implantation at three sites. Twenty-nine of thirty implants were effective, and four individuals were not implanted. 19.4 ± 7.7 years was the mean age. Doppler mean gradient was 28.8 ± 10.1 mm Hg, and 94% of patients had moderate or severe pulmonary regurgitation. One distal pulmonary artery guidewire perforation, one conduit rupture, and one broad complicated tachycardia occurred. Peak systolic conduit gradient decreased to 17.3 ± 7.3 mm Hg. Pulmonary regurgitation was mild in all cases. At six months, conduit Doppler mean gradient was 22.4± 8.1 mm Hg, and pulmonary regurgitation fraction as determined by magnetic resonance imaging was dramatically improved (3.3 ± 3.6% vs. 27.6 ± 13.3%, $p < 0.0001$). Eight of twenty-nine implants fractured stents. Three of these patients had recurring stenosis and received a second Melody valve. The authors concluded that experienced operators can safely and effectively implant the Melody valve for RVOT conduit dysfunction. During the trial follow-up, 100% of patients were free of additional procedures, and 79% of the 24 New York Heart Association (NYHA) functional class II patients improved. This trial was followed by another that led to FDA clearance of the Melody prosthesis under the HDE clause. The study authors stated that a longer follow-up and more patient experience are needed to determine this therapy's decisive role in conduit dysfunction treatment.

McElhinney et al. (2010) conducted a multicenter trial of 136 patients (median age 19 years) having undergone catheterization for Melody valve implantation. Implantation was attempted in 124 patients. TPV placement was not attempted in the other 12 due to coronary artery compression or other clinical or protocol contraindications. After conduit rupture, 1 valve was explanted and 1 patient died. Before implantation, the median peak RVOT gradient was 37 mmHg. Before implantation, 92 patients had moderate or severe pulmonary regurgitation. No patient had more than mild pulmonary regurgitation early after implantation or during follow-up. At 14 months, 77.8+/-4.3% were stent fracture-free. Valve dysfunction or reintervention was 93.5+/-2.4% at 1 year. Shorter freedom from dysfunction was associated with higher RVOT gradient at discharge and younger age. The results showed good short-term valve function and a high procedural success rate. This series of re-interventions for RVOT obstruction emphasizes patient selection, adequate obstruction relief, and stent fracture prevention and management.

McElhinney et al. (2011) reported patient-related and procedural risk factors in the US Melody Valve Trial. At the 39-month follow-up 60+/-9% of patients were Melody stent fracture (MSF)-free. On multivariable analysis, implant within an existing stent, new pre-stent, or bioprosthetic valve (combined variable) was associated with longer freedom from MSF ($p < 0.001$), while TPV compression ($p = 0.01$) and apposition to the anterior chest wall ($p = 0.02$) were associated with shorter freedom from MSF. At 27 months 86+/-4% of patients were RVOT intervention-free. At 2 years, 49+/-10% of MSF patients did not need RVOT reintervention. Reintervention factors resembled MSFs. MSF was common after TPV implant in this multicenter study, especially in patients with severely obstructed RVOT conduits and when the TPV was directly behind the anterior chest wall and/or compressed. MSF and reintervention were lower in TPV implant sites protected by pre-stents or bioprosthetic valves. The trial was originally intended to follow patients for 5 years after implantation or until ex-plantation, but it was modified in 2011 to allow patients who provided supplemental written informed consent to be followed for up to 10 years.

Cheatham et al. (2015) reported on outcomes up to 7 years after TPVI for the 148 patients in the U.S. Melody TPV study who received and were discharged with TPVs. At discharge, 140 patients had no pulmonary regurgitation and 5 had mild regurgitation on echocardiography. Four deaths occurred during a median follow-up of 4.5 years (range, 0.4-7.0 years). In the follow-up period, 32 patients needed RVOT reinterventions, 25 of which were TPV. Melody valve ex-plantation was needed in 11 individuals. The RVOT gradient was constant from early after valve implantation in 113 patients who were alive and reintervention-free at a median of 4.5 years post-implantation. Fourteen percent of patients were in NYHA class I before TPVI, while 17% were in class III or IV. At each annual post-implantation evaluation, at least 74% of patients were in class I and 1% to 2% were in class III or IV.

Melody TPV Post Approval Study

Armstrong et al. (2014) published 1-year follow-up results of the Melody TPVI Post Approval Study to assess short-term hemodynamic changes after device implantation. The prospective, non-randomized study used historical controls from the Melody IDE trial to determine whether the device's short-term effectiveness was noninferior to the IDE trial results. The study included 120 participants, 101 of whom attempted TPVI. The IDE trial criteria were used for patient selection, but the age (5 years old) and weight (30 kg) limitations were not included. A confined conduit tear was the most common procedure-related significant adverse event (AE) in 16 patients (13.3% of the total cohort of 120; 15.8% of those who had an attempted TPVI). At one year, the proportion of patients with NYHA class I heart failure increased from 35% to 89%. Of the 99 patients who had been 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 the entire cohort), and 82 had acceptable TPV hemodynamic function confirmed at 1 year (94.3% of those with evaluable echocardiographic data, 82.8% of the entire cohort). Following the procedure, 8% of patients experienced serious device-related AEs, the most common of which was endocarditis.

Gillespie et al. (2015) retrospectively reviewed data of TPVI after a Ross procedure from the Melody TPV trial and post-approval study and an additional European registry, the manufacturer-sponsored Melody TPV Post-Market Surveillance Study, conducted in Canada and Europe (NCT00688571). A prior Ross procedure was performed on 67 (19%) of the pooled sample (n = 358). In 56 of 67 (84%) of the Ross patients who underwent catheterization with the intent of TPVI, a Melody valve was successfully implanted. After TPVI, six patients (9%) had symptomatic coronary artery compression or did not undergo implantation due to compression risk. After TPVI, right ventricular hemodynamics improved, however 12 of 55 patients discharged with the Melody valve needed RVOT reinterventions.

Adverse Events (AEs)

Amat-Santos et al. (2015) assessed the incidence, characteristics, predisposing factors, and outcomes of prosthetic valve endocarditis (PVE) after transcatheter aortic and percutaneous pulmonary valve implantation (PPVI) replacement from 2000 to 2013. In 28 articles (n=60; 32 aortic valve, 28 pulmonary valve), aortic valve patients had a high logistic EuroSCORE of 30.4 ± 14.0. Melody was given to all pulmonary valve patients and Sapien/Sapien XT or CoreValve to aortic valve patients. Only aortic valve patients had in-hospital problems, and antibiotic prophylaxis data was lacking. Aortic valve patients were 80 ± 7 years old, while pulmonary valve patients were 19 ± 6 years old. In 71.9% of aortic valve replacement patients, PVE was found in the transcatheter valve, compared to 100% in the PPVI group. The median period between valve replacement and infective endocarditis was 5 months (IQR, 2 to 9 months). Enterococci were most common in the aortic group (34.4%) and Staphylococcus aureus in the pulmonary group (29.4%). Sixty percent of aortic valve patients with PVE were managed medically, although valve ex-plantation rates ranged from 23% to 57% and in-hospital mortality was 34.4%. Seventy-five percent of pulmonary valve patients were surgically treated, with 7.1% in-hospital mortality.

Virk et al. (2015) published clinical outcomes from 12 observational studies (n = 677) for periprocedural mortality (death within 30 days following PPVI), complications, and independence from RVOT reintervention. Analysis employed DerSimonian-Laird random-effects. Nine Melody, two Sapien, and one study with both devices were analyzed. Pooled periprocedural mortality was 1.4% (95% CI, 0.7% to 2.8%), while complication rates were low and included coronary artery compression (1.2%; 95%, 0.6 to 2.5), pulmonary artery obstruction (1.2%; 0.5% to 2.6%), valve embolization (2.4%; 1.3% to 4.3%), and conduit rupture (2.6%; 1.5% to 4.3%). 2.8% of patients underwent open surgery (95% CI, 1.7%–4.6%). Stent fracture was 12.4% (95% CI, 7.6% to 19.6%) and infective endocarditis 4.9% (95%, 3.2% to 7.6%) at latest follow-up. The freedom from RVOT reintervention ranged from 100% at 4 months to 70% at 70 months.

Medtronic issued a Class I Medical Device Recall in April 2022 recommending suspension of use for Harmony TPV's delivery system. It is possible that the capsule bond at the end of the delivery catheter may break during a procedure to place the TPV. This may cause procedure delays for the device to be replaced or additional surgeries for the patient. A capsule bond break may cause serious harm to the patient including preventing blood flow, completely blocking, tearing and/or splitting, or other types of damage to the patient's blood vessels. There have been 6 reported complaints from clinical cases, one injury, and no deaths associated with the use of this device. The recall is specific to the Harmony Delivery Catheter only and does not apply to the Harmony TPV (FDA 2022).

Edwards Sapien XT Transcatheter Heart Valve (Pulmonic)

Congenital Multicenter trial of Pulmonic valve regurgitation Studying the SAPIEN Interventional THV (COMPASSION). The study is a prospective, non-randomized, multicenter center study that assessed the safety and effectiveness of pulmonic implantation of the SAPIEN THV in patients with dysfunctional RVOT conduit requiring treatment for moderate or severe pulmonary regurgitation by transthoracic echocardiogram and/or RVOT conduit obstruction with a mean gradient of 35 mmHg or higher by transthoracic echocardiogram. Patients were treated between April 2008 and November 2014. The database supplement reflects data collected through March 2015 and includes 81 patients. Data from this clinical study were the basis for the PMA decision for the pulmonary valve implantation indication (Clinical Trails 2020).

Kenny et al. (2018) reported 3-year outcomes of the COMPASSION study. At the 3-year follow-up, 69 implantations in 81 patients accounted for 57 of 63 eligible individuals. Pulmonary stenosis (7.6%), regurgitation (12.7%), or both (79.7%) indicated implantation. 93.5% of patients improved in NYHA functional class. Peak conduit gradient reduced from 37.5 ± 25.4 to 17.8 ± 12.4 mmHg and mean right ventricular systolic pressure decreased from 59.6 ± 17.7 to 42.9 ± 13.4. 91.1% had mild regurgitation The SAPIEN valve had reduced rates of all-cause mortality, reintervention, endocarditis, and stent fractures at 3 years in patients with moderate to severe pulmonary regurgitation and/or RVOT conduit obstruction. 98.4% of patients were all-cause mortality-free at 3 years. At 3 years, 93.7% were reintervention-free and 97.1% endocarditis-free. The stents were unbroken. At 3-year follow-up, Edwards SAPIEN THV TPV replacement showed good valve performance and clinical outcomes.

Harmony Heart Valve

The FDA assessed the safety and effectiveness of the Harmony TPV device through a prospective, non-randomized, multi-center clinical study. The Harmony TPV was implanted in 70 individuals in the study (FDA 2021). Seventy individuals with severe pulmonary regurgitation and a clinical justification for pulmonary artery conduit or prosthetic

valve surgery participated in the experiment. Twenty were in the feasibility phase, 31 in the pivotal phase with the current TPV 22 and TPV 25 devices, and 19 in the pivotal cohort with an earlier version (cTPV 25). Technical success was achieved in 95.7% of implantations, and 89.2% of patients met the clinical criterion of satisfactory hemodynamic function at 6 months without reintervention. At 6 months, 1.7% of patients had severe pulmonary regurgitation down from 84.4% at baseline. Four out of seventy patients (5.7%) needed TPV ex-plantation, two of whom were in the feasibility phase and two with a previous device. No explants or deaths occurred with the existing devices in the crucial research. The 36-item short form survey showed the greatest improvement in physical functioning and role restrictions owing to physical health. All patients were scheduled for follow-up exams at the start of the trial, at implant operation, discharge, and post-implant at 1-month, 6-months, and annually for five years. As part of the post-approval study, the follow-up is now 10 years. No procedure- or device-related death within 30 days after the implant was the primary safety endpoint, which 100% of patients met. At 6 months, the key efficacy outcome was the proportion of patients with no additional surgical or interventional procedures linked to the device and adequate heart blood flow function. The primary efficacy endpoint was met by 89.2% of patients with echocardiography data. AEs observed during the clinical trial included irregular or abnormal heart rhythms (23.9%, including 14.1% ventricular tachycardia), leakage around the valve (8.5%, including 1.4% major leakage), minor bleeding (7.0%), pulmonary valve narrowing (4.2%), and implant movement (4.2%).

Other Valve Devices

There are other valves such as the Venus P-valve and the Pulsta TPV among others which are not currently approved for use in the United States.

Systematic Reviews

Ribeiro et al. (2020) conducted a meta-analysis and systematic review of 18 nonrandomized comparative studies of SPVI and TPVI. There were no RCTs identified. There were no significant differences in age or gender between the groups, but there were significant differences in anatomic and functional characteristics. Patients undergoing transcatheter pulmonary valve replacement (TPVR) were more likely to have pulmonary stenosis (29% vs 12%), whereas those undergoing SPVR were more likely to have pulmonary regurgitation (57% vs 22%). There were significant numerical differences in the presence of a native ventricle outflow tract/transannular patch (TPVR: 16%, SPVR: 60%), but this difference did not reach statistical significance. A meta-analysis found that the percutaneous approach reduced peri-procedural complications (16.5% vs 41.3%, p = 0.01) and length of hospital stay (- 4.32 days), but it increased the risk of infective endocarditis (5.8% vs 2.7%). There were no significant differences in early mortality, late mortality, or the need for reintervention. The difference in baseline characteristics between the two groups, as well as the possibility of selection bias, limited interpretation. The authors noted that several patients underwent SPVR because they were not candidates for TPVR due to RVOT anatomy and/or other cardiac defects.

Chatterjee et al. (2017) conducted a systematic review and meta-analysis of observational studies evaluating transcatheter pulmonary valve implantation. Nineteen studies (n = 1044) with 5 or more patients and at least 6 months of follow-up were included (Note: Previously cited studies Cheatham et al. 2015, Armstrong et al. 2014, Butera et al. 2013 and Eicken et al. 2011 are included in this review). Thirteen studies used the Melody valve, three used the Edwards Sapien or Sapien XT valves, and three used both the Melody and Edwards valve systems. The procedural success rate was 96.2%, with a conduit rupture rate of 4.1% and a coronary complication rate of 1.3%. The authors reported favorable updated estimates of procedural and follow-up outcomes after transcatheter pulmonary valve implantation. The authors also stated that widespread use of pre-stenting has improved long-term outcomes in these patients.

National and Specialty Organizations

The **American College of Cardiology (ACC), American Heart Association (AHA)** and six other societies published comprehensive guidelines on the management of patients with CHD (Stout et al. 2018). Recommendations for treatment included pulmonary stenosis, pulmonary regurgitation and tetralogy of Fallot.

ACC/AHA Guidelines on the Management of Patients with Tetralogy of Fallot		
Recommendation	**Strength of Recommendation**	**Level of Evidence**
Pulmonary valve replacement (surgical or percutaneous) for relief of symptoms is recommended for patients with repaired tetralogy of Fallot and moderate or	Strong	Non-randomized (moderate quality

greater pulmonary regurgitation with cardiovascular symptoms not otherwise explained.		evidence)
Pulmonary valve replacement (surgical or percutaneous) is reasonable for preservation of ventricular size and function in asymptomatic patients with repaired tetralogy of Fallot and ventricular enlargement or dysfunction and moderate or greater pulmonary regurgitation	Moderate	Non-randomized (moderate quality evidence)
Surgical pulmonary valve replacement may be reasonable for adults with repaired tetralogy of Fallot and moderate or greater pulmonary regurgitation with other lesions requiring surgical interventions.	Weak	Consensus of expert opinion
Pulmonary valve replacement, in addition to arrhythmia management, may be considered for adults with repaired tetralogy of Fallot and moderate or greater pulmonary regurgitation and ventricular tachyarrhythmia.	Weak	Consensus of expert opinion

International Guidelines

The **National Institute for Health and Care Excellence (NICE)** published an Interventional Procedures Guidance (IPG436): *Percutaneous pulmonary valve implantation for right ventricular outflow tract dysfunction* which indicates that the evidence on PPVI for RVOT dysfunction shows good short-term efficacy (NICE 2013). There is little evidence on long-term efficacy, but it is well documented that these valves may need to be replaced in the longer term. Regarding safety, there are well-recognized complications, particularly stent fractures in the longer term, which may or may not have clinical effects. Patients having this procedure are often in poor health and might otherwise need open heart surgery (typically re-operative) with its associated risks. The procedure should be performed only in specialist units and with arrangements in place for cardiac surgical support in the event of complications. Patient selection should be conducted by a multidisciplinary team including a cardiologist with a special interest in congenital heart disease, an interventional cardiologist, and a cardiothoracic surgeon with a special interest in CHD. Additionally, this is a technically challenging procedure that should only be performed by clinicians who have received training in interventional cardiology and CHD.

European Society of Cardiology (ESC). TPVI is an alternative to open heart surgery for patients with RVOT conduit stenosis/regurgitation, according to the ESC guidelines for the management of adult congenital heart disease. Transcatheter replacement, when technically feasible, provides outcomes comparable to surgical pulmonary valve replacement and is intended to extend the conduit's lifetime, thereby decreasing the number of reoperations over the lifetime of a patient (Baumgartner et al. 2021).

The **European Society of Cardiology (ESC) / Association for European Pediatric Cardiology (AEPC)** 2010 guidelines for the management of adult CHD include the following indications for surgical intervention or PPVI in patients with right ventricular to pulmonary artery conduits (Baumgartner et al. 2010):

- Intervention is recommended in symptomatic patients with right ventricular systolic pressure >60 mmHg (TR velocity >3.5 m/s; may be lower in cases with reduced flow) and/or moderate to severe pulmonic regurgitation.
- Intervention is suggested in asymptomatic patients with severe right ventricular outflow tract obstruction and/or severe pulmonic regurgitation when at least one of the following criteria is present:
  - Decrease in exercise capacity on cardiopulmonary exercise testing
  - Progressive right ventricular dilation
  - Progressive right ventricular systolic dysfunction
  - Progressive TR (at least moderate)
  - Right ventricular systolic pressure >80 mmHg (TR velocity >4.3 m/s)
  - Sustained atrial/ventricular arrhythmias

SUPPLEMENTAL INFORMATION

Table 1. Regulatory Status of TPVI 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.
Harmony™ TPV	Medtronic	Mar 2021	P200046	Pulmonary valve for pediatric and adult patients with severe pulmonary regurgitation.

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

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology) Code

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

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

12/13/2023 Policy reviewed. No changes to coverage criteria. Updated summary of medical evidence and references.
12/14/2022 Policy reviewed. No changes to coverage criteria. Updated references.
12/08/2021 Policy reviewed and revised. IRO Peer Review: IRO reviews, 11/30/2021; 12/1/2021. Practicing physician board-certified in Pediatric Cardiology; Interventional Cardiology. Updated references, clinical studies, and content of policy. Updates include:
- Added diagnosis of 'Dysfunctional non-conduit, patch-repaired RVOT' indication
- Added Harmony™ TPV (Medtronic) approved in March 2021 for the indication of pulmonary valve for pediatric and adult patients with severe pulmonary regurgitation
- Previous criteria were specific to Melody TPV (MedTronic) and Edwards SAPIEN™ XT Transcatheter Heart Valve; revised criteria to address TPVI devices
- Revised and updated 'Summary of Medical Evidence' section
- Added 'Table 1: Regulatory Status of TPVI Devices' in Supplemental Information section
- Added pregnancy to exclusion criteria
- Added exceptions statement for case-by-case review
- Assessed Sapien S3 valve for inclusion in medical necessity as percutaneous transcatheter pulmonary valve replacement, however its long-term effectiveness has not been established. References addressing Sapien S3 valve, including two studies reported off-label PPVI with the SAPIEN S3 valve with short follow-up, added to references section.

12/09/2020 Policy reviewed. No changes to coverage criteria. Updated references.
12/10/2019 Policy reviewed. Updated with inclusion of the Edwards Sapien XT Transcatheter Heart Valve FDA approval. Updated description of PPVI procedure, revised coverage criteria to include device specific criteria, updated contraindications section, added new references and clinical trial information and updated guideline information. IRO Peer Review: 10/13/2019. Practicing physician board certified in Pediatrics, Pediatric Cardiology.
07/10/2018 Policy reviewed. No changes to coverage criteria. Updated references.
09/19/2017 Policy reviewed. No changes to coverage criteria. Updated references.
11/2016 Policy reviewed. No changes to coverage criteria. Medical evidence summary and references sections updated.
12/16/2015 Policy reviewed. No changes.
10/30/2013 New policy. IRO Peer Review: 9/20/2013. Practicing physician board certified in Pediatrics, Pediatric Cardiology.

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