Cigna Medical Coverage Policy

Subject **Transcatheter Heart Valve Procedures**

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Coverage Policy

Cigna covers transcatheter aortic valve implantation using a U.S. Food and Drug Administration (FDA) approved device as medically necessary when the following device-specific criteria are met:

- **Edwards SAPIEN™ Transcatheter Heart Valve [Edwards Lifesciences, LLC, Irvine, CA] for ALL of the following:**
  - severe symptomatic calcified native aortic valve stenosis without severe aortic insufficiency
  - ejection fraction > 20%
  - EITHER of the following::
    - inoperable as determined by the heart team, including an experienced cardiac surgeon and a cardiologist,, and existing comorbidities would not preclude the expected benefit from correction of the aortic stenosis
  - operative candidate for aortic valve replacement but with a Society of Thoracic Surgeons predicted operative risk score ≥ 8%, or are judged by the heart team to be at a ≥ 15% risk of mortality for surgical aortic valve replacement

- **Edwards SAPIEN™ XT Transcatheter Heart Valve [Edwards Lifesciences, LLC, Irvine, CA] OR Medtronic CoreValve System Transcatheter Aortic Valve [Medtronic CoreValve LLC, Santa Rosa, CA]) for ALL of the following:**

  - symptomatic heart disease due to severe native calcific aortic stenosis (i.e., aortic valve area ≤ 1.0 cm^2 or aortic valve area index ≤ 0.6 $cm2/m^2$, a mean aortic valve gradient of ≥ 40mm Hg, or a peak aortic-jet velocity of ≥ 4.0 m/s)
  - appropriate native anatomy

- judged by a heart team, including a cardiac surgeon, to be at high (or greater) risk for open surgical therapy (i.e., Society of Thoracic Surgeons operative risk score ≥ 8% or at a ≥ 15% risk of mortality at 30 days).

Cigna does not cover transcatheter aortic valve implantation for any other indication because it is considered experimental, investigational or unproven.

Cigna covers transcatheter pulmonary valve implantation using the Medtronic Melody® Transcatheter Pulmonary Valve (Medtronic, Inc., Santa Ana, CA) as medically necessary when used in accordance with the U.S. FDA's Humanitarian Device Exemption (HDE) requirements when BOTH of the following criteria are met:

- 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
- dysfunctional RVOT conduit with a clinical indication for intervention, and EITHER of the following:
    - moderate or greater regurgitation
    - stenosis, with mean RVOT gradient ≥ 35 mmHg

Cigna does not cover transcatheter pulmonary valve implantation for any other indication because it is considered experimental, investigational or unproven.

Cigna does not cover percutaneous mitral valve repair (e.g., MitraClip Clip Delivery System (MitraClip CDS) (Abbott Vascular, Menlo Park, CA) because it is considered experimental, investigational or unproven.

General Background

Aortic Valve

Valvular aortic stenosis is a narrowing or obstruction of the aortic valve that prevents the valve leaflets from opening normally. In adults, obstruction usually develops gradually over many years during which the left ventricle adapts to the systolic pressure overload with progressive hypertrophy resulting in diastolic dysfunction, reduced coronary reserve, myocardial ischemia, and eventually, depressed contractility resulting in left ventricular systolic dysfunction. Heart failure or sudden death ultimately occurs in some patients. Generally patients are free from cardiovascular symptoms (i.e., angina, syncope, and heart failure) until late in the course of the disease. Once symptoms occur, however, the prognosis is poor; the interval between onset of symptoms and death is approximately two years in patients with heart failure, three years in those with syncope, and five years in those with angina. Medication is prescribed to alleviate symptoms. Surgical aortic valve replacement reduces symptoms and improves survival in patients with severe aortic stenosis, and is considered the surgical treatment of choice for most adults. Conventional valve replacement requires three to six hours of general anesthesia, a sternotomy, and heart-lung bypass. Patients are typically hospitalized for five to six days, and require twelve weeks for recovery. As many as a third of patients with severe heart valve disease are considered too high risk for conventional surgical valve replacement. Transcatheter aortic valve implantation (TAVI), also referred to as transcatheter aortic valve replacement (TAVR) or percutaneous aortic valve replacement, has been proposed as a less invasive alternative to open heart surgery.

Several techniques for TAVI have been described in the literature. In early stages of development, valves were delivered via the femoral vein using an antegrade approach, with the catheter directed to the heart thorough the venous system in the direction of blood flow. With this procedure, a catheter is passed through the septum to reach the aortic valve. More recently, valves have been implanted through the heart wall (i.e., transapical approach), and via the femoral artery using a retrograde approach, against the direction of blood flow. The transapical procedure is performed by a cardiac surgeon, using direct left ventricular apical puncture though a small thoracotomy, and does not require a sternotomy. Retrograde approaches via the subclavian or axillary artery or the ascending aorta may also be used (Williams, 2010; ECRI, 2012, FDA 2013).

U.S. Food and Drug Administration (FDA)–Edwards SAPIEN™ Transcatheter Heart Valve (Edwards Lifesciences, LLC, Irvine, CA): The Edwards SAPIEN™ Transcatheter Heart Valve model 9000TFX, 23 and

26 mm, and accessories (RetroFlex™ 3 Delivery System, models 9120FS23 and 9120FS26 RetroFlex Balloon Catheter, models 9120BC20 and 9120BC23 Crimper, models 9100CR23 and 9100CR26) received FDA approval through the PMA process on November 2, 2011. The SAPIEN Transcatheter Heart Valve was approved for transfemoral delivery in patients with severe symptomatic native aortic valve stenosis, determined by a cardiac surgeon to be inoperable for open aortic valve replacement and in whom existing comorbidities would not preclude the expected benefit from correction of the aortic stenosis.

On October 19, 2012, an additional PMA approval was granted, allowing a transapical delivery approach in addition to a transfemoral approach. Indications for use were also expanded. On September 23, 2013, the FDA approved removal of the access approach from the device labeling. As revised, the device is indicated for patients with severe symptomatic calcified native aortic valve stenosis without severe aortic insufficiency and with ejection fraction > 20% who have been examined by a heart team including an experienced cardiac surgeon and a cardiologist and found to be: 1) inoperable and in whom existing co-morbidities would not preclude the expected benefit from correction of the aortic stenosis; or 2) be operative candidates for aortic valve replacement but who have a predicted operative risk score ≥ 8% or are judged by the heart team to be at a ≥ 15% risk of mortality for surgical aortic valve replacement.

On June 16, 2014, The Edwards SAPIEN XT™ Transcatheter Heart Valve model 9300TFX, 23, 26, and 29 mm, and accessories received FDA PMA approval. This next-generation, lower profile system includes a 29 mm valve size for patients with a larger native annulus. The device is indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis (aortic valve area ≤ 1.0 cm^2,or aortic valve area index ≤ 0.6 cm^2, /m^2, a mean aortic valve gradient of ≥ 40 mm/Hg, or a peak aortic-jet velocity of ≥ 4.0 m/s), and with native anatomy appropriate for the 23, 26, or 29 mm valve system, who are judged by a heart team, including a cardiac surgeon, to be at high or greater risk for open surgical therapy (i.e., Society of Thoracic Surgeons operative risk score ≥ 8% or at a ≥ 15% risk of mortality at 30 days).

Medtronic CoreValve™ (MCS) System Transcatheter Aortic Valve (TAV) (Medtronic CoreValve LLC, Santa Rosa, CA): The MCS TAV models MCS-P4-23-AOA (23 mm CoreValve Evolut), MCS-P3-26-AOA (26 mm), MCS-P3-29-AOA (29 mm) and MCS-P3-31-AOA (31 mm); Delivery Catheter System (DCS), Models DCS-C4-18FR and DCS-C4-18FR-23); and Compression Loading System Model CLS-3000-18FR received FDA approval through the PMA process on January 17, 2014.

According to the FDA labeling, the Medtronic CoreValve™ system is indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis (aortic valve area ≤0.8 cm2, a mean aortic valve gradient of >40 mm Hg, or a peak aortic-jet velocity of >4.0 m/s) and with native aortic annulus diameters between 18 and 29 mm who are judged by a heart team, including a cardiac surgeon, to be at extreme risk or inoperable for open surgical therapy (predicted risk of operative mortality and/or serious irreversible morbidity ≥50% at 30 days).

In a PMA supplement approved on June 12, 2014, the FDA expanded the indications for the CoreValve system. According the revised approval, the CoreValve is indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis (aortic valve area ≤ 1.0 cm^2 or aortic valve area index ≤ 0.6 cm^2/m^2, a mean aortic valve gradient of ≥ 40mm Hg, or a peak aortic-jet velocity of ≥ 4.0 m/s) and with native anatomy appropriate for the 23, 26, 29, or 31 mm valve system who are judged by a heart team, including a cardiac surgeon, to be at high or greater risk for open surgical therapy (i.e., Society of Thoracic Surgeons operative risk score ≥ 8% or at a ≥ 15% risk of mortality at 30 days).

Literature Review–Transcatheter Aortic Valve Implantation: Abdel-Wahab et al. (2014) conducted a multicenter randomized trial to assess the comparative performance of the balloon-expandable device and the self-expandable device regarding overall device success. Patients with severe aortic stenosis and an anatomy suitable for the transfemoral TAVR procedure were randomly assigned to receive a balloon-expandable valve (Edwards Sapien XT) or a self-expandable valve (Medtronic CoreValve). The primary endpoint was device success; a composite endpoint including successful vascular access and deployment of the device and retrieval of the delivery system, correct position of the device, intended performance of the heart valve without moderate or severe regurgitation, and only one valve implanted in the proper anatomical location. Device success occurred in 116 of 121 patients (95.9%) in the balloon-expandable group and 93 of 120 patients (77.5%) in the self-expandable valve group (relative risk 1.24, 95% CI 112-137, p<.001). The difference in success was attributed to a significantly lower frequency of residual moderate to severe aortic regurgitation (4.1% vs. 18.3%,

p<.001) and less frequent need to implant more than one valve in the balloon expandable group. There were no significant differences in cardiovascular mortality, bleeding, or vascular complications. Placement of a new permanent pacemaker was less frequent in the balloon-expandable valve group (17.3% vas. 37.6%, p=.001).

Adams et al. (2014) conducted a multicenter, randomized non-inferiority trial to compare transcatheter aortic valve replacement (TAVR) using a self-expanding transcatheter aortic valve bioprosthesis (CoreValve) to surgical aortic valve replacement (n=795). Patients with severe aortic stenosis and symptoms of NYHA class II or higher were eligible if considered to be at increased risk for undergoing surgical AVR. Patients were determined to be at increased surgical risk if two cardiac surgeons and one interventional cardiologist estimated that the risk of death within 30 days after surgery was 15% or more and the risk of death or irreversible complications within 30 days was less than 50%. In the as-treated analysis, the primary end point, rate of death from any cause at one year was significantly lower in the TAVR group than in the surgical group (14.2% vs. 19.1%, p<0.001 for noninferiority, p=0.04 for superiority). Results were similar in the intention to treat analysis. TAVR was non-inferior in terms of echocardiographic indexes of valve stenosis, functional status, and quality of life. Major vascular complications and permanent pacemaker implantations were significantly more frequent in the TAVR group, while bleeding, acute kidney injury, and new onset or worsening atrial fibrillation were significantly more common the surgical group. There were five cases of cardiac perforation in the TAVR group, and rates of paravalvular regurgitation were significantly higher in the TAVR group at all points.

Popma et al. (2014) conducted a multicenter nonrandomized study to evaluate the safety and efficacy of the CoreValve for treatment of severe aortic stenosis in patients at extreme risk for surgery (n=489). The primary endpoint was a composite of all-cause mortality or major stroke at 12 months, compared to a pre-specified objective performance goal (OPG). The OPG was determined based on a weighted meta-analysis performed of seven balloon aortic valvuloplasty studies and an analysis of inoperable patients in the PARTNER trial. At 12 months, the rate of all-cause mortality or major stroke was 26.0% compared to 43% with the OPG. The rates of all-cause mortality at 30 days and 12 months were 8.4% and 24.3%, respectively, and the rates of major stroke at 30 days and 12 months were 2.3% and 4.3%, respectively.

Leon et al. (2010) evaluated transcatheter aortic valve implantation for aortic stenosis in patients in the PARTNER (Placement of AoRTic TraNscathetER Valves) trial who were not suitable candidates for surgery (cohort B, n=358). In this randomized, unblinded, controlled multi-center trial patients with severe aortic stenosis, considered by surgeons not to be suitable candidates for surgery, were randomly assigned to standard therapy, including balloon valvuloplasty (n=179), or transfemoral transcatheter implantation of the Edwards SAPPIEN heart-valve system (n=179). At one year, the rate of death from any cause (the primary endpoint) was 30.7% with TAVI vs. 50.7% with standard therapy (p<0.001). The rate of the composite end point of death from any cause or repeat hospitalization was 42.5% with TAVI vs. 71.6% with standard therapy (p<0.001). The rate of cardiac symptoms (New York Heart Association class III or IV) was lower in patients in the TAVI group than in the standard therapy group (25.2% vs. 58.0% (p<0.001). However, at 30 days, TAVI was associated with a higher incidence of major strokes (5.0% vs. 1.1%, p=0.06) and major vascular complications (16.2% vs. 1.1%, p<0.001). The authors acknowledged limitations of the study, including the fact that important patient subgroups were excluded, including those requiring treatment of coronary stenosis and those with severe peripheral vascular disease, and also noted that an assessment of the durability and long-term clinical safety and effectiveness of the bioprosthetic valves will require more prolonged follow-up. The authors stated that the results of this study cannot be extrapolated to other patients with aortic stenosis. Additional randomized trials are needed to compare TAVI with aortic valve replacement among high-risk patients with aortic stenosis for whom surgery is a viable option and among low risk patients with aortic stenosis.

Two-year outcomes of transcatheter aortic valve replacement in inoperable patients in the PARTNER trial (Cohort B) were reported by Makkar et al. (2012). The rates of death at two years were 43.3% n the TAVR group and 68.0% in the standard-therapy group (p < 0.001). The corresponding rate of cardiac death were 31.0% and 62.4% (p < 0.001).The survival advantage seen with TAVR at one year remained significant in patients who survived beyond the first year (p=0.02). The incidence of stroke was higher after TAVR then with standard therapy (13.8% vs. 5.5%, p=0.01), due in the first 30 days to more ischemic events, and beyond 30 days, to more hemorrhagic strokes. Rehospitalization rates were 35.0% in the TAVR group and 72.5% in the standard therapy group. TAVR was also associated with improved functional status (p <0.001).

In a parallel study (PARTNER Cohort A), Smith et al. (2011) randomly assigned 699 high-risk patients with severe aortic stenosis to TAVI using the SAPIEN heart valve system with either a transfemoral or transapical

approach (n=348) or surgical replacement (n=351). The rates of death from any cause were 3.4% in the TAVI group and 6.5% in the surgical group at 30 days (p=0.07) and 24.2% vs. 26.8%, respectively, at one year. (p=0.07). The rates of stroke were 3.8% in the TAVI group and 2.1% in the surgical group at 30 days (p=0.20) and 5.1% vs. 2.4%, respectively, at one year (p=0.07). Major vascular complications were significantly more frequent with TAVR at 30 days (11.0% vs. 3.2%, p<0.001). Adverse events occurring more frequently after surgical replacement included major bleeding (9.3% vs. 19.5%, p<0.001) and new-onset atrial fibrillation 8.6% vs. 16.0%). More patients in the TAVI group had an improvement in symptoms at 30 days, but there was no significant difference between groups at one year.

Limitations of the study included an unexpected frequency of withdrawals and decisions to forego the procedure in patients assigned to surgical replacement, and approximately 5% of patients assigned to TAVI did not undergo the procedure. A balanced perspective on early outcomes therefore requires analysis of both the intention-to-treat and as-treated populations. However, for rates of death, neurological events, and procedural hazards, the two groups did not differ significantly in the as-treated population. The authors stated that in the absence of long-term follow-up data, recommendations for individual patients must balance the appeal of avoiding the known risks of open heart surgery with the transcatheter approach, which has different and less well understood risks, particularly regarding stroke. Additional randomized controlled trials are needed to determine whether transcatheter replacement is equivalent to surgical replacement in terms of clinical benefit for lower-risk patients with aortic stenosis.

Kodali et al. (2012) reported two year outcomes following TAVR or surgical aortic valve replacement in the high-risk patients with severe aortic stenosis in the PARTNER trial, Cohort A, (described above) who could undergo surgery (n=699). Patients at 25 centers were randomly assigned to surgical aortic-valve replacement (n=351) or TAVR (n=348). Patients assigned to TAVR were treated by either the transfemoral (n=244) or transapical (n=104) approach on the basis of whether peripheral arteries could accommodate the large sheath required. Patients assigned to surgical replacement were stratified according to whether a transfemoral or transapical approach would have been used. At two years there was no significant difference in mortality between the groups; 33.9% in the TAVR group and 35% in the surgery group (p=0.78). Paravalvular regurgitation was more frequent after TAVR (p < 0.001) and even mild regurgitation was associated with increased late mortality. The two treatments were similar in terms of reduction in cardiac symptoms and improved hemodynamics, and while there was an early increase in the risk of stroke with TAVR, this was attenuated over time.

Rodes-Cabau et al. (2012) conducted a Canadian multicenter study of 339 patients considered to be inoperable or at very high surgical risk (Society of Thoracic Surgeons score: 9.8 ± 6.4%) who underwent TAVI with the Edwards valve (transfemoral: 48%, transapical: 52%). Follow-up was available in 99% of the patients. At a mean follow-up of 42 ±15 months 188 patients (55.5%) had died. The causes of late death (152 patients) were noncardiac (59.2%), cardiac (23.0%), and unknown (17.8%). Chronic obstructive pulmonary disease, chronic kidney disease, chronic atrial fibrillation, and frailty were predictors of late mortality. A mild decrease in valve area occurred at two year follow-up (p < 0.01), but was not clinically significant, and no further reduction in valve area was observed up to four years follow-up. There were no changes in residual aortic regurgitation and no cases of structural valve failure observed during the follow-up period.

Reynolds et al. (2011) conducted a prospective quality of life substudy in the PARTNER trial (detailed above). Health-related quality of life was assessed at baseline and at one, six and twelve months using the Kansas City Cardiomyopathy Questionnaire (KCCQ) and the 12-item Short Form-12 General Health Survey (SF-12). At baseline, mean KCCQ summary scores (35 ± 20) and SF-12 physical summary scores (28 ± 7)) were significantly depressed. The KCCQ summary scores improved in both groups, but improvement was greater after TAVI compared to control at 1 month (mean between-group difference, 13 points, p<0.001), six months (mean difference, 21 points; p<0.001) and twelve months (mean difference, 26 points; p<0.001)). At twelve months, TAVI patients also reported higher SF-12 physical and mental health scores with mean differences compared with control of 5.7 and 6.4 points, respectively (p<0.001 for both comparisons).

A prospective single-center registry (Wenaweser et al., 2011) assessed the role of TAVI compared to medical treatment and surgical aortic valve replacement (SAVR) in patients with severe aortic stenosis at increased surgical risk (n=442). Patients with severe aortic stenosis (age 81.7 ± 6 years, mean logistic European System for Cardiac Operative Risk Evaluation: 22.3 ± 14.6%) were allocated to medical treatment (n=78), SAVR (n=107), or TAVI (n=257) on the basis of a comprehensive evaluation protocol. Baseline characteristics of patients allocated to medical treatment and TAVI were similar, while patients allocated to SAVR were younger

and had a lower predicted peri-operative risk. Unadjusted rates of all-cause mortality at 30 months were lower for SAVR (22.4%) and TAVI (22.6%) compared to medical treatment (61.5%). Medical treatment, older age, peripheral vascular disease, and atrial fibrillation were significantly associated with all-cause mortality at 30 months in multivariate analysis.

Moat et al. (2011) published data from the United Kingdom Transcatheter Aortic Valve Implantation (U.K. TAVI) Registry. Data were collected prospectively on 870 patients undergoing 877 TAVI procedures through December 2009. Survival was 92.9% at 30 days, 78% at one year, and 73.7% at two years. In univariate analysis, survival was significantly adversely affected by renal dysfunction, presence of coronary artery disease, and a nontransfemoral approach. In the multivariate model, left ejection fraction of < 30%, presence of moderate/sever aortic regurgitation, and chronic obstructive pulmonary disease remained the only independent predictors of mortality.

ECRI
A 2014 ECRI Emerging Technology Evidence Report, Transcatheter Aortic Valve Implantation Using the Sapien Valve for Treating Severe Aortic Stenosis, evaluated clinical studies that compared the Sapien device to standard medical therapy or to aortic valve replacement (AVR), and provided the following findings to each of the key questions:

Key Question 1: How does transcatheter aortic valve implantation (TAVI) compare to standard medical therapy for treating inoperable aortic valve stenosis in terms of all-cause death, cardiac-death, and quality of life (QOL) at 30 days, one-year, and five-year follow-up?

Only one randomized controlled trial reported on comparative outcomes in inoperable patients between Sapien TAVI and standard medical therapy. Rates of death were similar at 30 days, but TAVI significantly reduced mortality rates at one year and at two years. Findings for QOL suggested that TAVI provided substantial benefits over standard medical therapy.

Key Question 2: How does TAVI compare to AVR for treating high-risk patients with aortic valve stenosis in terms of all-cause death, cardiac death, and QOL at 30 days, one year, and five -year follow-up?

Evidence from eight studies suggests that Sapien TAVI and AVR have similar death rates at 30 days, one year, and two years. Three studies reported on QOL, and findings were inconsistent across studies; two found improvements in the TAVI group, and one found no significant difference between the TAVI and AVR groups in functional status at 30-days follow-up.

Key Question 3: How does TAVI compare to AVR for treating high-risk patients with aortic valve stenosis in terms of perioperative outcomes of blood loss, need for transfusion, postoperative pain, and length of hospital stay?

Although findings were somewhat inconsistent across studies, perioperative outcomes with Sapien TAVI appear to be either equivalent or better than with AVR.

Key Question 4: What adverse events (AEs), including stroke and other vascular complications, are associated with TAVI, and how do AEs for TAVI compare to AEs for either standard medical therapy or AVR?

AEs associated with Sapien TAVI included stroke, major vascular complications, renal failure, myocardial infarction, conversion to open-heart surgery, major bleeding, multisystem organ failure, paravalvular regurgitation, pacemaker implantation, aortic regurgitation, valve embolism, coronary obstruction, endocarditis, valve malpositioning, rehospitalization, reintervention, circulatory failure, and wound infection.

Only one study compared TAVI to medical therapy and found that TAVI had higher rates of stroke, major vascular complications, and major bleeding. While there was no significant difference between groups at 30 days in cardiac reintervention (balloon aortic valvuloplasty and aortic-valve replacement), the medical therapy group had significantly higher rates of cardiac reintervention at both one- and 2-years follow-up.

Eight studies compared TAVI to AVR. Four of these studies compared transapical TAVI to AVR and found no significant difference between these groups for any of the AEs. The other four studies compared transfemoral

and transapical TAVI to AVR. All four studies reported on stroke, and one found that TAVI had higher rates. Three of these studies reported on major vascular complications, and two found that TAVI had higher rates. Three reported on renal failure, and one found that TAVI had higher rates. One study reported on grade of paravalvular regurgitation and found that TAVI had higher rates. Two studies reported on major bleeding, and one found that AVR had higher rates.

Professional Societies/Organizations: An ACCF/AATS/SCAI/STS Expert Consensus Document on Transcatheter Aortic Valve Replacement (TAVR) (Homes et al., 2012, in press) was published with involvement of twelve professional societies to examine the current state of the evidence, facilitate integration of this technology as one of the available therapeutic options for patients with aortic valvular stenosis, and enable responsible adoption and diffusion of this promising technology. The authors note that the document is focused on published data; but there is a single completed randomized trial, although others are in progress or planned. Much of the data is therefore based upon information from studies and registries, which are frequently retrospective and include self-reported clinical events rather than adjudicated events.

The expert consensus document states that TAVR offers new and potentially transformational technology for patients with severe aortic valvular stenosis who are either extremely high-risk candidates or inoperable for surgical aortic valve replacement (AVR) or who are inoperable due to associated comorbidities. In the future, this technology may be utilized in lower risk surgical candidates.

The consensus document summarizes current recommendations for treatment of patients with aortic stenosis, including surgical aortic valve replacement, transcatheter aortic valve replacement, balloon aortic valvuloplasty, and medical therapy (refer to Appendix A, below).The document provides the following observations and recommendations regarding transcatheter aortic valve replacement:

- Complex Technology: Although the technique and equipment continue to evolve, TAVR is a complex procedure with many interlocking steps that require meticulous attention to achieve optimal results and minimize complications.

- Team-Based Approach: A foundational requirement of TAVR is a team-based approach to patient care. Given the high-risk profile of patients, who often have multiple comorbidities, as well as the technical complexity of the procedure involved, this team-based care will need to include multiple contributors at different stages in the process but will be mainly centered around the primary cardiologist, the cardiovascular surgeon, and the interventional cardiologist. Patients and families must be included in the care team. Other team members will include cardiac anesthesiologists, heart failure specialists, structural heart disease physicians, imaging specialists and the nursing care team, among others.

- Patient Selection: In adults with severe, symptomatic, calcific stenosis of a trileaflet aortic valve who have aortic and vascular anatomy suitable for transcatheter aortic valve replacement (TAVR) and a predicted survival >12 months:

    - TAVR is recommended in patients with prohibitive surgical risk.
    - TAVR is a reasonable alternative to surgical aortic valve replacement (AVR) in patients at high surgical risk

Prohibitive surgical risk is defined as

- An estimated 50% or greater risk of mortality or irreversible morbidity at 30 days (as assessed by one cardiologist and two cardiothoracic surgeons), or other factors such as frailty, prior radiation therapy, porcelain aorta, and severe hepatic or pulmonary disease.

Suitable aortic and vascular anatomy is defined as:

- Both aortic annulus size and valve plane to coronary ostium height suitable for placement of an available TAVR.
- Adequate vascular access for passage of the TAVR system (femoral iliac, subclavian, axillary) or suitability for an apical implantation approach.

TAVR is not currently recommended because of limited available information in adults who have:

- An acceptable surgical risk for conventional surgical aortic valve replacement
- Known bicuspid aortic valve
- Failing bioprosthetic aortic valve
- Severe mitral annular calcification or severe mitral regurgitation
- Moderate aortic stenosis
- Other (e.g., severe aortic regurgitation and subaortic stenosis)

In the above groups, additional scientific data will need to be collected to ascertain risk/benefit ratio prior to integration into routine clinical care.

Summary–Transcatheter Aortic Valve Implantation: Transcatheter aortic valve implantation (TAVI) also referred to as transcatheter aortic valve replacement (TAVR) is a relatively new technology that has been proposed as a less invasive alternative to conventional surgical valve replacement. Conventional valve replacement requires general anesthesia, a sternotomy, and heart-lung bypass. A significant percentage of patients with severe aortic stenosis are not considered suitable candidates for surgical aortic valve replacement due to the presence of significant comorbidities. Although evidence published to date is limited, and long-term outcomes have not been fully defined, Transfemoral TAVI may be a reasonable alternative to open heart surgery in carefully selected patients with severe symptomatic aortic stenosis who meet the FDA-specified indications for use.

Pulmonary Valve

Transcatheter pulmonary valve implantation, also referred to as transcatheter pulmonary/pulmonic valve replacement, or percutaneous pulmonary/pulmonic valve implantation/replacement, has been explored for the treatment of pulmonary regurgitation and right ventricular outflow tract (RVOT) dysfunction. Transcatheter pulmonary valve implantation is performed under general anesthesia without cardiopulmonary bypass. A catheter system is inserted through a vein or artery, and a stent-mounted valve is positioned into the diseased valve or pulmonary conduit and deployed by balloon inflation RVOT dysfunction is usually associated with a congenital heart abnormality (e.g. Tetralogy of Fallot), and encompasses valve stenosis, valve incompetence (also referred to as valve insufficiency or regurgitation), and combined/mixed lesions. RVOT may cause hemodynamic instability, cyanosis, dyspnea, and reduced exercise tolerance. Depending on the severity and chronicity, RVOT may result in right ventricular hypertrophy and heart failure. Clinically significant untreated RVOT is a life-limiting condition.

Treatment of RVOT may include balloon valvuloplasty, although this may only be palliative. Repair or replacement of the valve is required for patients with severe stenotic lesions, predominantly incompetent lesions, or when prior valvuloplasty was unsuccessful. Pulmonary valve surgery requires cardiopulmonary bypass, and involves insertion of a pulmonary conduit, with or without a valve, to re-establish blood flow to the pulmonary artery. The use of valved conduits to reconstruct the right ventricular outflow tract in patients with congenital heart disease has allowed most such patients to survive to adulthood. Conduits require frequent replacement, however, due to patient growth and conduit degeneration. Placement of bare metal stents may be effective in postponing surgery, but is only useful in treating conduit stenosis, and may worsen pulmonary regurgitation. Most patients with stenosis also have some degree of regurgitation.

The goal of transcatheter pulmonary valve implantation, at a minimum, is to improve the hemodynamic function of the existing conduit, mitigate the adverse impact of pulmonary regurgitation and/or RVOT obstruction, and extend the longevity of the existing conduit and defer the need for conduit replacement. In some patients delaying surgical conduit reintervention may reduce the need for open heart surgeries required over the course of a lifetime. (Bonow: Braunwald's Heart Disease, 2011; NICE, 2007; FDA website).

U.S. Food and Drug Administration (FDA)–Medtronic Melody® Transcatheter Pulmonary Valve (Medtronic, Inc., Santa Ana, CA): The Medtronic Melody® Transcatheter Pulmonary Valve (Model PB10) and Medtronic Ensemble® Transcatheter Valve Delivery System (NU10).received FDA approval through the Humanitarian Device Exemption (HDE) program on January 25, 2010.

The Melody Transcatheter Pulmonary Valve 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 Right Ventricular Outflow Tract (RVOT) conduits with a clinical indication for intervention, and either:
    - Regurgitation: ≥ moderate regurgitation, or
    - Stenosis: mean RVOT gradient ≥ 35 mmHg

The Melody device consists of a segment of bovine jugular vein with a thinned down venous wall containing a native, central competent venous valve. This bovine valve is attached to a platinum/iridium stent with a length of 28 mm and diameter of 18 mm that can be crimped to a size of 6 mm and re-expanded up to 22 mm.

In order to receive HDE approval, a manufacturer must first be granted a Humanitarian Use Device (HUD) exemption by demonstrating that the device is designed to treat or diagnose a disease or condition that affects fewer than 4,000 people in the U.S. per year. Although data demonstrating the safety and probable clinical benefit are required for HDE approval, clinical trials evaluating the effectiveness of the device are not required. Following HDE approval, the hospital or health care facility institutional review board (IRB) must also approve the use of the device at that institution before the device may be used in a patient.

Literature Review–Transcatheter Pulmonary Valve Implantation: The Melody U.S. Clinical Trial (n=34) was designed to evaluate the safety, procedural success, and short-term effectiveness of the Melody transcatheter pulmonary valve in patients with dysfunctional right ventricular outflow tract conduits. Early results were published by Zahn et al. (2009). Patients underwent catheterization for intended Melody valve implantation at three centers between January and September, 2007. The mean age was 19.4 ± 7.7 years. Doppler mean gradient was 28.8 ± 10.1 mm Hg, and 94% of patients had moderate or severe pulmonary regurgitation (PR). Implantation was successful in 29 of 30 attempts, and not attempted in four patients. Complications included one conduit rupture requiring urgent surgery and device removal, one distal pulmonary artery guidewire perforation, and one instance of wide complex tachycardia. Peak systolic conduit gradient fell from 37.2 ± 16.3 mm Hg to 17.3 ± 7.3 mm Hg. None of the patients had more than mild PR. At 6-months, conduit Doppler mean gradient was 22.4± 8.1 mm Hg, and pulmonary regurgitation fraction as measured by magnetic resonance imaging was significantly improved (3.3 ± 3.6% vs. 27.6 ± 13.3%, p<0.0001). Stent fracture occurred in 8 of 29 implants. Three of these patients were subsequently treated with a second Melody valve for recurrent stenosis during follow-up. The authors concluded that implantation of the Melody valve for RVOT conduit dysfunction can be performed by experiences operators and appears safe, and has encouraging acute and short-term outcomes. Longer follow-up and a larger patient experience are needed to determine the ultimate role of this therapy in the treatment of conduit dysfunction.

McElhinney et al. (2010) evaluated short and medium-term outcomes in the expanded Melody U.S. Trial (n=136). Implantation was attempted in 124 patients, and was achieved successfully in all except one. Placement was not attempted in the other 12 patients due to the risk of coronary artery compression (n=6) or other clinical or protocol contraindications. There was one death from intracranial hemorrhage after coronary artery dissection, and one valve was explanted after conduit rupture. The median peak RVOT gradient was 37 mm Hg prior to implantation and 12 mm Hg immediately following implantation. Pulmonary regurgitation (PR) was moderate or severe in 92 patients prior to implantation, and no patient had greater than mild PR immediately after implantation or during follow-up (≥ one year in 65 patients). Freedom from stent fracture was 77.8% ± 4.3% at 14 months, and freedom from Melody valve dysfunction or reintervention was 93.5 ± 2.4% at one year. A higher RVOT gradient at discharge and younger age were associated with shorter freedom from dysfunction.

Vezmar et al. (2010) conducted a case series to evaluate the physiological and clinical consequences of percutaneous pulmonary valve implantation (PPVI) in patients with chronic right ventricular outflow tract (RVOT) obstruction and volume overload (n=28). Of 28 patients, 16 had the Melody valve implanted within a bioprosthetic valve. The procedure resulted in acute improvement in symptoms, hemodynamic status and objective findings of exercise performance. There were no acute device-related complications, with stent fractures were noted in 10.8% of patients. Early follow-up demonstrated persistent improvement in ventricular parameters, PR, and objective exercise capacity.

Eiken et al. (2011) published results of 102 consecutive percutaneous pulmonary valve implantations performed at two centers in Germany between 2006 and 2010. The median patient age was 21.5 years. Sixty-one patients

had undergone surgical correction of a Tetralogy of Fallot/pulmonary atresia with ventricular septal defect, and14 had a common arterial trunk; the remaining patients had been treated surgically for transposition of the great arteries (n=9) or aortic stenosis (n=8), or had a variety of other cardiac lesions (n=10). The majority of conduits (79) used during previous surgery were homografts. The median peak systolic RVOT gradient between the right ventricle and the pulmonary artery decreased immediately following the procedure from 37 mmHg (29–46 mmHg) to 14 mmHg (9–17 mmHg, p< 0.001). Pulmonary regurgitation assessed by MRI was reduced from a median of 16% (5–26%) to 1% (0–2%, p<0.001). The median end-diastolic RV-volume index also decreased significantly (p=0.001). One patient died due to compression of the left coronary artery. At a median follow-up of 357 days (99–388 days), the mean doppler gradient in the RVOT decreased from a pre-procedure median of 36 mmHg (26–44) to a median of 15 mmHg (12–20) at the latest follow-up (p<0.0001). The authors concluded that PPVI can be performed by an experienced structural heart disease interventionalist in patients with RVOT dysfunction. Medium and long term follow up needs to be assessed to document sustained benefit, however. It remains to be proved whether the improvements in hemodynamics persist, and the goal to reduce the number of cardiothoracic operations during the lifetime of the patient can be achieved.

Professional Societies/Organizations
ACC/AHA 2008 Guidelines for the Management of Adults with Congenital Heart Disease does not include recommendations for transcatheter pulmonary valve implantation.

ECRI
A 2012 ECRI Emerging Technology Evidence Report, Percutaneous Pulmonary Valve Implantation for Treating Right Ventricular Outflow Tract Dysfunction, evaluated the available evidence and provided the following findings to each key question:

Key Question 1: Does percutaneous pulmonary valve implantation (PPVI) significantly improve symptoms, quality of life, and cardiac function for patients with RVOT conduit dysfunction?

Studies using the Melody system indicate that PPVI improves symptoms as indexed by the New York Heart Association Classification system in the short-term (<6 months), but longer-term results are not available. No data were available to assess how PPVI affects quality of life. Studies using the Melody system also indicate that PPVI improves cardiac function on several measures (i.e., decreases RVOT pressure gradient, decreases regurgitation fraction through the pulmonary valve, and decreases right ventricular end-diastolic volume; data on maximal oxygen consumption are not consistent).

Key Question 2: How does PPVI compare to open heart valve replacement surgery for pulmonary valve dysfunction in terms of short-term (<6 months) outcomes (i.e., hospital stay, fluoroscopy duration, adverse events [AEs])?

One published comparative study using the Melody system reported that PPVI was associated with a shorter hospital stay (median of two days versus a median of seven days) and fewer AEs than surgical pulmonary valve replacement.

Key Question 3: How does PPVI compare to open heart valve replacement surgery for longer-term (>6 months) outcomes (i.e., quality of life, overall survival, long-term number of open heart surgeries per patient, time to reintervention, adverse events [AEs)]?

No data were available to address any of these outcomes.

Key Question 4: What AEs are associated with PPVI?

Published studies on 454 patients who received the Melody valve reported occurrence of 110 AEs, some of which were very serious or fatal. The most frequently occurring event was stent fracture (66 occurrences), which can be either benign with no loss of stent integrity or more serious, requiring explantation or reintervention with another percutaneous valve. One study that assessed the impact of the PPVI learning curve on clinical outcomes stated that the rate of stent fracture was not related to the interventionalist's procedural proficiency; instead, fractures are caused by insufficient radial strength to withstand the forces from the conduit. This AE is being managed by implanting a bare-metal stent to provide additional integrity immediately before implanting the Melody valve, although device redesigns are under way.

Summary–Transcatheter Pulmonary Valve Implantation: Transcatheter pulmonary valve implantation has been explored as an alternative to conventional valve surgery for the treatment of pulmonary regurgitation and right ventricular outflow tract (RVOT) dysfunction. These conditions often occur in patients with previously repaired pulmonary valves. Pulmonary valve surgery requires cardiopulmonary bypass, and involves insertion of a pulmonary conduit, with or without a valve, to re-establish blood flow to the pulmonary artery. Conduits require frequent replacement due to patient growth and conduit degeneration. Although the published evidence is limited, transcatheter pulmonary valve implantation appears to be a reasonable alternative in carefully selected patients. This procedure may provide improved hemodynamic function and extend the longevity of the existing conduit, and may defer the need for conduit replacement, resulting in a reduction in the number of open heart surgeries required over a lifetime.

Mitral Valve

Open mitral valve surgery is generally recommended for patients with significant symptomatic mitral regurgitation (MR) and those who have evidence of left ventricular dysfunction or enlargement. Although mitral valve regurgitation may recur within the first six months after surgical repair, the grade of MR generally remains stable beyond the first year of follow-up. Transcatheter treatments have been developed to treat valvular disease as an alternative to open surgical treatment.

U.S. FDA–MitraClip Clip Delivery System (MitraClip CDS) (Abbott Vascular, Menlo Park, CA): The MitraClip CDS received FDA approval through the PMA process on October 24, 2013. It is indicated for the percutaneous reduction of significant symptomatic mitral regurgitation (MR ≥ 3+) due to primary abnormality of the mitral apparatus (degenerative MR) in patients who have been determined to be at prohibitive risk for mitral valve surgery by a heart team, which includes a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, and in whom existing comorbidities would not preclude the expected benefit from reduction of the mitral regurgitation. The device is contraindicated in patients who cannot tolerate procedural anticoagulation or post procedural antiplatelet regimen, and those with active endocarditis of the mitral valve, rheumatic mitral valve disease, or evidence of intracardiac, inferior vena cava or femoral venous thrombus.

The MitraClip system consists of implant catheters and the MitraClip device, a permanent implant that attaches to the mitral valve leaflets. The procedure results in a double opening of the mitral valve that allows greater closure and reduces mitral regurgitation.

Literature Review: Percutaneous Mitral Valve Repair: Four-year results of a randomized controlled trial of percutaneous repair versus surgery for mitral regurgitation were published by Mauri et al., for the EVEREST II Investigators (2013). Patients with grade 3+ or 4+ mitral regurgitation (MR) were randomized to percutaneous repair with the MitraClip device (n=184) or conventional mitral valve surgery (n=95) in a 2:1 ratio. The rate of the composite endpoint of freedom from death, surgery, or grade 3+ or 4+ MR at four years in the intention-to-treat population was 39.8% vs. 53.4% in the percutaneous repair group and surgical groups, respectively (p=0.070).. Rates of death were 17.4% in the percutaneous repair group vs. 17.8% in the surgical group (p=0.914), and 3+ or 4+ MR was present in 21.7% in the percutaneous group vs. 24.7% in the surgical group (p=0.745). Surgery for mitral valve dysfunction was required in 29.4% in the percutaneous group vs. 2.2% in the surgical group at one year (p< 0.001) and 24.8% vs. 5.5% at four years (p< 0.001). The authors concluded that patients treated with percutaneous mitral valve repair more commonly required surgery to treat residual MR, although after the first year there were few surgeries required after either treatment, and there were no differences in the prevalence of moderate-severe and severe MR or mortality at four years.

Maisano et al. (2013) published results from the ACCESS EU, a prospective multicenter nonrandomized post-approval study of MitraClip therapy in Europe. A total of 567 patients with severe MR were treated with MitraCliip therapy at 14 European sites. Compared to patients in EVEREST II, patients in this study were older, presented with multiple comorbidities, and were determined to be at high surgical risk (similar to those enrolled in the EVEREST II high risk study, below.) A total of 19 patients died within 30 days after the procedure. The Kaplan Meier survival at one year was 81.8%. There were no device embolizations. Thirty six patients (6.3%) required MV surgery within 12 months of the procedure. The severity of MR improved at twelve months compared to baseline (p<0.001), with 78.9% of patients free from MR severity > 2. At 12 months, 71.4% of patients were in NYHA Class I or II.

The EVEREST II High Risk Study, an arm of the EVEREST II study, was conducted to assess the safety and effectiveness of the MitraClip device in patients with significant MR at high risk of surgical mortality. Outcomes of 78 patients with severe symptomatic MR and an estimated surgical mortality rate of 12% or more were retrospectively compared to 58 patients who were screened but not enrolled. The comparator group received standard care over the twelve month period, with 86% managed medically and 14% undergoing mitral valve surgery. Protocol-predicted surgical mortality in the study group and comparator group was 18.2% and 17.4%, respectively. There were six procedure-related deaths, although there was no significant difference in 30-day mortality between the study group and comparator group (7.7% and 8.3%, respectively). The twelve-month survival rate was 76% in the study group and 55% in the comparator group (p=0.047). Of surviving patients in the study group with matched baseline and 12-month data, 78% had an MR grade of ≤ 2+. NYHA class and quality of life improved in the majority of patients.

Summary: Percutaneous Mitral Valve Repair: Percutaneous mitral valve repair is an emerging technology. Although this approach may become an option for patients at high risk for traditional surgical repair there is currently insufficient evidence in the published medical literature to demonstrate the safety and efficacy of this procedure.

Use Outside the U.S.
The Edwards Sapien Transcatheter Aortic Heart Valve received CE mark certification in 2007, permitting commercial distribution in Europe. The device is also included in Health Canada's Medical Device Active License listing. According to the FDA summary, the device is approved for distribution in the 27 member states under the European Union, Croatia, Iran, Israel, Jordan, Kuwait, Monaco, Norway, Russia, Saudi Arabia, Singapore, South Africa, Switzerland, Thailand and Turkey.

The Medtronic Melody Transcatheter Pulmonary Valve received CE mark certification permitting commercial distribution in Europe in 2006. The Melody system is also included in Health Canada's Medical Device Active License listing.

The Edwards Sapien Pulmonic Transcatheter Heart Valve received CE mark in 2010, permitting commercial distribution in Europe for placement in the pulmonary position. (This device is undergoing clinical trials under an Investigational Device Exemption in the U.S. but is not yet FDA approved.

According to the FDA summary, the current Medtronic CoreValve System is commercially available in over 50 countries,

Several additional devices have received CE mark approval and are available outside the U.S., including but not limited to the following:

- Direct Flow Medical transcatheter valve
- JenaValve™ Transapical TAVI system (JenaValve Inc., Munich Germany)
- Engager™ Transcatheter Valve (Medtronic, Minneapolis MN)
- Lotus Valve System (Boston Scientific, Malborough MA)
- Portico™ Transcatheter Aortic Valve Implantation System (St. Jude Medical, St. Paul, MN)
- ACURATE TA™ (Symetris, Switzerland)

European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS): The ESC/EACTS 2012 Guidelines on the Management of Valvular Heart Disease state that based on current data, TAVI is recommended in patients with severe symptomatic aortic stenosis who are, according to the heart team, considered unsuitable for conventional surgery because of severe comorbidities. The guideline further states that among high-risk patients who are still candidates for AVR, the decision for TAVI should be individualized, in consideration of the respective advantages/disadvantages of both techniques. At the present stage, TAVI should not be performed in patients at intermediate risk for surgery and trials are required in this population."

National Institute for Health and Clinical Excellence (NICE) (United Kingdom)
NICE Interventional Procedure Guidance on transcatheter aortic valve implantation for aortic stenosis, updated in March, 2012, includes the following recommendations:

- Evidence on the safety of transcatheter aortic valve implantation (TAVI) for aortic stenosis shows the potential for serious but well-recognized complications.

- For patients with aortic stenosis who are considered to be unsuitable for surgical aortic valve replacement, the evidence on the efficacy of TAVI is adequate. For these patients, TAVI may be used with normal arrangements for clinical governance, consent and audit.

- For patients with aortic stenosis for whom SAVR is considered suitable but to pose a high risk, the evidence on the efficacy of TAVI is inadequate. For these patients TAVI should only be used with special arrangements for clinical governance, consent and data collection or research.

- For patients with aortic stenosis for whom SAVR is considered suitable and not to pose a high risk, the evidence on the efficacy of TAVI is inadequate. For these patients TAVI should only be used in the context of research.

- Patient selection should be carried out by a multidisciplinary team including interventional cardiologists, cardiac surgeons, a cardiac anesthetist and an expert in cardiac imaging. The multidisciplinary team should determine the risk level for each patient.

- TAVI is a technically challenging procedure that should be performed only by clinicians and teams with special training and experience in complex endovascular cardiac interventions. Units undertaking this procedure should have both cardiac and vascular surgical support for emergency treatment of complications.

NICE Interventional Procedure Guidance on percutaneous pulmonary valve implantation for right ventricular outflow tract dysfunction, updated in January 2013, includes the following recommendations:

- The evidence on percutaneous pulmonary valve implantation (PPVI) for right ventricular outflow tract (RVOT) dysfunction shows good short-term efficacy. 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. With regard to 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 very unwell and might otherwise need open heart surgery (typically reoperative) with its associated risks. Therefore, this procedure may be used with normal arrangements for clinical governance, consent and audit.

- 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 carried out 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 congenital heart disease.

- This is a technically challenging procedure that should be performed only by clinicians with training and experience in interventional cardiology and congenital heart disease.

Summary
Transcatheter aortic valve implantation (TAVI) has been evaluated as a less invasive alternative to conventional surgical valve replacement. Although evidence published to date is limited, and long-term outcomes have not been fully defined, TAVI may be a reasonable alternative to open heart surgery in carefully selected patients with severe symptomatic aortic stenosis when performed using a U.S. Food and Drug Administration (FDA)-approved implant used according to FDA-approved indications.

Transcatheter pulmonary valve implantation has been explored as an alternative to conventional valve surgery for the treatment of pulmonary regurgitation and right ventricular outflow tract (RVOT) dysfunction. These conditions often occur in patients with previously repaired pulmonary valves. Pulmonary valve surgery requires cardiopulmonary bypass, and involves insertion of a pulmonary conduit, with or without a valve, to re-establish blood flow to the pulmonary artery. Conduits require frequent replacement due to patient growth and conduit

degeneration. Although the published evidence is limited, transcatheter pulmonary valve implantation appears to be a reasonable alternative in carefully selected patients. This procedure may provide improved hemodynamic function and extend the longevity of the existing conduit, and may defer the need for conduit replacement, resulting in a reduction in the number of open heart surgeries required over a lifetime.

Percutaneous mitral valve repair has been proposed as a less invasive alternative to open valve surgery for the treatment of mitral regurgitation. There is insufficient evidence in the published medical literature to demonstrate the safety, efficacy and long-term outcomes of this procedure.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

Transcatheter Aortic Valve Implantation

Covered when medically necessary:

CPT®* Codes	Description
33361	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; percutaneous femoral artery approach
33362	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; open femoral artery approach
33363	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; open axillary artery approach
33364	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; open iliac artery approach
33365	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; transaortic approach (eg, median sternotomy, mediastinotomy)
33366	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; transapical exposure (e.g., left thoracotomy)
33367	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; cardiopulmonary bypass support with percutaneous peripheral arterial and venous cannulation (eg, femoral vessels) (List separately in addition to code for primary procedure)
33368	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; cardiopulmonary bypass support with open peripheral arterial and venous cannulation (eg, femoral, iliac, axillary vessels) (List separately in addition to code for primary procedure)
33369	Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; cardiopulmonary bypass support with central arterial and venous cannulation (eg, aorta, right atrium, pulmonary artery) (List separately in addition to code for primary procedure)

Transcatheter Pulmonary Valve Implantation

Covered when medically necessary when the Medtronic Melody® Transcatheter Pulmonary Valve (Medtronic, Inc., Santa Ana, CA) is used in accordance with the U.S. FDA's Humanitarian Device Exemption (HDE) requirements:

CPT* Codes	Description
0262T	Implantation of catheter-delivered prosthetic pulmonary valve, endovascular approach

Percutaneous Mitral Valve Repair

Experimental/Investigational/Unproven/Not Covered:

CPT* Codes	Description
0343T	Transcatheter mitral valve repair percutaneous approach including transseptal puncture when performed, initial prosthesis
0344T	Transcatheter mitral valve repair percutaneous approach including transseptal puncture when performed; additional prosthesis (es) during same session (List separately in addition to code for primary procedure.)
0345T	Transcatheter mitral valve repair percutaneous approach via the coronary sinus

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Appendix A: Current Treatment Recommendations for Patients With Aortic Stenosis
(ACCF/AATS/SCAI/STS Expert Consensus Document on Transcatheter Aortic Valve Replacement (TAVR); Homes et al., 2012)

Treatment	Indication	Complications
Surgical Aortic Valve Replacement	• Symptomatic severe AS (Class I, LOE: B) • Severe AS undergoing CABG, aortic surgery or other valve surgery (Class I, LOE: C) • Symptomatic moderate AS undergoing CABG, aortic surgery or other valve surgery (Class IIa, LOE: C) • Asymptomatic severe AS with hypotensive response to exercise (Class IIb; LOE: C) • Asymptomatic extremely severe AS (AVA <0.6 cm2, mean gradient >50 mm	• Mortality (3%) • Stroke (2%) • Prolonged ventilation (11%) Thromboembolism and bleeding • Prosthetic dysfunction • Perioperative complications are higher when surgical AVR is combined with CABG
Transcatheter Aortic Valve Replacement	• TAVR is recommended in patients with severe, symptomatic, calcific stenosis of a trileaflet aortic valve who have aortic and vascular anatomy suitable for TAVR and a predicted survival >12 months, and who have a prohibitive surgical risk	Mortality (3% to 5%) • Stroke (6% to 7%) • Access complications (17%) • Pacemaker insertion • 2% to 9% (Sapien) • 19% to 43%

	as defined by an estimated 50% or greater risk of mortality or irreversible morbidity at 30 days or other factors such as frailty, prior radiation therapy, porcelain aorta, and severe hepatic or pulmonary disease. • TAVR is a reasonable alternative to surgical AVR in patients at high surgical risk (PARTNER Trial Criteria: STS ≥ 8%*)	(CoreValve) • Bleeding • Prosthetic dysfunction • Paravalvular AR • Acute kidney injury • Other • Coronary occlusion • Valve embolization • Aortic rupture
Medical Therapy	• No specific therapy for asymptomatic AS • Medical therapy not indicated for symptomatic severe AS risk factors as indicated • Statins not indicated for preventing progression of AS • Diuretics, vasodilators and positive inotropes should be avoided in patients awaiting surgery because of risk of destabilization	• Hemodynamic instability

Key:
Class I: Conditions for which there is evidence for and/or general agreement that the procedure or treatment is beneficial, useful, and effective;
Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment
Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy

*The original PARTNER protocol specified inclusion criteria as a minimum STS-predicted risk of mortality of ≥ 10. During the trial enrollment phase, the minimum STS-predicted risk of mortality was changed to ≥ 8. In both instances, two surgeons had to document that the true predicted risk of mortality was ≥ 15.

AR indicates aortic regurgitation; AS, aortic stenosis; AVR, aortic valve replacement; CABG, coronary artery bypass graft; LOE, level of evidence; STS, Society of Thoracic Surgeons; and TAVR, transcatheter aortic valve replacement.