Transcatheter Heart Valve Replacement

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INSTRUCTIONS:

“Medical Policy assists in administering UCare benefits when making coverage determinations for members under our health benefit plans. When deciding coverage, all reviewers must first identify enrollee eligibility, federal and state legislation or regulatory guidance regarding benefit mandates, and the member specific Evidence of Coverage (EOC) document must be referenced prior to using the medical policies. In the event of a conflict, the enrollee’s specific benefit document and federal and state legislation and regulatory guidance supersede this Medical Policy. In the absence of benefit mandates or regulatory guidance that govern the service, procedure or treatment, or when the member’s EOC document is silent or not specific, medical policies help to clarify which healthcare services may or may not be covered. This Medical Policy is provided for informational purposes and does not constitute medical advice. In addition to medical policies, UCare also uses tools developed by third parties, such as the InterQual Guidelines®, to assist us in administering health benefits. The InterQual Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. Other Policies and Coverage Determination Guidelines may also apply. UCare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary and to provide benefits otherwise excluded by medical policies when necessitated by operational considerations.”
POLICY DESCRIPTION:
This policy describes the use of transcatheter aortic valve replacement (TAVR) for the treatment of severe aortic stenosis in patients considered to be high risk and not operable candidates for open heart surgery. This nonsurgical treatment procedure involves delivering and implanting a bioprosthetic valve via a peripheral artery.

COVERAGE RATIONALE / CLINICAL CONSIDERATIONS:

1. **AORTIC VALVE:**
   Transcatheter aortic valve replacement (TAVR) is considered **MEDICALLY NECESSARY** for patients with severe, symptomatic aortic stenosis who meet ALL the following criteria (CMS, 2012):
   
   - Patient is not a candidate for conventional, open valve replacement surgery.
   - The procedure is furnished with a complete aortic valve and implantation system that has received U.S. Food and Drug Administration (FDA) approval (e.g. Edwards SAPIEN).
   - Procedure is performed according to FDA approved labeled indications and contraindications.
   - Two cardiac surgeons have examined the patient and evaluated the patient’s suitability for surgical valve replacement.
   - The patient is under the care of a heart team.
   - The interventional cardiologist and cardiac surgeon must jointly participate in the TAVR procedure.
   - TAVR must be furnished in a hospital with the appropriate infrastructure that includes but is not limited to on-site heart valve surgery program, cardiac catheterization lab, non-invasive imaging, post-procedure intensive care facility, and appropriate volume requirements.
   - The heart team and hospital are participating in a national TAVR registry.

   The use of transcatheter aortic valve replacement (TAVR) for non-approved indications is covered if performed within a clinical trial under strict criteria set forth by CMS. TAVR is not covered for patients in whom existing comorbidities would preclude the expected benefit from correction of the aortic stenosis (Refer to CMS Clinical Trials for coverage guidelines on Category B devices).

   CMS issued a Medicare National Coverage Determination (NCD) on May 1, 2012 which allows coverage of TAVR under Coverage with Evidence Development (CED) with certain conditions. CMS considers TAVR as Category B devices and the Medicare Advantage plan is responsible to cover these devices when criteria are met (Refer to the Regulatory-Status/CMS section on this policy for NCD guidelines).

2. **PULMONARY VALVE:**
   Transcatheter pulmonary heart valve replacement (e.g., Melody®) is **CONSIDERED EXPERIMENTAL AND INVESTIGATIONAL** for treating right ventricular outflow tract dysfunction.

   There is insufficient evidence in the clinical literature demonstrating the long-term efficacy and durability of catheter-delivered prosthetic pulmonary heart valves for treating right ventricular outflow tract dysfunction.

3. **MITRAL VALVE:**
   Transcatheter mitral valve leaflet repair (e.g., MitraClip®) is **CONSIDERED EXPERIMENTAL AND INVESTIGATIONAL** for treating mitral regurgitation, due to lack of U.S. Food and Drug Administration
(FDA) approval.

There is insufficient evidence in the clinical literature demonstrating the long-term efficacy of catheter-delivered mitral valve leaflet repair devices for treating mitral regurgitation. Further results from prospective, randomized controlled trials are needed to determine device durability and the ideal candidates for the procedure.

Clinical Considerations:

Contraindications: The bioprosthesis and delivery system are contraindicated in patients who cannot tolerate an anticoagulation/antiplatelet regimen or who have active bacterial endocarditis or other active infections.

Possible Complications: At this time, TAVI is reserved for patients who are deemed high risk because of major comorbidities; therefore, the risk for complications is greater in this population of patients.

- Valve Malposition or Embolization: The incidence of valve malposition or embolization has decreased to ≤2% in recent studies. The design of the CoreValve bioprosthesis allows for repositioning when the valve is only partially deployed; however, both Edwards SAPIEN and the CoreValve devices are not repositionable once they are fully deployed.
- Conversion to Open Heart Surgery: Although the incidence of conversion to open heart surgery is low (<2%), TAVI should be performed only in centers that have urgent cardiac surgery capabilities. In the reviewed studies, conversion to open heart surgery was necessary because of valve embolization, apical rupture, pericardial tamponade, and unsuccessful balloon dilatation.
- Access Site Complications: The large size of the catheters used during TAVI has led to a high incidence (>10%) of access site complications. Transfemoral access can cause tears or avulsions of the femoral vessels and bleeding that can range from small hematomas to severe bleeding. Transapical access can cause life-threatening complications, including ventricular tears and major bleeding.
- Myocardial Infarction: The incidence of myocardial infarction ranges from 0.2% to 18%.
- Stroke: Currently, the incidence of stroke is <5%. Possible etiologies of stroke include athero-embolism from the aorta or aortic arch, calcific embolism from aortic valve, thromboembolism from catheters, air embolism from left ventricular cannulation, dissection of arch vessels, and prolonged hypotension.
- Need for Permanent Pacemaker: TAVI is highly associated with new-onset intraventricular conduction abnormalities that necessitate implantation of a permanent pacemaker. The incidence of pacemaker implantation is higher with the CoreValve system (>10%) than the Edwards SAPIEN device (<7%).
- Acute Renal Failure: Acute kidney injury is a common (incidence of 12% to 28%) complication of TAVI that has been identified as a predictor of mortality.

BACKGROUND:

The four natural valves of the heart (aortic, pulmonary, mitral and tricuspid) act as one-way valves to direct the flow of blood to the lungs and aorta. Heart valves with congenital defects or those that become diseased over time can result in either a leaky valve (regurgitation/incompetence/insufficiency) or a valve that does not open wide enough (stenosis).
Conventional treatment of structural heart valve disorders is surgical repair or replacement requiring open-heart surgery using cardiopulmonary bypass. Transcatheter (percutaneous or catheter-based) valve procedures use catheter technology to access the heart and manage heart valve disorders without the need for open-heart surgery and cardiopulmonary bypass. During the procedure, a compressed artificial heart valve or other device is attached to a wire frame and guided by a catheter to the heart. Once in position, the wire frame expands, allowing the device to fully open.

**AORTIC VALVE:**
Aortic stenosis is the narrowing of the aortic valve, which obstructs the blood flow from the left ventricle of the heart to the ascending aorta. The most common cause of aortic stenosis in the elderly is aortic sclerosis, a degenerative disease characterized by fibrosis and calcification of the aortic valve. Aortic sclerosis progresses to aortic stenosis in ≤ 15% of patients. Other potential causes of aortic valve disease include autoimmune disorders, carcinoid syndrome, metabolic disorders, weight-loss medications, and radiation therapy. In patients < 70 years of age, the most common cause of aortic stenosis is congenital bicuspid aortic valve. The prevalence of aortic stenosis in adults > 70 years of age is 4.6%. Patients with aortic stenosis typically have a heart murmur and may experience the following symptoms, depending on the stage of disease: fatigue, dyspnea, edema, angina, dizziness, exertional syncope, and arrhythmia. Aortic stenosis may be diagnosed by physical examination, echocardiography, and chest x-ray. Cardiac catheterization, cardiac magnetic resonance imaging, electrocardiography, and stress testing may also be performed. Asymptomatic aortic stenosis is not treated directly; however, other cardiovascular conditions, such as hypertension, hypercholesterolemia, coronary heart disease, arrhythmias, or heart failure, may contribute to the progression of aortic stenosis and need to be managed. Once aortic stenosis is symptomatic, valve repair or replacement is often necessary. The mean survival of patients with untreated asymptomatic aortic stenosis is approximately 3 years.

Surgical aortic valve replacement is the standard treatment for aortic stenosis. However, approximately 33% of patients are ineligible for surgery, which carries an operative mortality rate of ≤ 10%. Transcatheter aortic valve replacement (TAVR) or implantation (TAVI) is a nonsurgical method to correct aortic stenosis. TAVI is a viable option for patients with severe symptomatic aortic stenosis who are not candidates for conventional surgery. TAVI involves delivering and implanting a bioprosthetic valve via a peripheral artery.

Currently, there are two transcatheter valves in use in the United States: the Edwards SAPIEN Transcatheter Heart Valve (Edwards Lifesciences LLC) and the CoreValve® System (Medtronic Inc.). Of these, only the Edwards SAPIEN system has received marketing approval. The Edwards SAPIEN device is a balloon-expandable, stainless steel frame that supports a valve created from bovine pericardial tissue. The CoreValve device is a self-expandable, nitinol frame that supports a valve created from porcine pericardial tissue.

TAVI is performed in a sterile environment under general anesthesia using fluoroscopy, transesophageal echocardiography (TEE), and other imaging guidance; recently, some centers have reported performing TAVI-TF under local anesthesia. The optimal setting for TAVI is not yet established. However, it appears that the best outcomes are achieved when the procedure is performed by a specially trained and credentialed interdisciplinary team at a specialized heart center in a modified cardiac catheterization laboratory or hybrid operating room. Ideally, the TAVI team should be committed to a unique professional collaboration, and include members from cardiology, cardiac surgery, interventional cardiology, anesthesiology, and relevant imaging departments.
There are two access routes for TAVI: transfemoral and transapical. Since the transapical access route involves a thoracotomy, it was deemed to be an invasive procedure that was beyond the scope of this report. For transfemoral TAVI, surgical cut-down and placement of a femoral graft may be required because of the large size of the valve delivery systems. Alternatively, a direct percutaneous puncture may be performed. Once vascular access is achieved, the valve may be delivered via an antegrade approach through the right ventricle or via a retrograde approach through the aorta. Currently, the retrograde approach is preferred (Salinas et al., 2011). Balloon valvuloplasty is performed prior to deployment of the valve to facilitate implantation of the prosthetic valve. Rapid pacing is initiated via a transvenous pacemaker to reduce the risk of prosthetic valve displacement during implantation. Once the prosthetic valve is deployed, angiography or echocardiography is conducted to ensure successful implantation of the device and that all catheters are removed (McRae et al., 2009; Bande et al., 2010; Salinas et al., 2011).

**PULMONARY VALVE:**
The pulmonary valve directs blood flow from the right ventricle into the lungs. Disorders of the pulmonary valve are often due to congenital heart disease such as tetralogy of Fallot, pulmonary atresia, transposition of the great arteries and double-outlet right ventricle. Surgery to replace the valve with a bioprosthesis may also include a conduit (graft) to open the right ventricular outflow tract (RVOT). Over time, the valve conduit may fail, leading to pulmonary valve stenosis (narrowing), pulmonary valve regurgitation (incompetence/insufficiency) or a combination of the two. Because patients undergoing this procedure are typically children or adolescents, the bioprosthetic valve will require revisions as the patient grows. Transcatheter pulmonary valve implantation, a minimally invasive alternative to surgical valve repair or replacement, is designed to reduce the number of surgeries needed throughout a patient’s lifetime. Transcatheter pulmonary valves feature a metal, stent-like scaffold that contains a bioprosthetic valve. Access to the pulmonary valve is achieved via the femoral vein. The replacement valve is usually positioned within a preexisting pulmonary conduit (graft) (ECRI, 2011a; NICE, 2007; Medtronic Melody website).

**MITRAL VALVE:**
The mitral valve directs blood flow from the left atrium into the left ventricle. Mitral regurgitation (MR) occurs when the mitral valve does not close properly, allowing blood to flow backwards from the ventricle to the atrium. MR is sometimes referred to as mitral incompetence or mitral insufficiency. Left untreated, moderate to severe MR can lead to congestive heart failure. MR that cannot be managed conservatively may require surgical valve repair or replacement (NICE, 2009). The aim of transcatheter mitral valve repair is to keep the two valve leaflets more closely fitted together, thereby reducing regurgitation. The procedure, based on the surgical edge-to-edge technique, creates a double orifice using a clip instead of a suture to secure the leaflets. The device consists of a steerable guide catheter, including a clip delivery device and a two-armed, flexible metal clip covered in polyester fabric. Access to the mitral valve is achieved via the femoral vein.

### REGULATORY STATUS:

1. **U.S. FOOD AND DRUG ADMINISTRATION (FDA):**
   **AORTIC VALVE:**
   The SAPIEN Transcatheter Heart Valve System™ received FDA approval in November 2, 2011. Approval was granted for transfemoral delivery in patients with severe symptomatic native aortic valve stenosis, who are not eligible for open-heart procedures and have a calcified aortic annulus. The
product labeling also advises that a heart surgeon should be involved in determining whether a patient is an acceptable candidate for transcatheter valve replacement. Exclusion criteria are patients who are candidates for an open procedure, patients with congenital heart abnormalities, patients with an infection in the heart, and/or cannot tolerate anticoagulation/antiplatelet therapy post-implantation. The SAPIEN valve is available in two sizes: 23 and 26 mm (CDRH, 2012). In June 2012, the FDA Advisory Panel will review a Premarketing Authorization from Edwards Lifesciences regarding approval of the SAPIEN valve for patients with severe, symptomatic aortic stenosis who are at high risk for surgery (Edwards Lifesciences, 2012).


The FDA approved the Medtronic Melody® Transcatheter Pulmonary Valve and Ensemble Delivery System under the Humanitarian Device Exemption (HDE) on January 25, 2010 for the treatment of adults and children with previously implanted, poorly functioning pulmonary valve conduits.


**PULMONARY VALVE:**
The Medtronic Melody Transcatheter Pulmonary Valve and Ensemble Delivery System received FDA approval under the Humanitarian Device Exemption (HDE) program on January 25, 2010 (H080002). A HDE application is similar to a premarket approval (PMA) application, but is exempt from the effectiveness requirements. FDA approval of an HDE grants limited marketing approval for a Humanitarian Use Device (HUD). A HUD is a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects fewer than 4,000 individuals in the United States per year.

The Melody transcatheter pulmonary valve is approved for use as an adjunct to surgery in the management of pediatric and adult patients with the following clinical conditions:

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

b. Dysfunctional RVOT conduit with a clinical indication for intervention, and either:
   
   o Regurgitation: ≥ moderate regurgitation OR
   
   o Stenosis: mean RVOT gradient ≥ 35 mmHg


**MITRAL VALVE:**
Mitraclip Delivery System received Premarket Approval (PMA) 11/15/2013.

This device 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. Available:

ADDITIONAL PRODUCT:
Portico™ (St. Jude Medical) – not FDA approved at time of publication.

2. CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS):

National Coverage Determination (NCD) for TRANSCATHETER AORTIC VALVE REPLACEMENT (TAVR)
(20.32). Effective Date of this Version 5/1/2012. Implementation Date 1/7/2013.

Indications and Limitations of Coverage:
The Centers for Medicare & Medicaid Services (CMS) covers transcatheter aortic valve replacement
(TAVR) under Coverage with Evidence Development (CED) with the following conditions:
A. TAVR is covered for the treatment of symptomatic aortic valve stenosis when furnished according
to a Food and Drug Administration (FDA)-approved indication and when all of the following
conditions are met:
1. The procedure is furnished with a complete aortic valve and implantation system that has
received FDA premarket approval (PMA) for that system's FDA approved indication.
2. Two cardiac surgeons have independently examined the patient face-to-face and evaluated the
patient's suitability for open aortic valve replacement (AVR) surgery; and both surgeons have
documented the rationale for their clinical judgment and the rationale is available to the heart
team.
3. The patient (preoperatively and postoperatively) is under the care of a heart team: a cohesive,
multi-disciplinary, team of medical professionals. The heart team concept embodies
collaboration and dedication across medical specialties to offer optimal patient-centered care.
4. TAVR must be furnished in a hospital with the appropriate infrastructure that includes, but is
not limited to:
   • On-site heart valve surgery program,
   • Cardiac catheterization lab or hybrid operating room/catheterization lab equipped with a
fixed radiographic imaging system with flat-panel fluoroscopy, offering quality imaging,
   • Non-invasive imaging such as echocardiography, vascular ultrasound, computed
   tomography (CT) and magnetic resonance (MR),
   • Sufficient space, in a sterile environment, to accommodate necessary equipment for cases
with and without complications,
   • Post-procedure intensive care facility with personnel experienced in managing patients
who have undergone open-heart valve procedures,
   • Appropriate volume requirements per the applicable qualifications below.
5. There are two sets of qualifications; the first set outlined below is for hospital programs and
heart teams without previous TAVR experience and the second set is for those with TAVR
experience.
   • Qualifications to begin a TAVR program for hospitals without TAVR experience:
The hospital program must have the following:

- ≥ 50 total AVRs in the previous year prior to TAVR, including 10 high-risk patients, and;
- ≥ 2 physicians with cardiac surgery privileges, and;
- ≥ 1000 catheterizations per year, including 400 percutaneous coronary interventions (PCIs) per year.

**Qualifications to begin a TAVR program for heart teams without TAVR experience:**

The heart team must include:

- Cardiovascular surgeon with:
  1) ≥ 100 career AVRs including 10 high-risk patients; or,
  2) ≥ 25 AVRs in one year; or,
  3) ≥ 50 AVRs in 2 years, which include at least 20 AVRs in the last year prior to TAVR initiation; and,

- Interventional cardiologist with:
  1) Professional experience with 100 structural heart disease procedures lifetime; or,
  2) 30 left-sided structural procedures per year of which 60% should be balloon aortic valvuloplasty (BAV). Atrial septal defect and patent foramen ovale closure are not considered left-sided procedures; and,

- Additional members of the heart team such as echocardiographers, imaging specialists, heart failure specialists, cardiac anesthesiologists, intensivists, nurses, and social workers; and,

- Device-specific training as required by the manufacturer.

**Qualifications for hospital programs with TAVR experience:**

The hospital program must maintain the following:

- ≥ 20 AVRs per year or ≥ 40 AVRs every 2 years; and,
- ≥ 2 physicians with cardiac surgery privileges; and,
- ≥ 1000 catheterizations per year, including ≥ 400 percutaneous coronary interventions (PCIs) per year.

**Qualifications for heart teams with TAVR experience:**

The heart team must include:

- Cardiovascular surgeon and an interventional cardiologist whose combined experience maintains the following:
  1) ≥ 20 TAVR procedures in the prior year, or,
  2) ≥ 40 TAVR procedures in the prior 2 years; and,

- Additional members of the heart team such as echocardiographers, imaging specialists, heart failure specialists, cardiac anesthesiologists, intensivists, nurses, and social workers.

6. The heart team's interventional cardiologist(s) and cardiac surgeon(s) must jointly participate in the intra-operative technical aspects of TAVR.

7. The heart team and hospital are participating in a prospective, national, audited registry that:

- consecutively enrolls TAVR patients;
- accepts all manufactured devices;
- follows the patient for at least one year; and,
- complies with relevant regulations relating to protecting human research subjects, including 45 CFR Part 46 and 21 CFR Parts 50 & 56.

The following outcomes must be tracked by the registry; and the registry must be designed to permit identification and analysis of patient, practitioner and facility level variables that predict...
each of these outcomes:
- Stroke;
- All cause mortality;
- Transient Ischemic Attacks (TIAs);
- Major vascular events;
- Acute kidney injury;
- Repeat aortic valve procedures;
- Quality of Life (QoL).

The registry should collect all data necessary and have a written, executable analysis plan in place to address the following questions (to appropriately address some questions, Medicare claims or other outside data may be necessary):
- When performed outside a controlled clinical study, how do outcomes and adverse events compare to the pivotal clinical studies?
- How do outcomes and adverse events in subpopulations compare to patients in the pivotal clinical studies?
- What is the long term (5 year) durability of the device?
- What are the long term (5 year) outcomes and adverse events?
- How do the demographics of registry patients compare to the pivotal studies?

Consistent with section 1142 of the Act, the Agency for Healthcare Research and Quality (AHRQ) supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

B. TAVR is covered for uses that are not expressly listed as an FDA-approved indication when performed within a clinical study that fulfills all of the following:

1. The heart team's interventional cardiologist(s) and cardiac surgeon(s) must jointly participate in the intra-operative technical aspects of TAVR.

2. As a fully-described, written part of its protocol, the clinical research study must critically evaluate not only each patient's quality of life pre- and post-TAVR (minimum of 1 year), but must also address at least one of the following questions:
   - What is the incidence of stroke?
   - What is the rate of all cause mortality?
   - What is the incidence of transient ischemic attacks (TIAs)?
   - What is the incidence of major vascular events?
   - What is the incidence of acute kidney injury?
   - What is the incidence of repeat aortic valve procedures?

3. The clinical study must adhere to the following standards of scientific integrity and relevance to the Medicare population:
   - The principal purpose of the research study is to test whether a particular intervention potentially improves the participants' health outcomes.
   - The research study is well supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use.
   - The research study does not unjustifiably duplicate existing studies. The research study design is appropriate to answer the research question being asked in the study.
The research study is sponsored by an organization or individual capable of executing the proposed study successfully.

The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found in the Code of Federal Regulations (CFR) at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration (FDA), it also must be in compliance with 21 CFR Parts 50 and 56. In particular, the informed consent includes a straightforward explanation of the reported increased risks of stroke and vascular complications that have been published for TAVR.

All aspects of the research study are conducted according to appropriate standards of scientific integrity (see http://www.icmje.org).

The research study has a written protocol that clearly addresses, or incorporates by reference; the standards listed as Medicare coverage requirements.

The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life threatening as defined in 21 CFR §312.81(a) and the patient has no other viable treatment options.

The clinical research study is registered on the www.ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject.

The research study protocol specifies the method and timing of public release of all pre-specified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of Medical Journal Editors (http://www.icmje.org). However a full report of the outcomes must be made public no later than three (3) years after the end of data collection.

The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria affect enrollment of these populations, and a plan for the retention and reporting of said populations on the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.

The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention.

Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

Consistent with section 1142 of the Act, AHRQ supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

The principal investigator must submit the complete study protocol, identify the relevant CMS research question(s) that will be addressed, and cite the location of the detailed
analysis plan for those questions in the protocol, plus provide a statement addressing how the study satisfies each of the standards of scientific integrity (a. through m. listed above), as well as the investigator’s contact information, to the address below. The information will be reviewed, and approved studies will be identified on the CMS Website.

C. Nationally Non-Covered Indications

TAVR is not covered for patients in whom existing co-morbidities would preclude the expected benefit from correction of the aortic stenosis.

National Coverage Determination (NCD) for Transcatheter Mitral Valve Repair (TMVR) (20.33).

Effective date 8/7/2014. Implementation date: 4/6/2015. Available at:


Indications and Limitations of Coverage

The Centers for Medicare & Medicaid Services (CMS) covers TMVR for MR under Coverage with Evidence Development (CED) with the following conditions:

A. Treatment of significant symptomatic degenerative MR when furnished according to an FDA-approved indication and when all of the following conditions are met:
   1. The procedure is furnished with a complete TMVR system that has received FDA premarket approval (PMA) for that system’s FDA-approved indication.
   2. Both a cardiothoracic surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease have independently examined the patient face-to-face and evaluated the patient's suitability for mitral valve surgery and determination of prohibitive risk; and both surgeons have documented the rationale for their clinical judgment and the rationale is available to the heart team.
   3. The patient (pre-operatively and post-operatively) is under the care of a heart team: a cohesive, multi-disciplinary, team of medical professionals. The heart team concept embodies collaboration and dedication across medical specialties to offer optimal patient-centered care.

B. TMVR must be furnished in a hospital with the appropriate infrastructure that includes but is not limited to:
   1. On-site active valvular heart disease surgical program with >2 hospital-based cardiothoracic surgeons experienced in valvular surgery;
   2. Cardiac catheterization lab or hybrid operating room/catheterization lab equipped with a fixed radiographic imaging system with flat-panel fluoroscopy, offering catheterization laboratory-quality imaging,
   3. Non-invasive imaging expertise including transthoracic/transesophageal/3D echocardiography, vascular studies, and cardiac CT studies;
   4. Sufficient space, in a sterile environment, to accommodate necessary equipment for cases with and without complications;
   5. Post-procedure intensive care facility with personnel experienced in managing patients who have undergone open-heart valve procedures;
   6. Adequate outpatient clinical care facilities
   7. Appropriate volume requirements per the applicable qualifications below.

C. There are institutional and operator requirements for performing TMVR. The hospital must have
the following:

1. A surgical program that performs > 25 total mitral valve surgical procedures for severe MR per year of which at least 10 must be mitral valve repairs;

2. An interventional cardiology program that performs > 1000 catheterizations per year, including > 400 percutaneous coronary interventions (PCIs) per year, with acceptable outcomes for conventional procedures compared to National Cardiovascular Data Registry (NCDR) benchmarks;

3. The heart team must include:
   a. An interventional cardiologist(s) who:
      i. performs ≥ 50 structural procedures per year including atrial septal defects (ASD), patent foramen ovale (PFO) and trans-septal punctures; and,
      ii. must receive prior suitable training on the devices to be used; and,
      iii. must be board-certified in interventional cardiology or board-certified/eligible in pediatric cardiology or similar boards from outside the United States;
   b. Additional members of the heart team, including: cardiac echocardiographers, other cardiac imaging specialists, heart valve and heart failure specialists, electrophysiologists, cardiac anesthesiologists, intensivists, nurses, nurse practitioners, physician assistants, data/research coordinators, and a dedicated administrator;
   c. All cases must be submitted to a single national database;
   d. Ongoing continuing medical education (or the nursing/technologist equivalent) of 10 hours per year of relevant material;
   e. The cardiothoracic surgeon(s) must be board-certified in thoracic surgery or similar foreign equivalent.

4. The heart team interventional cardiologist or a cardiothoracic surgeon must perform the TMVR. Interventional cardiologist(s) and cardiothoracic surgeon(s) may jointly participate in the intra-operative technical aspects of TMVR as appropriate.

5. The heart team and hospital are participating in a prospective, national, audited registry that:
   1) consecutively enrolls TMVR patients; 2) accepts all manufactured devices; 3) follows the patient for at least one year; and, 4) complies with relevant regulations relating to protecting human research subjects, including 45 Code of Federal Regulations (CFR) Part 46 and 21 CFR Parts 50 & 56. The following outcomes must be tracked by the registry; and the registry must be designed to permit identification and analysis of patient-, practitioner-, and facility-level variables that predict each of these outcomes:
   a. All-cause mortality;
   b. Stroke;
   c. Repeat mitral valve surgery or other mitral procedures;
   d. Worsening MR;
   e. Transient ischemic events (TIAs);
   f. Major vascular events;
   g. Renal complications;
   h. Functional capacity;
   i. Quality of Life (QoL).

D. The registry should collect all data necessary and have a written executable analysis plan in place to address the following questions (to appropriately address some questions, Medicare claims or other outside data may be necessary):
• When performed outside a controlled clinical study, how do outcomes and adverse events compare to the pivotal clinical studies?
• How do outcomes and adverse events in subpopulations compare to patients in the pivotal clinical studies?
• What is the long-term (.5 year) durability of the device?
• What are the long-term (.5 year) outcomes and adverse events?
• How do the demographics of registry patients compare to the pivotal studies?

E. Consistent with section 1142 of the Social Security Act (the Act), the Agency for Healthcare Research and Quality (AHRQ) supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

F. TMVR for MR uses that are not expressly listed as an FDA-approved indication when performed within an FDA-approved randomized controlled trial that fulfills all of the following:
   • TMVR must be performed by an interventional cardiologist or a cardiac surgeon. Interventional cardiologist(s) and cardiothoracic surgeon(s) may jointly participate in the intra-operative technical aspects of TMVR as appropriate.
   • As a fully-described, written part of its protocol, the clinical research trial must critically evaluate the following questions at 12 months or longer follow-up:
     o What is the rate of all-cause mortality in the group randomized to TMVR compared to the patients randomized to control (surgical repair, optimal medical therapy, or other specified control group)?
     o What is the rate of re-operations (open surgical or transcatheter) of the mitral valve in the group randomized to TMVR compared to the patients randomized to control (surgical repair or other specified control group)?
     o What is the rate of severe MR in the group randomized to TMVR compared to the patients randomized to control (surgical repair or other specified control group)?

G. The randomized controlled trial must address all of the following questions at one year post-procedure:
   • What is the incidence of stroke?
   • What is the incidence of TIAs?
   • What is the incidence of major vascular events?
   • What is the incidence of renal complications?
   • What is the incidence of worsening MR?
   • What is the patient post-TMVR QoL?
   • What is the patient post-TMVR functional capacity?

H. The CMS-approved clinical trials and registries must adhere to the following standards of scientific integrity and relevance to the Medicare population:
   • The principal purpose of the research study is to test whether a particular intervention potentially improves the participant’s health outcomes.
   • The research study is well supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use.
   • The research study does not unjustifiably duplicate existing studies.
   • The research study design is appropriate to answer the research question being asked in the
study.

- The research study is sponsored by an organization or individual capable of executing the proposed study successfully.
- The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found in 45 CFR Part 46. If a study is regulated by the FDA, it also must be in compliance with 21 CFR Parts 50 and 56.
- All aspects of the research study are conducted according to appropriate standards of scientific integrity.
- The research study has a written protocol that clearly addresses, or incorporates by reference; the standards listed as Medicare coverage requirements.
- The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life threatening as defined in 21 CFR 312.81(a) and the patient has no other viable treatment options.
- The clinical research studies and registries are registered on the www.ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject. Registries are also registered in the AHRQ Registry of Patient Registries (RoPR).
- The research study protocol specifies the method and timing of public release of all prespecified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 12 months of the study primary completion date, which is the date the final subject had final data collection for the primary endpoint, even if the trial does not achieve its primary aim. The results must include number started/completed, summary results for primary and secondary outcome measures, statistical analyses, and adverse events. Final results must be reported in a publicly accessible manner; either in a peer-reviewed scientific journal (in print or on-line), in an on-line publicly accessible registry dedicated to the dissemination of clinical trial information such as ClinicalTrials.gov, or in journals willing to publish in abbreviated format (e.g., for studies with negative or incomplete results).
- The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria affect enrollment of these populations, and a plan for the retention and reporting of said populations on the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.
- The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

Consistent with section 1142 of the Act, AHRQ supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

The principal investigator must submit the complete study protocol, identify the relevant CMS research question(s) that will be addressed and cite the location of the detailed analysis plan for those questions in the protocol, plus provide a statement addressing how the study satisfies each of the standards of

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<th>Study Conduct</th>
<th>Compliance</th>
<th>Integrity</th>
<th>Protocol</th>
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scientific integrity (a. through m. listed above), as well as the investigator contact information, to the address below. The information will be reviewed, and approved studies will be identified on the CMS Website.

**Nationally Non-Covered Indications**
TMVR is non-covered for the treatment of MR when not furnished under CED according to the above-noted criteria. TMVR used for the treatment of any non-MR indications are non-covered. (This NCD last reviewed August 2014.)

No CMS National Coverage Determination (NCD) was identified for Transcatheter Pulmonary Valve. In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

**3. MINNESOTA DEPARTMENT OF HUMAN SERVICES (DHS):**
Minnesota DHS does not have a policy statement regarding transcatheter heart valve replacements in its Provider Manual or other specific provider references.

**CLINICAL EVIDENCE:**
The overall evidence for transcatheter aortic valve implantation (TAVI) is moderately large in size and consisted of two randomized controlled trials (RCTs), five comparison studies, and seven uncontrolled studies. Eight international registries were also reviewed. Individual study quality ranged from very poor to good. There were two well-designed, RCTs of TAVI using the Edwards SAPIEN device. The remaining studies were all poor to very poor in quality. The other comparison studies were case series studies, case control studies, or prospective studies that compared one TAVI device or approach with another. The overall body of evidence was low to moderate in quality. The limitations of the reviewed studies included apparent procedural learning curve, device manufacturer funding, author involvement with device manufacturer, small sample size, baseline differences between treatment groups, preferential use of one device over another, lack of randomization, and lack of a control or comparator group.

**APPLICABLE CODES:**
The Current Procedural Terminology (CPT®) codes and HCPCS codes listed in this policy are for reference purposes only. Listing of a service or device code in this policy does not imply that the service described by this code is a covered or non-covered health service. The inclusion of a code does not imply any right to reimbursement or guarantee claims payment. Other medical policies and coverage determination guidelines may apply.

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<th>HCPCS Codes</th>
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<td>ICD-9 Codes</td>
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<td>395.x*</td>
<td>Diseases of aortic valve</td>
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<td>0262T</td>
<td>Implantation of catheter-delivered prosthetic pulmonary valve, endovascular approach</td>
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<tr>
<td>0318T</td>
<td>Implantation of catheter-delivered prosthetic aortic heart valve, open thoracic approach, (e.g., transapical, other than transaortic)</td>
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<td>Transcatheter aortic valve replacement (TAVR/TAVI) with prosthetic valve; open axillary artery approach</td>
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<td>93799</td>
<td>Unlisted cardiovascular service or procedure</td>
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REFERENCES:

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POLICY HISTORY:

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QUESTIONS AND ANSWERS:
Q1:
A1:

ATTACHMENTS: