

Protocol

Transcatheter Aortic Valve Implantation for Aortic Stenosis

(701132)

Medical Benefit		Effective Date: 04/01/19	Next Review Date: 01/21
Preauthorization	No	Review Dates: 03/12, 01/13, 01/14, 01/15, 01/16, 01/18, 01/19, 01/20	

Preauthorization is not required.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none"> • With severe symptomatic aortic stenosis who are at prohibitive risk for open surgery 	Interventions of interest are: <ul style="list-style-type: none"> • Transcatheter aortic valve implantation 	Comparators of interest are: <ul style="list-style-type: none"> • Medical management 	Relevant outcomes include: <ul style="list-style-type: none"> • Overall survival • Symptoms • Morbid events • Treatment-related mortality • Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> • With severe symptomatic aortic stenosis who are at high risk for open surgery 	Interventions of interest are: <ul style="list-style-type: none"> • Transcatheter aortic valve implantation 	Comparators of interest are: <ul style="list-style-type: none"> • Surgical aortic valve repair 	Relevant outcomes include: <ul style="list-style-type: none"> • Overall survival • Symptoms • Morbid events • Treatment-related mortality • Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> • With severe symptomatic aortic stenosis who are at low or intermediate risk for open surgery 	Interventions of interest are: <ul style="list-style-type: none"> • Transcatheter aortic valve implantation 	Comparators of interest are: <ul style="list-style-type: none"> • Surgical aortic valve repair 	Relevant outcomes include: <ul style="list-style-type: none"> • Overall survival • Symptoms • Morbid events • Treatment-related mortality • Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> • With valve dysfunction and aortic stenosis or regurgitation after aortic valve repair 	Interventions of interest are: <ul style="list-style-type: none"> • Transcatheter aortic "valve-in-valve" implantation 	Comparators of interest are: <ul style="list-style-type: none"> • Surgical aortic valve repair • Medical management 	Relevant outcomes include: <ul style="list-style-type: none"> • Overall survival • Symptoms • Morbid events • Treatment-related mortality • Treatment-related morbidity

DESCRIPTION

Transcatheter aortic valve implantation (TAVI; also known as transcatheter aortic valve replacement) is a potential treatment for patients with severe aortic stenosis. Many patients with aortic stenosis are elderly and/or have multiple medical comorbidities, thus indicating a high, often prohibitive, risk for surgery. This procedure is being evaluated as an alternative to open surgery, or surgical aortic valve replacement (SAVR), for high-risk

patients with aortic stenosis and as an alternative to nonsurgical therapy for patients with a prohibitive risk for surgery.

SUMMARY OF EVIDENCE

For individuals who have severe symptomatic aortic stenosis who are at prohibitive risk for open surgery who receive TAVI, the evidence includes a randomized controlled trial (RCT) comparing TAVI with medical management in individuals at prohibitive risk of surgery, a single-arm prospective trial, multiple case series, and multiple systematic reviews. Relevant outcomes are overall survival, symptoms, morbid events, and treatment-related mortality and morbidity. For patients who are not surgical candidates due to excessive surgical risk, the PARTNER B trial reported on results for patients treated with TAVI by the transfemoral approach compared with continued medical care with or without balloon valvuloplasty. There was a large decrease in mortality for the TAVI patients at one year compared with medical care. This trial also reported improvements in other relevant clinical outcomes for the TAVI group. There was an increased risk of stroke and vascular complications in the TAVI group. Despite these concerns, the overall balance of benefits and risks from this trial indicate that health outcomes are improved. For patients who are not surgical candidates, no randomized trials have compared the self-expandable valve with best medical therapy. However, results from the single-arm CoreValve Extreme Risk Pivotal Trial met trialists' prespecified objective performance goal. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have severe symptomatic aortic stenosis who are at high risk for open surgery who receive TAVI, the evidence includes two RCTs comparing TAVI with surgical repair in individuals at high risk for surgery, multiple nonrandomized comparative studies, and systematic reviews of these studies. Relevant outcomes are overall survival, symptoms, morbid events, and treatment-related mortality and morbidity. For patients who are high risk for open surgery and are surgical candidates, the PARTNER A trial reported noninferiority for survival at one year for the balloon-expandable valve compared with open surgery. In this trial, TAVI patients also had higher risks for stroke and vascular complications. Nonrandomized comparative studies of TAVI vs. open surgery in high-risk patients have reported no major differences in rates of mortality or stroke between the two procedures. Since the publication of the PARTNER A trial, the CoreValve High Risk Trial demonstrated noninferiority for survival at one and two years for the self-expanding prosthesis. This trial reported no significant differences in stroke rates between groups. In an RCT directly comparing the self-expandable with the balloon-expandable valve among surgically high-risk patients, the devices had similar 30-day mortality outcomes, although the self-expandable valve was associated with higher rates of residual aortic regurgitation and need for a new permanent pacemaker. Evidence from RCT and nonrandomized studies has suggested that TAVI with a self-expanding device is associated with higher rates for permanent pacemakers postprocedure. However, survival rates appear to be similar between device types, and the evidence does not support the superiority of one device over another in all patients. Two sex-specific studies were also identified in a literature search with the objective of observing mortality rates in women undergoing TAVI or SAVR. Results were varied, and further study is needed. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have severe symptomatic aortic stenosis who are at intermediate risk for open surgery who receive TAVI, the evidence includes three RCTs comparing TAVI with surgical repair including individuals at intermediate surgical risk, two RCTs only in patients with intermediate risk, and multiple systematic reviews and nonrandomized cohort studies. Relevant outcomes are overall survival, symptoms, morbid events, and treatment-related mortality and morbidity. Five RCTs have evaluated TAVI in patients with intermediate risk for open surgery. Three of them, which included over 4,000 patients combined, reported noninferiority of TAVI vs. SAVR for their composite outcome measures (generally including death and stroke). A subset analysis of patients (n=383) with low and intermediate surgical risk from a fourth trial reported higher rates of death at two years

for TAVI vs. SAVR. The final study (N=70) had an unclear hypothesis and reported 30-day mortality rates favoring SAVR (15% vs. 2%, $p=0.07$) but used a transthoracic approach. The rates of adverse events differed between groups, with bleeding, cardiogenic shock, and acute kidney injury higher in patients randomized to open surgery and permanent pacemaker requirement higher in patients randomized to TAVI. Subgroup analyses of meta-analyses and the transthoracic arm of the Leon et al RCT has suggested that the benefit of TAVI may be limited to patients who are candidates for transfemoral access. Although several RCTs have two years of follow-up postprocedure, it is uncertain how many individuals require reoperation. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have severe symptomatic aortic stenosis who are at low risk for open surgery who receive TAVI, the evidence includes two RCTs comparing TAVI with surgical repair in individuals selected without specific surgical risk criteria but including patients at low surgical risk, systematic reviews, and nonrandomized cohort studies. Relevant outcomes are overall survival, symptoms, morbid events, and treatment-related mortality and morbidity. Limited data are available comparing SAVR with TAVI in patients who had severe aortic stenosis with low risk for open surgery. A systematic review including the low surgical risk patients of these two RCTs, and four observational studies, with propensity score matching, reported that the 30-day and in-hospital mortality rates were similar for TAVI (2.2%) and SAVR (2.6%). However, TAVI was associated with increased risk of mortality with longer follow-up (median, two years; 17.2% vs. 12.7%). TAVI was associated with reduced risk for bleeding, renal failure and, an increase in vascular complications and pacemaker implantation compared with SAVR. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have valve dysfunction and aortic stenosis or regurgitation after open surgical aortic valve repair who receive transcatheter aortic “valve-in-valve” implantation, the evidence includes case series (largest with 459 patients) and systematic reviews of case series. Relevant outcomes are overall survival, symptoms, morbid events, and treatment-related mortality and morbidity. These case series have reported high rates of technical success of valve implantation and improvement in heart failure symptoms for most patients. However, they have also reported high rates of short-term complications and high rates of mortality at one year postprocedure. There is a lack of evidence comparing valve-in-valve replacement with alternative treatment approaches. The evidence is insufficient to determine the effects of the technology on health outcomes.

Clinical input obtained in 2016 supported the use of transcatheter aortic “valve-in-valve” replacement for individuals who have degeneration of a surgically implanted aortic valve and who are at high or prohibitive risk for open repair.

POLICY

Transcatheter aortic valve replacement with an U.S. Food and Drug Administration (FDA)-approved transcatheter heart valve system, performed via an approach consistent with the device’s FDA-approved labeling, may be considered **medically necessary** for patients with native valve aortic stenosis when all of the following conditions are present:

- Severe aortic stenosis (see Policy Guidelines) with a calcified aortic annulus; AND
- New York Heart Association heart failure Class II, III or IV symptoms; AND
- Left ventricular ejection fraction greater than 20%; AND
- Patient is not an operable candidate for open surgery, as judged by at least two cardiovascular specialists (cardiologist and/or cardiac surgeon); or patient is an operable candidate but is at high or intermediate risk for open surgery (see Policy Guidelines).

Transcatheter aortic valve replacement with a transcatheter heart valve system approved for use for repair of a degenerated bioprosthetic valve may be considered **medically necessary** when all of the following conditions are present:

- Failed (stenosed, insufficient, or combined) of a surgical bioprosthetic aortic valve; AND
- New York Heart Association heart failure class II, III or IV symptoms; AND
- Left ventricular ejection fraction greater than 20%; AND
- Patient is not an operable candidate for open surgery, as judged by at least two cardiovascular specialists (cardiologist and/or cardiac surgeon); or patient is an operable candidate but is at high risk for open surgery (see Policy Guidelines section).

Transcatheter aortic valve replacement is considered **investigational** for all other indications.

POLICY GUIDELINES

The FDA definition of extreme risk or inoperable for open surgery is:

- Predicted risk of operative mortality and/or serious irreversible morbidity 50% or higher for open surgery

The FDA definition of high risk for open surgery is:

- Society of Thoracic Surgeons predicted operative risk score of 8% or higher; or
- Judged by a heart team, which includes an experienced cardiac surgeon and a cardiologist, to have an expected mortality risk of 15% or higher for open surgery.

The FDA definition of intermediate risk is:

- Society of Thoracic Surgeons predicted operative risk score of 3% to 7%.

For the use of the Sapien or CoreValve devices, severe aortic stenosis is defined by the presence of one or more of the following criteria:

- An aortic valve area of less than or equal to one cm²
- An aortic valve area index of less than or equal to 0.6 cm²/m²
- A mean aortic valve gradient greater than or equal to 40 mm Hg
- A peak aortic-jet velocity greater than or equal to four m/s

BACKGROUND

AORTIC STENOSIS

Aortic stenosis is defined as narrowing of the aortic valve opening, resulting in obstruction of blood flow from the left ventricle into the ascending aorta. Progressive calcification of the aortic valve is the most common etiology in North America and Europe, while rheumatic fever is the most common etiology in developing countries.¹ Congenital abnormalities of the aortic valve, most commonly a bicuspid valve, increase the risk of aortic stenosis, but aortic stenosis can also occur in a normal aortic valve. Risk factors for calcification of a congenitally normal valve mirror those for atherosclerotic vascular disease, including advanced age, male gender, smoking, hypertension, and hyperlipidemia.¹ Thus, the pathogenesis of calcific aortic stenosis is thought to be similar to that of atherosclerosis, i.e., deposition of atherogenic lipids and infiltration of inflammatory cells, followed by progressive calcification.

The natural history of aortic stenosis involves a long asymptomatic period, with slowly progressive narrowing of the valve until the stenosis reaches the severe stage. At this time, symptoms of dyspnea, chest pain, and/or dizziness/syncope often occur, and the disorder progresses rapidly. Treatment of aortic stenosis is primarily surgical, involving replacement of the diseased valve with a bioprosthetic or mechanical valve by open heart surgery.

Disease Burden

Aortic stenosis is a relatively common disorder in elderly patients and is the most common acquired valve disorder in the United States. Approximately 2% to 4% of people older than 65 years of age have evidence of significant aortic stenosis,¹ increasing up to 8% of people by age 85 years.² In the Helsinki Aging Study (1993), a population-based study of 501 patients, ages 75 to 86 years, the prevalence of severe aortic stenosis by echocardiography was estimated to be 2.9%.³ In the United States, more than 50,000 aortic valve replacements are performed annually due to severe aortic stenosis.

Aortic stenosis does not cause substantial morbidity or mortality when the disease is mild or moderate in severity. By the time it becomes severe, there is an untreated mortality rate of approximately 50% within two years.⁴ Open surgical repair is an effective treatment for reversing aortic stenosis, and artificial valves have demonstrated good durability for up to 20 years.⁴ However, these benefits are accompanied by perioperative mortality of approximately 3% to 4% and substantial morbidity,⁴ both of which increase with advancing age.

Unmet Needs

Many patients with severe, symptomatic aortic stenosis are poor operative candidates. Approximately 30% of patients presenting with severe aortic stenosis do not undergo open surgery due to factors such as advanced age, advanced left ventricular dysfunction, or multiple medical comorbidities.⁵ For patients who are not surgical candidates, medical therapy can partially alleviate the symptoms of aortic stenosis but does not affect the underlying disease progression. Percutaneous balloon valvuloplasty can be performed, but this procedure has less than optimal outcomes.⁶ Balloon valvuloplasty can improve symptoms and increase flow across the stenotic valve but is associated with high rates of complications such as stroke, myocardial infarction, and aortic regurgitation. Also, restenosis can occur rapidly, and there is no improvement in mortality. As a result, there is a large unmet need for less invasive treatments for aortic stenosis in patients at increased risk for open surgery.

Treatment

Transcatheter aortic valve implantation has been developed in response to this unmet need and was originally intended as an alternative for patients for whom surgery was not an option due to prohibitive surgical risk or for patients at high risk for open surgery. The procedure is performed percutaneously, most often through the transfemoral artery approach. It can also be done through the subclavian artery approach and trans-apically using mediastinoscopy. Balloon valvuloplasty is first performed to open up the stenotic area. This is followed by passage of a bioprosthetic artificial valve across the native aortic valve. The valve is initially compressed to allow passage across the native valve and is then expanded and secured to the underlying aortic valve annulus. The procedure is performed on the beating heart without cardiopulmonary bypass.

REGULATORY STATUS

Two manufacturers have transcatheter aortic valve devices with Food and Drug Administration (FDA) approval. Regulatory status data for these devices are listed in Table 1.

Table 1. FDA-Approved Transcatheter Aortic Valve Device Systems

Device and Indication	Manufacturer	Date Cleared	PMA
Edwards SAPIEN Transcatheter Heart Valve System™	Edwards Lifesciences	11/11	P100041

Device and Indication	Manufacturer	Date Cleared	PMA
<ul style="list-style-type: none"> Severe native aortic valve stenosis determined to be inoperable for open aortic valve replacement (transfemoral approach) Expanded to include high-risk aortic stenosis (transapical approach) Expanded to include replacement of bioprosthetic valve in high risk for death or severe complications of repeat surgery Expanded to include severe aortic stenosis with intermediate surgical risk 		10/12 06/17 08/16	
Edwards SAPIEN XT Transcatheter Heart Valve (model 9300TFX) and accessories		07/14	P130009
<ul style="list-style-type: none"> Severe native aortic valve stenosis at high or greater risk for open surgical therapy Expanded to include failure of bioprosthetic valve in high or greater risk for open surgical therapy Expanded to include severe aortic stenosis with intermediate surgical risk 		10/15 08/16	P130009/S034
Medtronic CoreValve System™	Medtronic CoreValve	01/14	P130021
<ul style="list-style-type: none"> Severe native aortic stenosis at extreme risk or inoperable for open surgical therapy Expanded to include high risk for open surgical therapy Expanded to include intermediate risk for open surgical therapy 		06/16 07/17	P130021/S002 P130021/S033
Medtronic CoreValve Evolut R System™		06/15	P130021/S014
<ul style="list-style-type: none"> Design iteration for valve and accessories Expanded to include intermediate risk for open surgical therapy 		07/17	P130021/S033
Medtronic CoreValve Evolut PRO System™		03/17	P130021/S029
<ul style="list-style-type: none"> Design iteration for valve and accessories (includes porcine pericardial tissue wrap) Expanded to include intermediate risk for open surgical therapy 		07/17	P130021/S033

FDA: Food and Drug Administration; PMA: postmarket approval.

Other transcatheter aortic valve systems are under development. The following repositionable valves are under investigation:

- Lotus™ Aortic Valve Replacement System (Boston Scientific)⁷
- Portico™ Transcatheter Aortic Valve (St. Jude Medical)
- JenaValve™ (JenaValve Technology); designed for transapical placement

On June 1, 2017, the FDA cleared the Sentinel® Cerebral Protection System (Claret Medical Inc. and Boston Scientific) which is indicated for use as an embolic protection device to capture and remove thrombus and tissue debris while performing transcatheter aortic valve replacement procedures. The diameters of the arteries at the site of filter placement should be between 9 – 15 mm for the brachiocephalic and 6.5 – 10 mm in the left common carotid. The device received a de novo classification as a class II device (DEN 160043). The FDA order, therefore, classifies the Sentinel® Cerebral Protection System, and substantially equivalent devices of this generic type, into class II under the generic name, temporary catheter for embolic protection during transcatheter intracardiac procedures.

Several additional embolic protection devices have been under investigation; TriGuard and Embrella.

RELATED PROTOCOL

Transcatheter Pulmonary Valve Implantation

Services that are the subject of a clinical trial do not meet our Technology Assessment and Medically Necessary Services Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment and Medically Necessary Services Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

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We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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