**Transcatheter Aortic Valve Implantation for Aortic Stenosis**

(701132)

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<tr>
<th>Medical Benefit</th>
<th>Effective Date: 04/01/17</th>
<th>Next Review Date: 01/19</th>
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<tr>
<td>Preauthorization</td>
<td>Yes</td>
<td>Review Dates: 03/12, 01/13, 01/14, 01/15, 01/16, 01/18</td>
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**Preauthorization is 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.

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<th>Populations</th>
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<td>Relevant outcomes include: • Overall survival • Symptoms • Morbid events • Treatment-related mortality • Treatment-related morbidity</td>
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**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 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 one randomized controlled trial (RCT) comparing TAVI with medical management in individuals at prohibitive risk of surgery, one 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 results for patients treated with TAVI by the transfemoral approach compared to 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 on 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 the authors’ 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 versus open surgery in high-risk patients have reported no major differences in rates of mortality or stroke between the two procedures. Since publication of the PARTNER A trial, the CoreValve High Risk Trial demonstrated noninferiority for survival at one year 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 clearly support the superiority of one device over another in all patients. 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 or intermediate 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, one RCT 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. Two RCTs, one investigator-initiated, have evaluated TAVI in patients in low or intermediate risk for open surgery, and both reported no significant differences in their composite outcome measure between groups. 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. In addition, given the limited follow-up beyond a year postprocedure, it is uncertain how many individuals require reoperation. 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 aortic valve repair who receive transcatheter aortic “valve-in-valve” implantation, the evidence includes case series (largest included 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.

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 (NYHA) 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).

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
- NYHA 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 investigative for all other indications.

Policy Guidelines

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 extreme risk or inoperable for open surgery is:

- Predicted risk of operative mortality and/or serious irreversible morbidity 50% or higher for open surgery.
For the use of the Sapien or CoreValve device, 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 cm$^2$
- An aortic valve area index of less than or equal to 0.6 cm$^2$/m$^2$
- 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. Congenital abnormalities of the aortic valve, most commonly a bicuspid valve, increase the risk for 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. 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.

Burden of Illness

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, increasing up to 8% of people by age 85 years. 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%. 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. Open surgical repair is an effective treatment for reversing aortic stenosis, and artificial valves have demonstrated good durability for up to 20 years. However, these benefits are accompanied by a perioperative mortality of approximately 3% to 4% and substantial morbidity, 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. 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. Balloon valvuloplasty can improve symptoms and increase flow across the stenotic
Protocol
Transcatheter Aortic Valve Implantation for Aortic Stenosis

Transcatheter Aortic Valve Implantation

TAVI has been developed in response to this unmet need and is intended as an alternative for patients for whom surgery is 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 transapically 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.

Two transcatheter aortic valve devices have FDA approval. The Edwards SAPIEN Transcatheter Heart Valve System is a tri-leaflet bioprosthetic porcine valve contained within a stainless steel frame. This device first received FDA approval in 2011, with expanded indications granted in 2012 and 2013.

The CoreValve ReValving System and the second-generation Evolut R system are porcine bioprosthetic valves sewn within a self-expanding nitinol frame, which received FDA approval in 2014. The CoreValve is most commonly inserted via the transfemoral artery approach, but can also be inserted via a non-iliofemoral approach (subclavian artery or direct aortic access). The Evolut R system incorporates a repositionable valve and an in-line catheter design, reducing the diameter of the device delivery system.

Several embolic protection devices, which are designed to collect embolic debris distal to the TAVI apparatus and to prevent ischemic stroke, are under investigation. No devices have FDA approval for use in the United States. Examples include the TriGuard (Keystone Heart, Caesarea, Israel) and the Sentinel Cerebral Protection System (Claret Medical, Santa Rosa, CA).

Regulatory Status

In November 2011, the SAPIEN Transcatheter Heart Valve System™ (Edwards LifeSciences, Irvine, CA) was originally approved by the FDA through the premarket approval process for patients with severe aortic stenosis who are not eligible for open-heart procedures and have a calcified aortic annulus. Approval was granted for both the transfemoral and transapical approach. For the transfemoral approach, patient indications were broadened to include patients at high risk for open surgery. For the transapical approach, approval was granted for patients at high risk for open surgery. In September 2012, FDA expanded the indications for the transapical approach to include both inoperable patients and patients at high risk for open surgery. As a result, the SAPIEN Transcatheter Heart Valve System™ is approved for both high-risk and inoperable patients when used by either the transapical or transfemoral approach. In June 2014, the next-generation SAPIEN XT Transcatheter Heart Valve (model 9300TFX) was approved by FDA for use with the NovaFlex+ delivery system. In October 2015, FDA expanded the indication for the SAPIEN valve to include treatment of a failed surgical bioprosthesis (TAV- in-SAV or “valve-in-valve”).

In August 2016, the SAPIEN XT valve and introducers were approved with an expanded indication to include individuals at intermediate surgical risk for open aortic valve replacement (i.e., predicted risk of surgical mortality ≥ 3% at 30 days based on the Society of Thoracic Surgeons [STS] Risk Score and other clinical comorbidities unmeasured by the STS Risk Calculator). The earlier generation Sapien devices also received the expanded indication for intermediate surgical risk patents.
In January 2014, the CoreValve® Transcatheter Aortic Valve Replacement System (Medtronic, Minneapolis, MN) was approved by FDA through the premarket approval process for patients with symptomatic heart disease due to severe native calcific aortic stenosis 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. In June 2014, the FDA expanded the indications for the CoreValve® to include patients at high risk for open surgery. FDA labeling indicates that the device can be delivered via femoral, subclavian/axillary, or ascending aortic access. In March 2015, the FDA further expanded the indications for the CoreValve® to include treatment of a failed surgical bioprosthesis (TAV-in-SAV or “valve-in-valve”). A second-generation CoreValve® device, the CoreValve Evolut™ R System, received FDA approval in June 2015.

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

- Lotus™ Aortic Valve Replacement System (Boston Scientific, Marlborough, MA)
- Portico™ Transcatheter Aortic Valve (St. Jude Medical, St. Paul, MN)
- JenaValve™ (JenaValve Technology, Munich); designed for transapical placement
- Direct Flow Medical Transcatheter Aortic Valve System (Direct Flow Medical, Santa Rosa, CA).

Related Protocol
Transcatheter Pulmonary Valve Implantation

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

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


