Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy # 00181
Original Effective Date: 09/22/2005
Current Effective Date: 11/16/2016

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Endovascular Grafts for Abdominal Aortic Aneurysms are addressed separately in medical policy 00035.

When Services Are Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:
• Benefits are available in the member’s contract/certificate, and
• Medical necessity criteria and guidelines are met.

Based on review of available data, the Company may consider endovascular stent grafts using devices approved by the U.S. Food and Drug Administration (FDA) to be eligible for coverage in the following situations:
• Treatment of descending thoracic aortic aneurysms (TAAs) without dissection (see Note below);
• Treatment of acute, complicated (organ or limb ischemia or rupture) Type B thoracic aortic dissection.

Note: Endograft placement relies on nonaneurysmal aortic segments proximal and distal to the aneurysm and/or dissection for anchoring, and a maximal graft diameter that varies by device. The GORE TAG⃣ endoprosthesis is approved by FDA for “≥ 2cm non-aneurysmal aorta proximal and distal to the aneurysm and an “aortic inner diameter of 23–37mm.” The Talent ™ Thoracic Stent Graft System is approved by FDA for “non-aneurysmal aortic proximal and distal neck lengths ≥ 20mm” and “non-aneurysmal aortic diameter in the range of 18–42mm.” The Zenith TX2⃣ device is approved by FDA for non-aneurysmal aortic segments “of at least 25mm in length” and “diameter measured outer wall to outer wall of no greater than 38mm and no less than 24mm.”

Based on review of available data, the Company considers endovascular stent grafts for the treatment of rupture of the descending thoracic aorta to be eligible for coverage.

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of endovascular stent grafts for the treatment of thoracic aortic lesions that do not meet the above criteria, including but not limited to thoracic aortic arch aneurysms to be investigational.*

Background/Overview
Thoracic endovascular aneurysm repair (TEVAR) involves the percutaneous placement of a stent graft in the descending thoracic or thoracoabdominal aorta. It is a less invasive alternative to open surgery for the
Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy # 00181
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treatment of TAA, dissection, or rupture, and thus has the potential to reduce the morbidity and mortality of open surgery. Endovascular stenting may also be an alternative treatment to medical therapy for thoracic aortic aneurysms or thoracic aorta dissections.

Thoracic Aortic Aneurysms
Aortic aneurysms are arterial dilations that are associated with age, atherosclerosis, and hypertension, as well as some congenital connective tissue disorders. The likelihood of significant sequelae of aortic aneurysm is dependent on location, size, and underlying disease state. Left untreated, these aneurysms tend to enlarge over time, increasing the risk of rupture or dissection. Of greatest concern is the tendency for aortic aneurysms to rupture, with severe consequences including death. Another significant adverse occurrence of aortic aneurysm is aortic dissection, in which an intimal tear permits blood to enter the potential space between the intima and the muscular wall of the aorta. Stable dissections may be managed medically; however, dissections which impinge on the true lumen of the aorta, or occlude branching vessels are a surgical emergency.

The indications for the elective surgical repair of aortic aneurysms are based on estimates of the prognosis of the untreated aneurysm balanced against the morbidity and mortality of the intervention. The prognosis of TAA is typically reported in terms of the risk of rupture according to size and location, i.e., the ascending or descending or thoracoabdominal aorta. While several studies have estimated the risk of rupture of untreated aneurysms, these studies have excluded patients who underwent surgical repair; therefore, the true natural history of thoracic aneurysms is unknown. Clouse and colleagues performed a population-based study of TAA diagnosed in Olmstead County, Minn., between the period of 1980 and 1994. A total of 133 patients were identified; the primary clinical endpoints were cumulative rupture risk, rupture risk as a function of aneurysm size, and survival. The cumulative risk of rupture was 20% after 5 years. The 5-year risk of rupture as a function of aneurysm size at recognition was 0% for aneurysms less than 4 cm in diameter, 16% for those 4 to 5.9 cm, and 31% for aneurysms 6 cm or more. Interestingly, 79% of the ruptures occurred in women. Davies and colleagues reported on the yearly rupture or dissection rates in 721 patients with TAA. A total of 304 patients were dissection-free at presentation; their natural history was followed up for rupture, dissection, and death. Patients were excluded from analysis once the operation occurred. Not surprisingly, the authors reported that aneurysm size had a profound impact on outcomes. For example, based on their modeling, a patient with an aneurysm exceeding 6 cm in diameter can expect a yearly rate of rupture or dissection of at least 6.9% and a death rate of 11.8%. In a previous report, the authors suggested surgical intervention of a descending aorta aneurysm if its diameter measured 6.5 cm.

Surgical morbidity and mortality are typically subdivided into elective versus emergency repair with a focus on the incidence and risk of spinal cord ischemia, considered one of the most devastating complications, resulting in paraparesis or paraplegia. The operative mortality of surgical repair of aneurysm of the descending and thoracoabdominal aorta is estimated at 6–12% and 10–15%, respectively, while mortality associated with emergent repair is considerably higher. In elective cases, predictors of operative mortality include renal insufficiency, increasing age, symptomatic aneurysm, presence of dissection, and other comorbidities, such as cardiopulmonary or cerebrovascular disease. The risk of paraparesis or paraplegia is estimated at 3–15%. Thoracoabdominal aneurysms, larger aneurysms, presence of dissection, and diabetes are predictors of paraplegia. A number of surgical adjuncts have been explored over the years to
reduce the incidence of spinal cord ischemia, including distal aortic perfusion, cerebrospinal fluid drainage, hypothermia with circulatory arrest, and evoked potential monitoring. However, the optimal protective strategy is still uncertain.

This significant morbidity and mortality makes definitive patient selection criteria for repair of thoracic aneurysms difficult. Several authors have recommended an individual approach based on balancing the patients’ calculated risk of rupture with their anticipated risk of postoperative death or paraplegia. However, in general, surgical repair is considered in patients with adequate physiologic reserve when the thoracic aneurysm measures from 5.5 to 6 cm in diameter or in patients with smaller symptomatic aneurysms.

**Thoracic Aortic Dissection**

Aortic dissection can be subdivided into type A, which involves the aortic arch, and type B, which is confined to the descending aorta. Type A dissections are usually treated surgically, while type B dissections are usually treated medically, with surgery indicated for serious complications, such as visceral ischemia, impending rupture, intractable pain, or sudden reduction in aortic size. Dissections associated with obstruction and ischemia can also be subdivided into an obstruction caused by an intimal tear at branch vessel orifices, or by compression of the true lumen by the pressurized false lumen. It has been proposed that endovascular therapy can repair the latter group of dissections by redirecting flow into the true lumen. The success of endovascular stent grafts of abdominal aortic aneurysms has created interest in applying the same technology to the aneurysms and dissections of the descending or thoracoabdominal aorta.

As noted previously, type A dissections (involving the ascending aorta) are treated surgically. There is more controversy regarding the optimal treatment of type B dissections (i.e., limited to the descending aorta). In general, chronic, stable type B dissections are managed medically, although some surgeons recommended a more aggressive approach for younger patients in otherwise good health. When serious complications arise from a type B dissection, i.e., shock or visceral ischemia, surgical intervention is usually indicated. However, although there is an estimated 50% 1-year survival rate in those treated with an open surgical procedure, it is not clear whether that is any better or worse than those treated medically. The advent of stent grafting, with the potential of reducing the morbidity and mortality of an open surgical procedure, may further expand the number of patients considered for surgical intervention.

**Thoracic Aortic Rupture**

Rupture of the thoracic aorta is a life-threatening emergency that is nearly always fatal if untreated. Thoracic artery rupture can result from a number of factors. Aneurysms can rupture due to progressive dilatation and pressure of the aortic wall. Rupture can also occur as a result of traumatic injury to the aorta, such as occurs with blunt chest trauma. Penetrating injuries that involve the aorta can also lead to rupture. Penetrating ulcers can occur in the setting of widespread atherosclerotic disease and lead to aortic rupture.

Emergent repair of thoracic artery rupture is indicated in many cases in which there is free bleeding into the mediastinum and/or complete transection of the aortic wall. In some cases of aortic rupture, where the aortic media and adventitia are intact, watchful waiting with delayed surgical intervention can be performed. With the advent of TEVAR, the decision making for intervention may be altered, as there may be a greater tendency to intervene on borderline cases due to the potential for less adverse events with TEVAR.
Thoracic Endovascular Aneurysm Repair
Thoracic endovascular aneurysm repair is an alternative to open surgery. Thoracic endovascular aneurysm repair has been proposed for prophylactic treatment of aneurysms that meet criteria for surgical intervention, as well as for patients in need of emergency surgery for rupture or complications related to dissection. The standard open surgery technique for TAA is open operative repair with graft replacement of the diseased segment. This procedure requires lateral thoracotomy, use of cardiopulmonary bypass, long operation times, and is associated with a variety of peri- and postoperative complications, with spinal cord ischemia considered the most devastating.

Thoracic endovascular aneurysm repair is performed through a small groin incision to access the femoral artery, followed by delivery of catheters across the diseased portion of the aorta. A tubular stent graft composed of fabric and metal is then deployed under fluoroscopic guidance. The stent graft is then fixed to the proximal and distal portions of the aorta. Approximately 15% of patients do not have adequate femoral access, and the procedure can be performed by a retroperitoneal approach in these cases.

Potential complications of TEVAR are bleeding, vascular access site complications, spinal cord injury with paraplegia, renal insufficiency, stroke, and cardiopulmonary complications. Some of these complications are similar to those encountered with open repair, such as paraplegia and cardiopulmonary events, and others are unique to TEVAR, such as access site complications.

FDA or Other Governmental Regulatory Approval
U.S. Food and Drug Administration
A number of endovascular grafts are approved for use in TAA (FDA product code: MIH).

In March 2005, the Gore TAG Thoracic Endoprosthesis (W.L. Gore and Associates Inc. Flagstaff, AZ) was approved by the FDA through the premarket approval (PMA) process for endovascular repair of aneurysms of the descending thoracic aorta. Use of this device requires patients to have adequate iliac/femoral access, aortic inner diameter in the range of 23 to 37 mm, and 2 cm or more nonaneurysmal aorta proximal and distal to the aneurysm. In January 2012, FDA granted an expanded indication for the Gore TAG system to include isolated lesions of the thoracic aorta. Isolated lesions refer to aneurysms, ruptures, tears, penetrating ulcers and/or isolated hematomas, but do not include dissections. Indicated aortic inner diameter is 16 to 42 mm, with 20 mm or more of nonaneurysmal aortic distal and proximal to the lesion.

In May 2008, the Zenith TX2 TAA Endovascular Graft (Cook Inc., Bloomington, IN) was approved by FDA through the PMA process for the endovascular treatment of patients with aneurysms or ulcers of the descending thoracic aorta. Indicated aortic inner diameter is in the range of 24 to 38 mm.

In June 2008, the Talent Thoracic Stent Graft System (Medtronic Vascular, Santa Rosa, CA) was approved by FDA through the PMA process for the endovascular repair of fusiform and saccular aneurysms/penetrating ulcers of the descending thoracic aorta. Indicated aortic inner diameter is in the range of 18 to 42 mm.

In September 2012, FDA approved the Relay® Thoracic Stent-Graft with Plus Delivery System (Bolton Medical, Sunrise, FL) through the PMA process for the endovascular repair of fusiform aneurysms and
Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy # 00181
Original Effective Date: 09/22/2005
Current Effective Date: 11/16/2016

Saccular aneurysms/penetrating atherosclerotic ulcers in the descending thoracic aorta in patients having appropriate anatomy, including:

- Iliac or femoral access vessel morphology that is compatible with vascular access techniques, devices and/or accessories
- Nonaneurysmal aortic neck diameter in the range of 19-42 mm
- Nonaneurysmal proximal aortic neck length between 15-25 mm and nonaneurysmal distal aortic neck length between 25-30 mm depending on the diameter stent-graft required.

In October 2012, FDA granted approval for the Valiant™ Thoracic Stent Graft with the Captivia® Delivery System (Medtronic Vascular, Santa Rosa, CA) to include isolated lesions of the thoracic aorta. Isolated lesions refer to aneurysms, ruptures, tears, penetrating ulcers and/or isolated hematomas, but not including dissections. Indicated aortic diameter is 18 to 42 mm for aneurysms and penetrating ulcers, and 18 to 44 mm for blunt traumatic injuries. In January 2014, FDA-approved indications for the Valiant Thoracic Stent Graft with the Captivia Delivery System were expanded into include all lesions of the descending thoracic aorta, including type B dissections. The Valiant graft is intended for the endovascular repair of all lesions of the descending aorta in patients having appropriate anatomy including:

- Iliac/femoral access vessel morphology that is compatible with vascular access techniques, devices, and/or accessories;
- Nonaneurysmal aortic diameter in the range of 18 to 42 mm (fusiform and saccular aneurysms/penetrating ulcers), 18 to 44 mm (blunt traumatic aortic injuries) or 20 to 44 mm (dissections) and;
- Nonaneurysmal aortic proximal and distal neck lengths 20 mm or more (fusiform and saccular aneurysms/penetrating ulcers), landing zone 20 mm or more proximal to the primary entry tear (blunt traumatic thoracic aortic injury [BTAI], dissection). The proximal extent of the landing zone must not be dissected.

The expanded approval was based on the Medtronic Dissection Trial, a prospective, nonrandomized study to evaluate the performance of the Valiant stent graft for acute, complicated type B dissection, which included 50 patients enrolled at 16 sites.

Other devices are under development, and in some situations, physicians have adapted other commercially available stent grafts for use in the thoracic aorta.

Centers for Medicare and Medicaid Services (CMS)
There is no national coverage determination.

**Rationale/Source**
This policy is updated regularly with searches of the MEDLINE database. The most recent literature review was performed for the period through March 28, 2016. The following is a summary of key findings.

Controlled trials of specific patient groups treated with specific procedures are required to determine if endovascular approaches are associated with equivalent or improved outcomes compared to surgical repair. For patients who are candidates for surgery, open surgical resection of the aneurysm with graft
Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy # 00181
Original Effective Date: 09/22/2005
Current Effective Date: 11/16/2016

replacement is considered the gold standard for treatment of aneurysms or dissections. Some patients who would not be considered candidates for surgical therapy due to unacceptable risks might be considered candidates for an endovascular graft. In this situation, the outcomes of endovascular grafting should be compared to optimal medical management. Comparative mortality rates are of high concern, as are the rates of serious complications such as the incidence of spinal cord ischemia.

Randomization to treatment groups is also very important in this area. This is due to the numerous patient factors (i.e., age, co-morbidities, location, size of the aneurysm, presence or absence of dissection) and procedure variables involved in surgical repair that are potential confounders of outcome. Selection for either open or endovascular repair involves a complex set of patient and anatomical considerations. As a result, studies are highly prone to selection bias if there is not randomized assignment.

Aneurysms of the Descending Thoracic Aorta
There are no randomized controlled trials (RCTs) of endovascular repair versus open surgery for thoracic aneurysms. The best evidence consists of non-randomized comparative studies and systematic reviews of these studies. The following review includes representative prospective, non-randomized studies and selected systematic reviews.

Systematic Reviews
A systematic review of the evidence for endovascular repair of thoracic aneurysms was published by the Cochrane Peripheral Vascular Diseases Group in January 2009 and was based on the literature to October 2008. No RCTs comparing endovascular repair to open surgical interventions for thoracic aneurysms were found in the medical literature. Reports from non-randomized studies suggest that endovascular repair is technically feasible and may reduce early negative outcomes, including death and paraplegia. However, endovascular repair is associated with late complications not often seen in open surgery, such as the development of leaks, graft migration, and need for re-intervention. Patients receiving endovascular grafts also more require frequent surveillance with computed tomography (CT) scans and have increased radiation exposure.

In 2016, Biancari et al published a meta-analysis of TEVAR for aneurysms of the descending thoracic aorta in the elderly (mean, 72.6 years; 95% confidence interval [CI], 71.3 to 73.9 years). No RCTs were identified, and the review did not compare TEVAR with open surgical repair in this more fragile population. The 11 observational studies (673 patients, 6 retrospective) reported technical success in 91.0% of procedures with vascular access complications requiring repair in 9.7% of cases. Endoleak was observed in 10.5% of patients. Survival rates were 96.0% at 30 days, 80.3% at 1 year, 77.3% at 2 years, and 74.0% at 3 years. TEVAR as an emergency procedure was performed in about one-third of the population, and had a significantly higher 30-day mortality rate than elective TEVAR (17.1% vs 1.8; relative risk [RR], 3.83; 95% CI, 1.18 to 12.40; p=0.025). By 3 years, reintervention was needed in 9.7% of patients, with death secondary to aneurysm rupture and/or fistula in 3.2% of patients. Interpretation of these results is difficult due to the lack of comparison with open repair.

Non-randomized Comparative Studies
TAG 99-01 Study
Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy # 00181
Original Effective Date: 09/22/2005
Current Effective Date: 11/16/2016

The TAG 99-01 study was a controlled trial of patients with aneurysms of the descending thoracic aorta treated with either surgical repair (n = 94; 50 historical, and 44 concurrent) or stent grafting (n = 140) at 17 sites in the United States. Patients for both the graft group and the control group were selected using the same inclusion and exclusion criteria. After fractures in the wire frame of the TAG endoprosthesis were discovered in TAG 99-01, 51 patients underwent stent grafting with a modified TAG endoprosthesis at 11 sites in the subsequent TAG 03-03 study. The primary outcomes assessed in both TAG 99-01 and TAG 03-03 were the number of patients who had 1 or more major adverse events and the number of patients who did not experience device-related events 12 months’ post-device deployment. The number of patients in the TAG 99-01 device group who experienced equal to or greater than 1 major adverse event (42%) was significantly lower (p < 0.001) than the surgical repair control group (77%) at 1-year follow-up. Major adverse events included major bleeding, neurologic; pulmonary; renal function; and vascular complications. In the TAG 99-01 device group, 4 of 140 patients (3%) experienced paraplegia or paraparesis versus 13 of 94 patients (14%) in the control group.

In the 12-month follow-up of TAG 99-01, 8 patients (3%) had 1 or more major adverse device-related events, while the 12- to 24-month follow-up in this group only noted 1 major adverse device-related event. No major adverse device-related events occurred in the 30-day follow-up of the TAG 03-03 group. Information on 142 patients from the TAG 99-01 trial was published by Makaroun and colleagues; however, the authors did not report on comparative data with the surgical control group, citing regulatory requirements pending FDA review. The Makaroun et al. report of the TAG 99-01 study reported favorable aneurysm-related (97%) and overall survival (OS) (75%) rates and concluded that the GORE TAG device was a safe alternative treatment for descending TAAAs.

These same authors have also reported 5-year outcomes of the TAG 99-01 trial. In this follow-up of 140 endograft patients and 96 non-contemporaneous controls, the authors concluded that endovascular treatment was superior to surgical repair at 5 years in anatomically suitable patients. At 5 years, aneurysm-related mortality was lower for TAG patients at 2.8% compared with open controls at 11.7% (p = 0.008). No differences in all-cause mortality were noted, with 68% of TAG patients and 67% of open controls surviving to 5 years. Endoleaks in the TAG group decreased from 8.1% at 1 month to 4.3% at 5 years. Five TAG patients have undergone major aneurysm-related re-interventions at 5 years (3.6%). For this study, significant sac size change was defined as 5 mm or greater increase or decrease from the 1-month baseline measurement. Migration was defined as 10 mm or more cranial or caudal movement of the device inside the aorta. Compared with the 1-month baseline, sac size at 60 months decreased in 50% and increased in 19% of TAG patients. At 5 years, there have been no ruptures, 1 migration, no collapse, and 20 instances of fracture in 19 patients, all before the revision of the TAG graft. They also noted that although sac enlargement was concerning, a modified device may be helping to resolve this issue.

VALOR and VALOR II Studies
The Evaluation of the Medtronic Vascular Talent Thoracic Stent Graft System for the Treatment of Thoracic Aortic Aneurysms (VALOR) trial was a nonrandomized study conducted at 38 sites within the United States to assess the Talent stent graft. The VALOR trial enrolled patients who were candidates for open surgical repair and compared 195 TAA patients (age, 70.2±11.1 years; male 59%) with 189 retrospective open surgical repair controls (age, 69.6±9.1 years; male: 52.4%). Patients in the Talent
Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy # 00181
Original Effective Date: 09/22/2005
Current Effective Date: 11/16/2016

Endovascular graft group had smaller TAA size and were less likely to have a previous aortic aneurysm (37/195 vs 70/189 in the surgery group). Talent subjects were also less likely to have comorbid conditions including angina (pooled relative risk [RR], 1.6; 95% confidence interval [CI], 1.0 to 2.6), coronary artery disease (pooled RR=1.2; 95% CI, 1.0 to 1.5), or previous myocardial infarction (MI; pooled RR=1.3; 95% CI, 1.0 to 1.6). Thirty-day (Talent group, 4/195 vs surgery group, 15/189; p<0.1) and 12-month mortality (Talent group, 31/192 vs surgery group, 39/189; p<0.01) were lower in the endovascular graft group than the open surgery group. Fewer endovascular graft patients required blood transfusions (Talent, 22% vs surgery, 93%). Endovascular graft patients had a shorter intensive care unit stay (Talent, 2±5.5 days vs surgery, 8±8.5 days) and overall hospital stay (Talent, 6±11.5 days vs surgery, 17±15 days).

The Evaluation of the Clinical Performance of the Valiant Thoracic Stent Graft in the Treatment of Descending Thoracic of Degenerative Etiology in Subjects Who Are Candidates for Endovascular Repair (VALOR II) was a prospective nonrandomized study at 24 sites that was designed to evaluate the Valiant thoracic stent graft, as opposed to the VALOR study which was an evaluation of the Talent stent graft. VALOR II enrolled 160 patients who underwent stent grafting with the Valiant device, using similar enrollment criteria to VALOR. Outcomes were compared with those from the VALOR study. Stent-graft delivery was technically successful in 154 patients. One hundred fifty-one patients were evaluated at 12 months postprocedure; all-cause mortality at 12 months associated with the Valiant stent graft was statistically noninferior to the Talent stent graft (12.6% vs 16.1%) and exceeded the primary effectiveness goal of 12-month successful aneurysm treatment (defined as absence of aneurysm growth >5 mm and of secondary procedures for type I/III endoleak).

In 2014, Matsumoto et al reported rates of secondary procedures over 3 years of follow up for patients enrolled in the VALOR and VALOR II studies. Three-year follow-up evaluation was available for 127 patients (65.5%) in the TEVAR arm of VALOR and 96 (61.8%) in VALOR II. Freedom from secondary procedures at 3 years was 85.1% (95% CI, 78.5% to 89.8%) in the TEVAR arm of VALOR and 94.9% (95% CI, 88.8% to 97.7%) in VALOR II (p<0.001). The overall 3-year difference between groups in secondary procedure rates were driven by differences in early (within 1 year) reintervention rates. This comparison suggests that the newer-generation stent-graft device may be associated with fewer subsequent reinterventions; however, the nonrandomized comparison and potential differences between patients in VALOR and VALOR II makes it difficult to draw firm conclusions about the relative efficacy of different devices.

Goodney et al
These authors used Medicare claims data from 1998-2007 to compare TEVAR with open surgery in patients with aneurysms of the descending aorta. This study included both intact and ruptured aneurysms. A total of 13,998 patients with intact aneurysms were identified; 11,565 were treated with open surgery and 2,433 with TEVAR. There were baseline differences between the 2 groups, with the TEVAR group being older and more likely to have a variety of medical comorbidities. The authors performed 2 comparisons, an unadjusted comparison of outcomes in all patients and a propensity-matched comparison in a subset of 1,100 patients.
Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy # 00181
Original Effective Date: 09/22/2005
Current Effective Date: 11/16/2016

Thirty-day mortality was slightly lower among TEVAR patients compared to open surgery, but this difference did not reach statistical significance (6.1% vs. 7.1%, p = 0.07). In the propensity-matched comparison, there was no difference in 30-day mortality between the TEVAR and open surgery group (4.5% vs. 4.2%, p = 0.78). Long-term survival was reported by Cox proportional hazards analysis. At 5 years, survival in the TEVAR group was lower than for the open surgery group (62% vs. 72%, p = 0.001). In the propensity-matched comparison, the TEVAR group also had lower OS at 5 years compared to the open surgery group (73% vs. 81%, p = 0.007).

Matsumara et al
The Zenith TX2 device also received PMA from the FDA based on results of Matsumara et al. The study was a prospective cohort study that compared 160 TEVAR patients (aged: 72+/-.9.6 years; male: 72%) to 70 open surgery patients (aged: 68+/-.12 years; male 60%). The study arms were comparable in previous history of cardiovascular and other vascular disease. The TEVAR patients had a lower American Society of Anesthesiologist classification (p < 0.01) and higher Society of Vascular Surgery/International Society of Cardiovascular Surgery risk score (p = 0.03).

The 30-day survival rate for the endovascular group was non-inferior (p < 0.01) to the control group (98.1% vs. 94.3%, respectively). The 30-day severe morbidity composite index (cumulative mean number of events per patient) was significantly lower in the endovascular group compared to the control group (0.2 ± 0.7 vs. 0.7 ± 1.2; p < 0.01). At 12 months, aneurysm growth was identified in 7.1% of the endovascular patients, endoleak occurred in 3.9% (4/103 patients), and migration in 2.8% (3/107 patients). At 12 months, aneurysm growth was identified in 7.1% of the endovascular patients, endoleak occurred in 3.9% (4/103 patients), and migration in 2.8% (3/107 patients).

In 2014, Matsumara et al published 5-year follow-up from the Zenith TX2 prospective cohort study described earlier. The 70 patients in the open surgical control group underwent clinical evaluation before discharge or at 1 month and then at 12 months and yearly thereafter up to 5 years. Follow-up beyond 1 year was unavailable for 24 patients due to institutional review board restrictions and for 4 additional patients who were lost to follow-up. TEVAR patients had follow-up at 1, 6, and 12 months postprocedure and yearly thereafter. Of the 160 TEVAR patients, 2 did not have successful device deployment and only had follow-up to 30 days, and an additional 32 were lost to follow-up. Five-year survival was 62.9% for the TEVAR group and 62.8% for the open surgical group (nonsignificant difference between groups). Kaplan-Meier estimates of freedom from severe morbidity composite index was significantly higher in the TEVAR group than the open surgical control group (87.3% vs 64.3% at 1 year and 79.1% vs 61.2% at 5 years; log-rank test, p<0.001). Secondary interventions occurred at similar rates between the endovascular and open surgical control patient groups during follow-up through 5 years. While this study is somewhat limited by some loss to follow-up, it suggests that the early morbidity benefit associated with TEVAR persists over time and that rates of secondary interventions may be comparable with open surgical repair.

Other Studies
In addition to the prospective studies described above, some additional studies have compared open and endovascular repair using either large administrative databases or retrospective comparative designs. Orandi et al published a comparative analysis of 1030 patients undergoing open surgery and 267
Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy #  00181
Original Effective Date:  09/22/2005
Current Effective Date:  11/16/2016

undergoing endovascular repair using the Nationwide Inpatient Sample database. In-hospital mortality was similar between open and endovascular patients (adjusted odds ratio [OR], 1.2; 95% CI, 0.73 to 2.12). Dick et al reported a post hoc analysis of prospectively collected data for clinical and quality-of-life outcomes in 52 patients undergoing endovascular repair with 70 patients undergoing open surgical repair, with no significant differences in perioperative mortality rates or overall quality-of-life scores. Other representative retrospective studies of TEVAR for aortic aneurysms are those by Cazavet et al, Iba et al, and Arnaoutakis et al.

Section Summary
There are no RCTs of TEVAR versus open surgery for elective repair of TAAs, with the best evidence on this question consisting of non-randomized, comparative studies. The main limitation of these studies is non-comparability of groups, with group differences demonstrated between endovascular and surgical patients in nearly all cases. In some instances, TEVAR patients appear to be less severely ill than open surgery patients, but in other instances, the TEVAR population appears to be more severely ill. These group differences preclude definitive conclusions about the comparative efficacy of endovascular versus open surgery for repair of thoracic aneurysms.

The results of these studies are consistent in showing equivalent or reduced short-term mortality and fewer early complications for TEVAR. The consistency of this finding across populations with different characteristics lends support to the conclusion that TEVAR is a safer procedure in the short term. The likely short-term benefits of TEVAR are mitigated by longer-term outcomes that are less favorable for TEVAR. Longer-term mortality appears to be roughly similar for patients undergoing TEVAR or open surgery, and some studies report that long-term survival is better following open surgery. Thoracic endovascular aneurysm repair patients have a higher rate of long-term complications, primarily from endoleaks, and a higher re-intervention rate. Thoracic endovascular aneurysm repair patients also require closer monitoring after intervention, with more frequent imaging studies.

Dissection of the Descending Aorta (Type B Dissection)
Acute, Uncomplicated Type B Aortic Dissections
Randomized Controlled Trials
One RCT (the ADSORB trial) compared TEVAR with best medical therapy for patients with acute, uncomplicated dissections. In 2014, initial results of the ADSORB trial, which randomized 61 patients with uncomplicated acute type B aortic dissection to best medical therapy (n=31) or best medical therapy plus endovascular repair with the Gore TAG stent graft (n=30), were published. Eligible patients had acute (randomized within 14 days of symptom onset), uncomplicated type B dissection without evidence of connective tissue disease. The median time from onset of symptoms to randomization was 4.8 and 4.6 days for the best medical therapy and the TEVAR group, respectively. Treatment crossovers occurred in 3 patients from the best medical therapy group to the TEVAR group. Fourteen subjects failed due to inadequate/no imaging, and were counted in the 1-year efficacy end point calculations as failures. The study’s primary end point was a composite of (1) incomplete or no false lumen thrombosis at 1 year, (2) aortic dilation at 1 year, or (3) aortic rupture through the 1-year follow-up period. At 1 year, 15 (50.0%) of the 30 TEVAR patients had at least 1 end point event and all 31 best medical therapy patients had at least 1 end point event (p<0.001). In the control group, 30 patients had no false lumen thrombosis and 14 had
Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy # 00181
Original Effective Date: 09/22/2005
Current Effective Date: 11/16/2016

There were no deaths within 30 days postprocedure; during follow-up, 1 death (cardiac arrest) occurred in the TEVAR group.

Nonrandomized Comparative Studies
One retrospective study compared outcomes of endovascular repair with medical therapy for acute type B aortic dissections. Of 88 patients presenting with acute dissection over a 12-year period, 50 were treated medically and 38 were treated with endovascular repair. Overall mortality was reported for a mean follow-up of 33 to 36 months and did not differ between the medical therapy group (24%) and the endovascular group (23.7%; p=NS).

Section Summary: Acute, Uncomplicated Type B Aortic Dissections
One RCT reported short-term improvements in aortic remodeling and risk of aortic dilation and rupture in patients with acute, uncomplicated aortic dissections treated with TEVAR, compared with those treated with best medical management. However, this trial was underpowered to evaluate mortality differences, and limitations include a high rate of failure of imaging follow-up. Single-arm series report relatively high success rates and favorable long-term results compared with historical controls undergoing open surgery.

Acute, Complicated Type B Aorta Dissections
Systematic Reviews
In 2014, Moulakakis et al reported results of a systematic review and meta-analysis of studies on the management of complicated and uncomplicated type B aortic dissection, including medical management, open surgical repair, and endovascular repair. “Complicated dissections” were defined as those with aortic rupture, visceral and renal ischemia, lower extremities ischemia, or spinal cord ischemia, or with expansion to the aortic arch or proximal descending aorta with a total diameter of 4.5 cm or more. The review included 30 studies on TEVAR, 15 studies on best medical therapy, and 9 studies on surgical repair. For the 2531 patients with acute complicated type B aortic dissection treated with TEVAR, the pooled 30-day/in-hospital mortality rate was 7.3% (95% CI, 5.3 to 9.6%). Survival rates ranged from 62% to 100% at 1 year and from 61% to 87% at 5 years. For the 1276 patients with acute complicated type B aortic dissection treated with open repair, the pooled 30-day/in-hospital mortality rate was 19.0% (95% CI, 16.8% to 21.1%). Survival rates ranged from 74.1% to 86.0% at 1 year and from 44.0% to 82.6% at 5 years. Direct comparisons between treatment groups are not reported, and the study does not account for between-group differences (other than treatment modality), which limits conclusions that may be drawn.

Randomized Controlled Trials
There are no RCTs for treatment of acute, complicated type B dissections, which is the group for which endovascular repair is often targeted.

Nonrandomized Controlled Trials
Fattori et al compared long-term survival between TEVAR and best medical therapy for type B acute aortic dissections among 1129 patients enrolled in an international registry of acute aortic dissections. The multinational registry included 24 referral centers in 12 countries; the registry was designed to provide an unbiased representative population of patients with acute aortic dissection. A total of 3865 patients were enrolled from December 26, 1995, to January 20, 2012. The present study included 1129 patients with type...
Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy # 00181
Original Effective Date: 09/22/2005
Current Effective Date: 11/16/2016

B acute aortic dissections, who underwent either medical therapy (n=853) or endovascular stent-graft placement (n=276). Patients who underwent TEVAR were matched in a 2:1 manner to medical therapy patients based on a propensity score created from a multivariable binary logistic regression model for the conditional probability for endovascular treatment versus medical treatment. The groups differed significantly at baseline: patients receiving endovascular treatment were more likely to present with clinical signs of malperfusion, such as leg pain (21.7% vs 8.4%, p<0.001) and limb ischemia (20.6% vs 4.8%, p<0.001), were more likely to have preoperative acute renal failure (21.4% vs 12.4%, p<0.001), any pulse deficit on presentation (28.3% vs 13.4%, p<0.001), and complicated dissections (defined by the presence of shock, periaortic hematoma, signs of malperfusion, stroke, spinal cord ischemia, mesenteric ischemia/infarction, and/or acute renal failure (61.7% vs 37.2%, p<0.001). Kaplan-Meier survival estimates at 5 years showed that patients who underwent TEVAR (15.5%) had a lower death rate than best medical therapy patients (29.0%; p=0.018).

Observational Studies
A number of case series have been reported, and some have reported long-term results for use of TEVAR in complicated type B aortic dissection.

White et al analyzed 1-year outcome after TEVAR in patients with complicated type B aortic dissection who had rupture or malperfusion and symptom onset 14 days or less (acute), 15 to 30 days (subacute), and 31 to 90 days (chronic) until required intervention. Their report focused on the acute cohort. Clinical data were systematically collected from 5 physician-sponsored investigational device exemption clinical trials between 2000 and 2008. Adverse events were reported early (≤30 days) and late (>30 days). In this study, there were 99 complicated type B aortic dissection patients: 85 were acute, 11 were subacute, and 3 were chronic. Among the acute patients, 31.8% had rupture and 71.8% had malperfusion, including 55.7% lower extremity, 36.1% renal, 19.7% visceral, 8.2% other, and 3.3% spinal cord (patients may have had >1 source). Rupture and malperfusion were both reported for 3 acute patients. Early major adverse events occurred in 37.6% of patients, including death (10.6%), stroke (9.4%), renal failure (9.4%), and paralysis (9.4%); late adverse events included vascular (15.8%), cardiac (10.5%), gastrointestinal (6.6%), and hemorrhage (5.3%). The point-estimate mortality rate was 10.8 (95% CI, 4.1 to 17.5) at 30 days and 29.4 (95% CI, 18.4 to 40.4) at 1 year, when 34 patients remained at risk. The authors concluded that emergency TEVAR for patients with complicated type B aortic dissection (malperfusion or rupture) provides acceptable mortality and morbidity results out to 1 year.

Steuer et al published a retrospective, single-center, consecutive case series from Europe. In this study, during the period 1999 to 2009, TEVAR was carried out in 50 patients with nontraumatic acute complicated type B dissection and in another 10 patients with acute complications, including rupture, end-organ ischemia, and acute dilatation during the primary hospitalization but more than 14 days after onset of symptoms. Within 30 days, 2 (3%) deaths, 1 (2%) paraplegia, and 3 (5%) strokes were observed. Five-year survival was 87% and freedom from reintervention at 5 years was 65%. The authors concluded that, in patients with acute complicated type B aortic dissection, TEVAR can be performed with excellent early and long-term survival.

Hanna et al published a retrospective case series of long-term follow-up (median follow-up, 33.8 months) of
Section Summary: Type B Aorta Dissections
For patients with acute, complicated type B dissections, there is limited evidence from a systematic review of case series and a propensity-matched study which reported a significant early survival advantage for patients treated with TEVAR. This evidence is limited by the noncomparability of treatment groups. The single-arm series have reported relatively high success rates and short-term survival that is possibly better than expected with open surgery.

Chronic Type B Aortic Dissections
Systematic Reviews
Thrumurthy et al performed a systematic review of endovascular repair for chronic type B dissections, defined as dissections that present with symptoms for more than 14 days. There were 17 publications included in this review, consisting of 1 RCT (the INSTEAD trial, discussed next) and 16 single-arm series. Of the 16 single-arm series, 2 were prospective and 14 were retrospective. At a median of 24 months of follow-up, mortality was 9.2% for patients treated with TEVAR, with a range of 0% to 41% across studies. A total of 8.1% of patients had endoleaks at this follow-up, and there was an increasing rate of endoleaks with longer follow-up times. Delayed aortic rupture occurred in 3.0% of patients. Freedom from reintervention occurred in a range of 40% to 100% at 24-month follow-up.

Randomized Controlled Trials
One RCT, the Investigation of Stent Grafts in Patients with type B Aortic Dissection (INSTEAD) trial has compared stents to best medical therapy for patients with chronic, stable dissections. The INSTEAD trial was reported in 2010. This trial compared endovascular stenting with medical management for stable thoracic aortic dissections. Stable or uncomplicated type B dissections differ from acute lesions in that there is no evidence of ischemia or extension over the time of observation that would necessitate emergency surgery. Patients were randomly assigned to elective stent-graft placement in addition to optimal medical management (n=72) or to optimal medical management alone (n=68) to maintain arterial pressure below 120/80 mm Hg. The primary end point of all-cause mortality at 1 year was not statistically significant between the 2 groups: cumulative survival was 91.3% in the endovascular group and 97.0% in the medical-only group (p=0.16). In addition, aorta-related mortality did not differ (5.7% and 3.0%, respectively; p=0.42). There were 2 cases of ischemic spinal cord injury with stent grafting and in the medical group. Seven (10.6%) patients in the medical group did cross over to the stent-graft group due to deterioration in
condition, and 1 patient from each group required open surgical intervention within the 12-month study period. An additional stent graft for false lumen expansion was required in 6 patients. A secondary measure of aortic remodeling did occur more frequently in the endovascular repair group (91.3% vs 19.4%, respectively; p<0.001), but the clinical significance is unknown. Three adverse neurologic events occurred in the endovascular group compared with in the medical-only arm. The authors concluded that elective stent-graft placement does not improve survival at 1 year and called for larger studies with extended follow-up.

In 2013, Nienaber et al published long-term follow-up results from the INSTEAD trial (INSTEAD-XL). Patients were followed for a minimum 5 years (maximum, 8 years); the median interval until death or latest follow-up was 69 months (interquartile range, 62-83 months); there was no loss to follow-up. Twenty-one additional TEVAR procedures were performed in the 5-year follow-up period, 14 in the optimal medical therapy group (5 emergency cases), with conversion to open repair in 4 cases, and 7 in the TEVAR group, with conversion to open repair in 3 cases. The risk of all-cause mortality was not statistically significantly different between groups at 5 years postrandomization (11.1% in the endovascular repair group vs 19.3% in the optimal medical therapy group, p=0.13). However, Kaplan-Meier curves demonstrated a survival benefit in the endovascular repair group between 2 and 5 years postrandomization (100% in the endovascular group vs 83.1% in the optimal medical therapy group, p<0.001). Patients randomized to endovascular repair had lower aorta-specific mortality (6.9% vs 19.3%, p=0.04) and progression of aortic pathology (27.05% vs 46.1%, p=0.04). For the combined end point of disease progression (aorta-specific death, crossover/conversion, secondary procedures) and aorta-specific events at 5 years of follow-up, freedom from the combined end point was 53.9% with medical therapy alone and 73.0% with TEVAR. Landmark analysis was performed to compare hazard ratios (HRs) for events occurring from randomization until 24 months postrandomization with events occurring beyond 24 months postrandomization to assess for a time-dependent response to treatment. In landmark analysis, groups had similar patterns of freedom from progression of aortic disease from randomization until 2 years of follow-up (76.1% vs 75.5%; HR=0.997; 95% CI, 0.51 to 1.95; p=0.994). However, from 2 to 5 years of follow-up, the TEVAR group was more likely to have freedom from progression than the medical therapy group (95.9% vs 71.9%; HR=0.112; 95% CI, 0.03 to 0.49; p=0.004).

The INSTEAD-XL findings suggest that, in stable patients with type B aortic dissection, preemptive endovascular repair may be associated with an excess risk of morbidity and mortality in the immediate postprocedural period, which is outweighed by a longer term survival benefit. The authors noted that best medical management did not prevent late complications of aortic dissections, including expansion, rupture, and late crossover/conversion to emergent TEVAR.

Nonrandomized Comparative Trials
A number of studies have compared outcomes for open and endovascular repair or endovascular repair and best medical therapy using prospective or retrospective nonrandomized cohort studies. Some of these studies use propensity score matching to attempt to adjust for factors other than repair strategy that may have differed between groups.

Andersen et al compared open and endovascular repair for chronic type B aortic dissection in a
Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy # 00181
Original Effective Date: 09/22/2005
Current Effective Date: 11/16/2016

A retrospective review of 107 patients treated at a single center. The study included 75 (70%) patients who underwent endovascular procedures, 44 of which were TEVAR, 27 of which were hybrid aortic arch, and 4 of which were hybrid thoracoabdominal aortic aneurysm repair; this group was compared with 32 (30%) patients who underwent open procedures. The institutional preference was to perform an endovascular repair for chronic type B aortic dissection in all non–connective tissue disease patients with suitable anatomy. Twenty-one (n=18) patients underwent nonelective repair, most commonly due to impending aneurysm rupture. Rates of stroke, paraplegia, and operative mortality were 0%, 0%, and 4%, respectively, following endovascular-based repairs, and were 16%, 9%, and 6%, respectively, following open repair. Cumulative 1- and 5-year survival rates were 86% (95% CI, 78% to 95%) and 65% (95% CI, 52% to 80%), respectively, following endovascular-based repairs, and were 88% (95% CI, 77% to 100%) and 79% (95% CI, 65% to 96%), respectively, following open repair. However, the heterogeneity among endovascular and open repair groups in terms of dissection location and repair type precludes direct comparisons between open and endovascular repair specifically for chronic type B thoracic aortic dissections without concomitant abdominal aortic pathology.

Van Bogerijen et al reported results of a retrospective, single-center study comparing TEVAR and open repair among 122 patients with chronic type B aortic dissection who were treated between 1993 and 2013. Compared with the 90 patients who had open repairs, the 30 patients who underwent TEVAR were older, more likely to be female, have chronic obstructive pulmonary disease or prior abdominal aortic aneurysm repair, have only intramural hematoma, and were less likely to have aortic arch involvement. For the study's primary outcome of late mortality, the 5-year survival was 78.1% in the TEVAR group compared with 86.7% in the open repair group (p=0.232). In multivariable analysis after propensity score adjustment for patient-related and treatment-related factors, the repair type was not significantly associated with late mortality. The open repair group had higher 3-year treatment efficacy (96.7% vs 87.5%, p=0.02), a result that remained significant after in multivariable analysis with propensity score adjustment.

Jia et al performed a prospective, multicenter, nonrandomized comparative study of TEVAR versus optimal medical therapy (OMT) for chronic type B thoracic aortic dissections. A total of 208 patients were treated with TEVAR and 95 patients were treated with OMT. In the TEVAR group, there were no periprocedural deaths, and serious complications (retrograde type A dissection, brachial artery pseudoaneurysm, paraplegia, MI) occurred in 12 (5.8%) patients. Estimated survival at 2 and 4 years was 87.5% and 82.7% with TEVAR, compared with 77.5% and 69.1% with OMT, both respectively, but this difference in survival was not statistically significant (p=0.068). The estimated freedom from aorta-related death at 2 and 4 years was 91.6% and 88.1% for the TEVAR group compared with 82.8% and 73.8% with OMT, both respectively, a difference that was statistically significant (p=0.039).

**Section Summary: Chronic Type B Aortic Dissections**

For patients with chronic, stable dissections of the thoracic aorta, 1 RCT reported that short-term outcomes do not differ significantly between TEVAR and best medical management. However, over 5 years of follow up, patients who undergo preemptive endovascular repair may demonstrate reduced morbidity and mortality.
Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy # 00181
Original Effective Date: 09/22/2005
Current Effective Date: 11/16/2016

Tears and Rupture of the Descending Aorta

Systematic Reviews

In 2010, Jonker and colleagues published a systematic review and meta-analysis of studies published between 1996 and 2009 to evaluate outcomes of open surgical repair (n = 81) versus endovascular repair (n = 143) for ruptured descending TAA. The 30-day mortality was 19% for patients treated with endovascular repair, compared to 33% for patients treated with open repair (p = 0.016). The 30-day incidence of MI was 3.5% for those treated with endovascular repair versus 11.1% in patients treated with open repair (p < 0.05). Rates of stroke and paraplegia were also increased in the surgically treated patients but did not reach statistical significance. Additional vascular interventions were performed in 9.1% of endovascular patients versus 2.3% of surgical patients (p = 0.169). Regarding safety, during a median follow-up of 17 ± 10 months, 5 additional patients in the endovascular group died of aneurysm-related causes, endoleak was reported in 11.1% of patients, and endograft migration was reported in 1 patient. The authors noted that the durability and development of endovascular-related complications remain concerns and that further surveillance of the endografts is required. These data need to be interpreted with caution given the non-random treatment assignment.

Lee et al. summarized data on use of TEVAR for repair of traumatic thoracic aortic injuries to aid development of practice guidelines. The systematic review included 7,768 patients from 139 studies. This review found the mortality rate was significantly lower in patients who underwent endovascular repair, followed by open repair, and nonoperative management (9%, 19%, and 46%, respectively, p < 0.01). Based on the overall very low quality of evidence, the committee suggests that endovascular repair of thoracic aortic transection is associated with better survival and decreased risk of spinal cord ischemia, renal injury, graft, and systemic infections, compared with open repair or nonoperative management. In addition to the low quality of the evidence, the authors also note that these conclusions should be tempered by the lack of suitable (anatomic fit) devices, which can lead to severe complications, and to the lack of follow-up data.

A 2015 Cochrane review searched for published or unpublished RCTs to determine whether TEVAR for blunt traumatic thoracic aortic rupture would reduce mortality and morbidity compared with open surgical repair. The authors did not identify any RCTs meeting their selection criteria.

Nonrandomized Comparative Studies

This non-randomized study by Azizzadeh et al compared outcomes of TEVAR and open surgery using prospectively collected data in 106 consecutive patients between 2002 and 2010 at one institution. This time interval covered the period of adoption for TEVAR at this institution, in which the proportion of patients treated with TEVAR increased from 0% to 100%. As a result, the number of procedures done in each group over time varied; 56 patients underwent open surgery and 50 underwent TEVAR. Primary outcomes were in-hospital death and complications. Death occurred in 5/56 (8.9%) patients undergoing open surgery, compared to 2/50 (4.0%) patients undergoing TEVAR. The overall likelihood of complications, including death, was significantly lower in the TEVAR group (OR 0.33, 95% CI 0.11-0.97). Also, the number of patients with at least one complication was greater in the open surgery group compared to TEVAR (69.6% vs. 48%).
Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy # 00181
Original Effective Date: 09/22/2005
Current Effective Date: 11/16/2016

Canaud et al compared outcomes of endovascular and open surgical repair in 75 patients with acute traumatic rupture of the thoracic aorta at one tertiary care center. Open surgery was performed on 35 patients during the time period of 1990-2000, and endovascular repair was performed on 40 patients between 2001 and 2010. Early mortality was lower in the endovascular group compared to open surgery (2.5% vs. 11.4%), but this difference did not reach statistical significance. Serious adverse events occurred in 20% of patients in the endovascular group compared to 14.2% in the open surgery group, which was also not a significant difference. There were no cases of paraplegia or stroke in either group.

Goodney et al used Medicare claims data from 1998-2007 to compare TEVAR with open surgery in patients with aneurysms of the descending aorta. This study included both intact and ruptured aneurysms. A total of 1,307 patients with ruptured aneurysms were identified, 1,008 were treated with open surgery and 299 with TEVAR. There were baseline differences between the 2 groups, with the TEVAR group being older and more likely to have a variety of medical comorbidities. Thirty-day mortality was significantly lower among TEVAR patients compared to open surgery (28.4% vs. 45.6%, p = 0.0001). Long-term survival was reported by Cox proportional hazards analysis. At 5 years, survival was low in both groups with no significant difference between the TEVAR and open surgery groups (23% vs. 26%, p = 0.37).

Gopaldas et al used the U.S. Nationwide Inpatient Sample database to identify patients who underwent procedures to repair a thoracic artery rupture. A total of 923 patients were identified between the period of 2006-2008, 364 (39.4%) who underwent TEVAR and 559 (60.6%) who underwent open repair. Patients undergoing TEVAR were older and had a significantly higher burden of comorbidities compared to patients undergoing open repair. Overall mortality was 23.4% for TEVAR and 28.6% for open repair, which was not significantly different. There were also no differences in complication rates. Thoracic endovascular aneurysm repair patients were more likely to have routine discharge from the hospital to home compared to open surgery patients (OR: 3.3, p < 0.001).

In 2013, Klima et al retrospectively compared outcomes and complications associated with for open repair with endovascular repair for blunt aortic trauma for 49 patients treated at a single nonuniversity hospital from 2004 to 2011. Twenty-one patients underwent open repair, while 28 patients were managed with TEVAR; groups did not differ at baseline with regard to age, sex, or injury severity. Hospital length of stay, intensive care unit length of stay, and ventilator time were similar between groups, but patients in the open repair group had higher in-hospital mortality than the TEVAR group (33% vs 7%, p=0.028).

Observational Studies

FDA- Approval Studies (Single-arm)

Data from two uncontrolled clinical series of patients with isolated thoracic artery lesions was reviewed by the FDA as part of the expanded approval for thoracic endografts in 2012. The TAG 08-02 study used the Gore TAG endograft to treat 51 patients with aortic transection due to blunt aortic injury. All 51 patients had successful implantation of the CORE TAG endograft, although 6 patients (11.8%) required deployment of two stent grafts for adequate coverage. There were 4 deaths within 30 days of treatment (7.8%, 95% CI 3.1-18.5%). Serious adverse events with reported in 39.2% of subjects at 30 days, with the most common events being pleural effusion (5.9%) respiratory failure (5.9%). The primary effectiveness outcome was the number of patients with major device-related events in the first 30 days requiring reintervention. There were
Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy #  00181
Original Effective Date:  09/22/2005
Current Effective Date:  11/16/2016

no patients who had such an event requiring reintervention. Two patients were identified with type II endoleaks, but neither patient required reintervention.

A similar study (RESCUE) was submitted to the FDA using the Valiant Thoracic stent graft in 50 patients with blunt aortic trauma. All patients had successful deployment of the stent, with 2 patients requiring 2 devices. There were 4 deaths within 30 days of the procedure for a perioperative mortality of 8.0%. Serious adverse events occurred in 12.0% of patients, the majority of these were procedure-related events such as femoral artery dissection, localized hematoma, and/or hemothorax. There were 3 patients who required left subclavian artery revascularization to treat arm ischemia.

Other Single-arm Studies
Since FDA’s approval of thoracic endografts for traumatic aortic rupture, a number of single-arm studies have reported outcomes for TEVAR for this indication. Martinelli et al reported an in-hospital mortality rate of 7.4% in a cohort of 27 patients who underwent TEVAR for blunt aortic trauma. Piffaretti et al reported an in-hospital mortality rate of 6.5% in a cohort of 35 patients who underwent TEVAR for blunt aortic trauma, with no subsequent mortality over a median follow-up of 72 months. Steuer et al reported that in patients who underwent TEVAR and survived the concomitant injuries from the initial trauma, 5-year survival was 81%, with reintervention needed in 16%.

Section Summary
FDA approval was granted for endovascular stent-graft treatment of thoracic artery ruptures in 2012. The evidence on TEVAR for treatment of thoracic artery rupture consists of single-arm series and nonrandomized comparative studies. There are no RCTs, but RCTs are likely difficult to complete for this indication because of the emergent nature. The available evidence suggests that there are fewer early deaths and complications with TEVAR than with open surgery, but these data are limited by noncomparability of groups. The longer term outcomes are uncertain, with no discernible differences between TEVAR and open surgery.

Pathology of the Ascending Aorta
Compared with its use for descending aortic pathologies, TEVAR has been less widely studied for management of ascending aortic pathologies. Only small case series for use of TEVAR for ascending aortic pathologies were identified. For example, Vallabhajosyula et al retrospectively reported outcomes for 6 patients who underwent endovascular repair for ascending aorta pseudoaneurysm (n=4) or acute type A aortic dissection (n=2). Roselli et al described a series of 22 patients who underwent TEVAR of the ascending aorta for acute type A aortic dissection (n=9), intramural hematoma (n=2), pseudoaneurysm (n=9), chronic dissection (n=2), or aortocardiac fistula (n=2). Appoo et al reported imaging-related outcomes for 16 patients who underwent TEVAR for aortic arch or ascending aorta.

Section Summary
The evidence related to the use of TEVAR for ascending aortic pathologies is limited to small case studies that include heterogeneous patient populations.

Mixed Populations
Several studies have evaluated TEVAR in heterogeneous groups of patients.
Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy #  00181
Original Effective Date:  09/22/2005
Current Effective Date:  11/16/2016

In 2005, the National Institute of Clinical Excellence (NICE) conducted a systematic review of 27 case series and 2 comparative observational studies of endovascular repair in the treatment of thoracic aortic disease. Data from the included studies demonstrated technical success in approximately 93% of cases. The short-term (30-day) mortality rate was 5% (range 0-14%), and with a mean follow-up period of 14 months, overall mortality rate was 12% (range 3-24%) across studies. The most frequent technical complications were endoleaks (13%), injury to the access site (6%), and stent fracture (6%). Stroke occurred in 6% and paraplegia in 2% of patients. The evidence base primarily consists of case series that include heterogeneous groups of patients with incomplete outcome data. However, the review concluded that the safety of the procedure must be weighed against the fact that mortality is very high if patients with TAA are untreated and that endovascular stent placement is a suitable alternative to open surgery in appropriately selected patients with aneurysm or dissection.

In 2009, Cambria and colleagues reported on 59 patients who received TEVAR for emergent repair of thoracic aorta pathology due to acute complicated type B dissection, traumatic aortic tear, and ruptured degenerative aneurysm. The authors’ own literature review prospectively postulated a combined mortality/paraplegia rate of 12.6% for TEVAR, compared to 29.6% for open surgery for each of the 3 diagnostic conditions, or arms, of the study. Based on pre-study power analysis, it was estimated that 52 test subjects would be required overall to detect a difference of 17% in the composite outcome; 20 subjects were enrolled in each arm, subject to anatomic considerations; at the time of presentation, the final number of subjects drafted was 59 due to a solitary patient reclassification. The combined 30-day mortality/paraplegia endpoint was observed in 13.6% of study participants (7 deaths and 1 paraplegia), significantly lower than the literature-based rate for open surgery (29.6%) previously stated (p = 0.008). Not surprisingly, 30-day complications in addition to the composite endpoint were high: 48 (81%) patients experienced at least one major complication. Of these, 11 (18.6%) were attributable to device failure or complication. During mean follow-up time of 409 ± 309 days, an additional 12 patients had died, 1 patient was converted to open surgery, and 2 patients had major, device-related events. For the entire study group, survival at 1 year was 66% (n = 40). Regression analysis revealed that age and concurrent chronic obstructive pulmonary disease were predictive of death at 1 year.

Naughton et al. reported on 100 patients with “acute thoracic aortic catastrophies” treated with either TEVAR (n=76) or open surgery (n=24). Conditions included ruptured aneurysms (n=41), traumatic transection (n=27), complicated acute type B dissections (n = 20), penetrating ulcers (n=4), intramural hematoma (n=3), penetrating injury (n=3), and embolizing lesions (n=2). Patients in the open surgery group were older and had more prior episodes of aortic surgery. Overall mortality at 30 days was lower for the TEVAR group compared to open surgery (8% vs. 29%, p = 0.007). Respiratory complications (16% vs. 48%, p < 0.05) were also lower in the TEVAR group. There were no significant differences in postoperative adverse events or mean length of stay.

In 2013, Alsc et al reported outcomes from for 48 patients treated with TEVAR for a “descending thoracic acute aortic syndrome,” including 19 ruptured aneurysms, 12 acute dissections, and 17 traumatic ruptures. Ten patients died during the peri-procedural hospitalization (mortality rate, 20.8%), but no later deaths were reported in the 33 patients for whom longer-term follow-up was available. Reintervention in the first month postprocedure was required in 8 patients (16.7%), and late reintervention was required in 5 patients.
Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy # 00181
Original Effective Date: 09/22/2005
Current Effective Date: 11/16/2016

(10.4%).

In 2014, Sood et al published a comparison of open repair, hybrid repair, and TEVAR for a mixed population of patients with thoracic aorta aneurysms (n=83) or dissections (n=15) treated at a single institution from 1993 to 2013. Patients treated with TEVAR were older and more likely to have a history of tobacco use. For the study’s primary outcome of all-cause late mortality, Kaplan-Meier analysis showed no significant difference in 5-year survival between TEVAR patients and open/hybrid repair patients.

Botsios et al reported outcomes for 21 patients who underwent emergency TEVAR for nontraumatic rupture of the descending thoracic aorta, due to underlying degenerative aneurysms (n=11), complicated type B dissection (n=9), or erosion due to neoplasia (n=1). Thirty-day mortality was 9.5%; over a median follow-up of 65.6 months (range, 1.5-44 months), 10 additional patients died, leading to a late mortality rate of 52.6%. Late mortality was more likely to be related to nonaortic causes, with 2 aorta-related deaths and 8 non-aorta-related deaths.

Wiedemann et al reported short- and medium-term outcomes for 300 patients who underwent TEVAR at a single institution for a range of thoracic aortic conditions, including 137 descending thoracic aneurysms, 80 type B dissections (60 acute, 20 chronic), 59 perforating aortic ulcer, and 24 traumatic aortic transections. Thirty-day mortality was 5% (15 patients) with no statistically significant differences between the 4 groups. Median follow-up was reported as 44 years, although this may be a typographic error. In Kaplan-Meier analysis, OS at 1, 5, and 10 years was 86%, 63%, and 44%, respectively, with significant differences between groups and the lowest survival for descending thoracic aneurysms.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this policy are listed in Table 1.

Table 1. Summary of Key Trials

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Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy # 00181
Original Effective Date: 09/22/2005
Current Effective Date: 11/16/2016

| NCT00435942a | Phase II Clinical Study of the Safety and Efficacy of the Relay Thoracic Stent-Graft in Patients With Thoracic Aortic Pathologies | 120 | May 2015 (unknown) |

NCT: national clinical trial.

a Denotes industry-sponsored or cosponsored trial.

Summary of Evidence

For individuals who have type B (descending) thoracic aortic aneurysms who receive endovascular repair, the evidence includes nonrandomized comparative studies and systematic reviews. Relevant outcomes are overall survival, morbid events, and treatment-related morbidity and mortality. The available nonrandomized comparative studies have consistently reported reduced short-term morbidity and mortality compared with surgical repair. Although these types of studies are subject to selection bias and other methodologic limitations, the consistency of the findings of equivalent or reduced short-term mortality and fewer early complications across populations with different characteristics supports the conclusion that TEVAR is a safer procedure in the short term. The likely short-term benefits of TEVAR are mitigated by less favorable longer term outcomes, but longer term mortality appears to be roughly similar for patients undergoing TEVAR or open surgery. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have type B (descending) aortic dissections who receive endovascular repair, the evidence includes RCTs, systematic reviews, and nonrandomized comparative studies. Relevant outcomes are overall survival, morbid events, and treatment-related morbidity and mortality. For acute uncomplicated type B dissections, 1 RCT has reported short-term improvements in aortic remodeling and a decreased risk of aortic dilation and rupture in patients treated with TEVAR compared with best medical management. However, this trial was underpowered to evaluate mortality differences, and limitations include a high TEVAR failure rate based on imaging follow-up. For acute complicated type B dissections, there are no RCTs. Short- and intermediate-term results from a systematic review of observational studies that compared TEVAR with open surgery suggest a benefit for TEVAR in complicated (organ or limb ischemia or rupture) type B dissection. However, this evidence is limited by selection bias and baseline differences between groups, and therefore is not definitive on the efficacy of TEVAR versus open surgery. For chronic type B dissections, the evidence from 1 RCT did not demonstrate short-term outcome benefits associated with TEVAR; however, after more than 5 years of follow-up, TEVAR was associated with a survival benefit beginning 2 years post-procedure. Additional evidence from high-quality trials is needed to determine whether TEVAR improves outcomes for patients having type B aortic dissections. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have traumatic descending aortic tears or rupture who receive endovascular repair, the evidence includes nonrandomized comparative studies and systematic reviews. Relevant outcomes are overall survival, morbid events, and treatment-related morbidity and mortality. For traumatic thoracic aortic injury and rupture, nonrandomized comparative data has suggested a benefit for TEVAR in reducing periprocedural morbidity and mortality. Although it is expected that RCTs will be difficult to conduct for this indication due to its emergent nature, the risks of bias in the available nonrandomized studies is high. The evidence is insufficient to determine the effects of the technology on health outcomes.
Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy # 00181
Original Effective Date: 09/22/2005
Current Effective Date: 11/16/2016

For individuals who have ascending aortic disorders who receive endovascular repair, the evidence includes small case series. Relevant outcomes are overall survival, morbidity events, and treatment-related morbidity and mortality. For patients with ascending aortic pathologies, including dissections, aneurysms, and other disorders, the evidence on use of TEVAR is limited to small series that assess heterogeneous patient populations. The evidence is insufficient to determine the effects of the technology on health outcomes.

References
23. Matsumura JS, Cambria RP, Dake MD et al. International controlled clinical trial of thoracic endovascular aneurysm repair with the
Endovascular Stent Grafts for Disorders of the Thoracic Aorta

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Policy History
Original Effective Date:  09/22/2005
Current Effective Date:  11/16/2016
09/07/2005  Medical Director review
09/20/2005  Medical Policy Committee review
09/22/2005  Quality Care Advisory Council approval

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Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy # 00181
Original Effective Date: 09/22/2005
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05/03/2006 Medical Director review
05/17/2006 Medical Policy Committee review. Format revision, including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.
11/07/2007 Medical Director review
11/05/2008 Medical Director review
11/18/2008 Medical Policy Committee approval. Coverage eligibility unchanged.
11/12/2009 Medical Policy Committee approval
11/04/2010 Medical Policy Committee review
11/03/2011 Medical Policy Committee review
11/16/2011 Medical Policy Implementation Committee approval. Eligible for coverage statements reformatted to clarify the intent that use is for specific types of aneurysms without dissection, for complicated Type B dissections and for traumatic aortic injury (when specific conditions are met). Added a Note to the coverage section for clarification.
11/01/2012 Medical Policy Committee review
11/07/2013 Medical Policy Committee review
11/20/2013 Medical Policy Implementation Committee approval. Eligible for coverage indication added for acute rupture of the thoracic aorta.
11/06/2014 Medical Policy Committee review
11/21/2014 Medical Policy Implementation Committee approval. Title changed from "Endovascular Stent Grafts for Thoracic Aortic Aneurysms or Dissections" to "Endovascular Stent Grafts for Disorders of the Thoracic Aorta". Coverage eligibility unchanged.
08/03/2015 Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
10/29/2015 Medical Policy Committee review
11/16/2015 Medical Policy Implementation Committee approval. Updated INV statement.
11/03/2016 Medical Policy Committee review
01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes
Next Scheduled Review Date: 11/2017

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Endovascular Stent Grafts for Disorders of the Thoracic Aorta

Policy # 00181
Original Effective Date: 09/22/2005
Current Effective Date: 11/16/2016

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<tbody>
<tr>
<td>CPT</td>
<td>33880, 33881, 33883, 33884, 33886, 33889, 33891, 75956, 75957, 75958, 75959, 93982</td>
</tr>
<tr>
<td>HCPCS</td>
<td>No codes</td>
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*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

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2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

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A. In accordance with nationally accepted standards of medical practice;

B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient’s illness, injury or disease; and

C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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