Endovascular Therapies for Extracranial Vertebral Artery Disease

Policy # 00466
Original Effective Date: 06/17/2015
Current Effective Date: 06/20/2016

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.

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 endovascular therapy, including percutaneous transluminal angioplasty (PTA) with or without stenting, for the management of extracranial vertebral artery disease to be investigational.*

Background/Overview
Vertebral artery diseases, including atherosclerotic stenosis, dissections, and aneurysms, can lead to ischemia of the posterior cerebral circulation. Conventional management of extracranial vertebral artery diseases may include medical therapy, including antiplatelet or anticoagulant medications, medications to reduce atherosclerotic disease risk (eg, statins), and/or surgical revascularization. Endovascular therapies have been investigated as an alternative to conventional management.

Overview of Vertebrobasilar Circulation Ischemia
Ischemia of the vertebobasilar or posterior circulation accounts for about 20% of all strokes. Posterior circulation strokes may arise from occlusion of the innominate and subclavian arteries, the extracranial vertebral arteries, or the intracranial vertebral, basilar, or posterior cerebral arteries. Compared with carotid artery disease, relatively little is known about the true prevalence of specific causes of posterior circulation strokes, particularly the prevalence of vertebral artery disease. Reports from 1 stroke registry have estimated that, in 9% of cases, posterior circulation strokes are due to stenosis of the proximal vertebral artery. Patients who experience strokes or transient ischemic attacks of the vertebobasilar circulation face a 25% to 35% risk of stroke within the subsequent 5 years. In particular, the presence of vertebral artery stenosis increases the 90-day risk of recurrent stroke by about 4-fold.

Relevant Clinical Anatomy and Pathophysiology
Large artery disease of the posterior circulation may be due to atherosclerosis (stenosis), embolism, dissection, or aneurysms. In about a third of cases, posterior circulation strokes are due to stenosis of the extracranial vertebral arteries or the intracranial vertebral, basilar, or posterior cerebral arteries. The proximal portion of the vertebral artery in the neck is the most common location of atherosclerotic stenosis in the posterior circulation. Dissection of the extracranial or intracranial vertebral arteries may also cause posterior circulation ischemia. In contrast, posterior cerebral artery ischemic events are more likely to be secondary to embolism from more proximal vessels.

The vertebral artery is divided into 4 segments, V1-V4, of which segments V1-V3 are extracranial. V1 originates at the subclavian artery and extends to the 5th or 6th cervical vertebrae; V2 crosses the bony...
Endovascular Therapies for Extracranial Vertebral Artery Disease

Policy # 00466
Original Effective Date: 06/17/2015
Current Effective Date: 06/20/2016

canal of the transverse foramina from C2-C5; V3 starts as the artery exits the transverse foramina at C2 and ends as the vessel crosses the dura mater and becomes an intracranial vessel. The most proximal segment, V1, is the most common location for atherosclerotic occlusive disease to occur, while arterial dissections are most likely to involve the extracranial vertebral artery just before the vessel crosses the dura mater. Compared with the carotid circulation, the vertebral artery system is more likely to be associated with anatomic variants, including a unilateral artery.

Atherosclerotic disease of the vertebral artery is associated with conventional risk factors for cerebrovascular disease. However, risk factors and the underlying pathophysiology of vertebral artery dissection and aneurysms differ. Extracranial vertebral artery aneurysms and dissections are most often secondary to trauma, particularly those with excessive rotation, distraction, or flexion/extension, or iatrogenic injury, such as during cervical spine surgeries. Spontaneous vertebral artery dissections are rare, and in many cases are associated with connective tissue disorders, including Ehlers-Danlos syndrome type IV, Marfan syndrome, autosomal-dominant polycystic kidney disease, and osteogenesis imperfecta type I.

Management of Extracranial Vertebral Artery Disease
The optimal management of occlusive extracranial vertebral artery disease is not well defined. Medical therapy with antiplatelet or anticoagulant medications is a mainstay of therapy to reduce stroke risk. Medical therapy also typically involves risk reduction for classical cardiovascular risk factors. However, no randomized trials have compared specific antiplatelet or anticoagulant regiments.

Surgical revascularization may be used for vertebral artery atherosclerotic disease, but open surgical repair is considered technically challenging due to poor access to the vessel origin. Surgical repair may involve vertebral endarterectomy, bypass grafting, or transposition of the vertebral artery, usually to the common or internal carotid artery. Moderately sized, single-center case series of surgical vertebral artery repair from 2012 and 2013 report rates of overall survival of 90.7% and 77.3% at 3 and 6 years postoperatively, and arterial patency rates of 80% after 1 year of follow-up. Surgical revascularization may be used in cases of symptomatic vertebral artery stenosis that is not responsive to medical therapy, particularly when bilateral vertebral artery stenosis is present or when unilateral stenosis is present in the presence of an occluded or hypoplastic contralateral vertebral artery. Surgical revascularization may also be considered in patients with concomitant symptomatic carotid and vertebral disease who do not have relief of vertebrobasilar ischemia after carotid revascularization.

The management of extracranial vertebral artery aneurysms or dissections is controversial due to uncertainty about the risk of thromboembolic events associated with aneurysms/dissections. Antiplatelet therapy is typically used; surgical repair, which may include vertebral bypass, external carotid autograft, and vertebral artery transposition to the internal carotid artery, or endovascular treatment with stent placement or coil embolization may also be used.

Given the technical difficulties related to surgical access of the extracranial vertebral artery, endovascular therapies have been investigated for extracranial vertebral artery disease. Endovascular therapy may consist of PTA, with or without stent implantation.
FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

There are currently no endovascular therapies approved by the U.S. FDA specifically for the treatment of extracranial vertebral artery disease. A variety of stents approved for use in the carotid or coronary circulation have been used for extracranial vertebral artery disease, which may be self- or balloon-expandable.

Two devices have been approved by FDA through the humanitarian device exemption process for intracranial atherosclerotic disease. This form of FDA approval is available for devices used to treat conditions with an incidence of 4000 or less per year; FDA only requires data showing "probable safety and effectiveness." Devices with their labeled indications are as follows:

1. Neurolink System® (Guidant, Santa Clara, CA). "The Neurolink system is indicated for the treatment of patients with recurrent intracranial stroke attributable to atherosclerotic disease refractory to medical therapy in intracranial vessels ranging from 2.5 to 4.5 mm in diameter with ≥50% stenosis and that are accessible to the stent system."

2. Wingspan™ Stent System (Boston Scientific, Fremont, CA). "The Wingspan Stent System with Gateway PTA Balloon Catheter is indicated for use in improving cerebral artery lumen diameter in patients with intracranial atherosclerotic disease, refractory to medical therapy, in intracranial vessels with ≥50% stenosis that are accessible to the system."

Centers for Medicare and Medicaid Services (CMS)

Centers for Medicare and Medicaid Services has a national coverage determination (NCD) that addresses the use of PTA in the treatment of atherosclerotic obstructive lesions of the lower or the upper extremities (not including the head or neck vessels), of a single coronary artery, of renal arteries, and of AV dialysis fistulas and grafts. It also addresses the use of PTA concurrent with carotid stent placement in FDA investigational device exemption clinical trials, in FDA-approved postapproval studies, and in patients at high risk for carotid endarterectomy.

The NCD states that all other indications for PTA, with or without stenting, to treat obstructive lesions of the vertebral and cerebral arteries remain noncovered.

Rationale/Source

This evidence review was created in February 2015 and has been updated with a search of the literature in the MEDLINE database through March 28, 2016.

Assessment of efficacy for therapeutic interventions involves a determination of whether the intervention improves health outcomes. The optimal study design for this purpose is a randomized controlled trial (RCT) that includes clinically relevant measures of health outcomes. Improvements in intermediate outcome measures may also be adequate to determine efficacy if there is an established link between the intermediate outcome and true health outcomes. Nonrandomized comparative studies and uncontrolled studies can sometimes provide useful information on health outcomes, but are prone to biases such as noncomparability of treatment groups, placebo effect, and variable natural history of the condition.
Endovascular Therapies for Extracranial Vertebral Artery Disease

Policy #  00466
Original Effective Date:  06/17/2015
Current Effective Date:  06/20/2016

Appropriate comparators for studies evaluating vertebral artery stenting for vertebral artery stenosis include surgical repair and/or medical management.

**Angioplasty and Stenting for Extracranial Vertebral Artery Stenosis**

The evidence base for the efficacy of endovascular interventions for vertebral artery stenosis consists of a large number of case series, most of which are small and retrospective. A very small number of controlled trials have been published. The emphasis for this review will be on controlled trials.

**Systematic Reviews**

Three systematic reviews of published studies were identified. Two systematic reviews included all the published studies, while the third selected only RCTs. These systematic reviews were published prior to the Vertebral Artery Stenting Trial (VAST), which is described in the Randomized Controlled Trials subsection.

In 2012, Antoniou et al reported results of a systematic review of studies evaluating PTA, stenting, or both for proximal vertebral artery stenosis. The authors included randomized and nonrandomized trials comparing endovascular treatment with open surgical repair or endovascular treatment with best medical care for proximal vertebral artery stenosis, along with prospective and retrospective case series with at least 5 patients of endovascular treatment for proximal vertebral artery stenosis. The review included 42 publications reporting on unique data sets, 40 of which were retrospective case studies or retrospective reviews of prospectively collected data, and 2 of which were comparative studies (1 RCT by Coward et al, 1 nonrandomized study by Karaskevich et al) comparing vertebral artery angioplasty and stenting with medical treatment. The selected studies reported outcomes for endovascular treatment (PTA, stenting, or both) of 1117 vertebral arteries in 1099 patients, with a mean of 26 patients (range, 5-117) per study. Indications for treatment differed across studies, but most included a requirement for vertebral artery stenosis, ranging from at least 50% to at least 70% occlusion, in conjunction with symptoms of posterior circulation disease. Most studies used a definition of “technical success” of less than 20% residual stenosis of the treated segment of the vertebral artery at the end of the procedure. The authors’ assessment of the literature was that it was of poor overall quality, and demonstrated heterogeneity in the selection of patients for revascularization, the characteristics of the populations used, and revascularization techniques.

Reported technical success rates were 36% to 100% among the studies, with a weighted mean value of 97%. Thirty-seven studies reported follow-up outcomes at a mean follow-up time of 6 to 54 months. During follow-up, recurrent symptoms of vertebrobasilar insufficiency developed in 65 (8%) patients. Twenty-one patients died (mean late mortality rate, 2%), with 1 death only reported to be associated with insufficiency of the posterior cerebral circulation. Restenosis in the previously treated segment of the vertebral artery occurred in 183 of the 789 patients who underwent follow-up imaging, for an accumulated restenosis rate of 23% (range, 0%-58%). However, restenosis was defined inconsistently in these studies.

A 2011 systematic review had a smaller evidence base but reported no differences in conclusions. These 2 systematic reviews include all of the published evidence available at the time. Conclusions from these reviews are limited largely as a result of the poor quality of the underlying evidence base.
A third systematic review, published by Cochrane in 2005, included only studies that randomized patients to endovascular treatment or best medical therapy in patients with vertebral artery stenosis. This review identified 1 RCT that met the inclusion criteria, the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) study. The vertebral artery arm of this trial randomized 16 subjects with symptomatic vertebral artery stenosis to endovascular therapy with best medical care or to best medical care alone. The CAVATAS study is detailed in the Randomized Controlled Trials subsection.

Randomized Controlled Trials
VAST is the largest RCT published to date on stenting versus medical therapy in patients with symptomatic vertebral artery disease. This multicenter phase 2 trial included 115 patients who had transient ischemic attack (TIA) or minor stroke attributed to vertebral artery stenosis. Randomization to stenting or medical therapy was stratified by center and level of stenosis: 83.5% of patients had extracranial lesions and the rest had intracranial lesions. The median interval between symptoms and randomization was 25 days, with a median interval between randomization and stenting of 7 days. Stent selection was by surgeon preference. All patients received best medical therapy and were followed yearly by telephone. The primary outcome was the composite of vascular death, stroke, or myocardial infarction (MI) within 30 days. Secondary outcomes were stroke in the territory of the symptomatic artery, the composite outcome measure during follow-up, and the degree of restenosis. Median follow-up was 3.0 years (range, 1.3-4.1 years).

Endovascular therapy plus best medical therapy was not superior to best medical therapy alone in this trial. The primary outcome occurred in 3 (5%) of 57 patients (95% confidence interval [CI], 0 to 11) in the stenting group and 1 (2%) of 58 patients (95% CI, 0 to 5) in the medical treatment group. Of these 4 patients, all had a vertebrobasilar stroke and 2 of the 4 occurred in the group of 9 patients with intracranial stenosis who received endovascular therapy. One of the strokes in the stenting group was fatal. During follow-up, the composite primary outcome occurred in 11 (19%) patients in the stenting group and 10 (17%) patients in the medical therapy group. The periprocedural risk of a major vascular event in the stenting group was 5%. The trialists questioned the need and feasibility of a phase 3 trial, given the low risk of recurrent stroke with best medical therapy. However, recruitment of 540 patients for the phase 3 Vertebral artery Ischaemia Stenting Trial (VIST) should have been completed as of March 2016. Enrollment was originally planned for 1302 patients. In VIST, patients with symptomatic extracranial or intracranial vertebral artery stenosis and vertebrobasilar transient ischemic attacks or stroke in the previous 3 months were to be randomly assigned to vertebral artery stenting or best medical therapy alone.

CAVATAS incorporated data from 3 separate randomized trials, 2 of which compared endovascular treatment to carotid endarterectomy or medical treatment alone for patients with carotid stenosis who were considered surgical candidates or who were not suitable for endarterectomy, respectively. In the third trial, discussed here, 17 patients with symptomatic vertebral artery stenosis were randomized to endovascular treatment or best medical management alone. The mean interval between symptom onset and randomization was 92 days (range, 5-376 days). Analysis included 8 patients allocated to endovascular treatment and 8 patients allocated to best medical treatment alone. Endovascular treatment was technically successful in all 8 patients on the first attempt. Severity of vessel stenosis was reduced immediately after angioplasty or stenting, from a median of 73% to a median of 25% (interquartile range, 0%-50%; p=0.003).
During the 30-day postprocedure period or postrandomization period, 2 subjects in the endovascular group experienced symptomatic posterior circulation TIAs, compared with no subjects in the control group (p=0.47). There were no periprocedural strokes or deaths in either group and no patient experienced the primary outcome event of vertebrobasilar territory stroke. Six endovascular patients had follow-up catheter angiography, and 3 of the 6 patients had restenosis greater than 50%. Two of the 6 patients had additional posterior circulation TIAs during follow-up, and 4 had no further TIAs (median stenosis severity, 59%; p=0.64). Over a mean follow-up of 4.7 years, 3 patients in each treatment arm died of MI, vascular death, or carotid territory stroke and 1 endovascular patient had a nonfatal carotid territory stroke. This study failed to demonstrate a benefit for endovascular intervention, although it was underpowered to detect all but a very large treatment benefit.

Nonrandomized Comparative Studies
One additional nonrandomized study comparing outcomes for patients with symptomatic vertebral ostial stenosis treated with medical therapy alone or vertebral artery stenting, which was included in the Antoniou et al review, was identified. The study included 39 consecutive patients at a single institution from 2000 to 2008 treated for vertebral ostial stenosis, 10 stenting and 29 with best medical therapy, with treatment decisions left to the treating physician. All patients had a history of posterior circulation stroke or TIA, with no alternative causes of stroke identified. Patients in the medical therapy group received therapies including aspirin (n=20), clopidogrel (n=1), vitamin K antagonists (n=5), combination of aspirin and clopidogrel (n=3), statin therapy (n=20), and antihypertensive drugs (n=18). All patients receiving vertebral artery stenting received aspirin and clopidogrel for 12 months, with aspirin continued indefinitely. Patients treated medically were older (68 vs 60 years; p=0.04), had less severe neurologic deficits on admission (National Institutes of Health Stroke Score 1 vs 2.5; p=0.03), and were less often current smokers (10% vs 60%; p=0.03). In the medical group, 1 patient died from basilar artery thrombosis 22 days after the index event. In the stenting group, 1 patient experienced a TIA 1 day after the procedure. There were no hemorrhagic strokes, strokes in the anterior circulation, MI, or reinterventions within 30 days after the index event. At 4-year follow-up, stented patients had a nonsignificantly lower risk of the combined end point of TIA and nonfatal and fatal posterior circulation strokes (10% vs 45%; relative risk, 0.25; 95% confidence interval, 0.03 to 1.85; p=0.095).

Noncomparative Studies
A large number of noncomparative studies, most often enrolling few patients, have described outcomes for patients treated with endovascular therapies for extracranial vertebral artery disease. Some of the cohort studies that report on prospectively collected complication and restenosis rates are shown in Table 1.

Section Summary
The evidence on the overall efficacy of endovascular therapies for extracranial vertebral artery stenosis includes a phase 2 RCT (115 patients) that compared endovascular therapy to best medical therapy alone for vertebral artery stenosis. This trial found no advantage of endovascular intervention compared to best medical therapy alone, with a periprocedural adverse event rate of 5% for the invasive procedures. A larger phase 3 trial comparing endovascular therapy to medical therapy for vertebral artery stenosis is ongoing, although the lack of benefit of endovascular therapy demonstrated in VAST raises questions about the need for a phase 3 trial. Evidence from noncomparative studies have indicated that vertebral artery stenting can
be performed with high rates of technical success and low periprocedural morbidity and mortality, and that vessel patency can be achieved in a high percentage of cases. However, long-term follow-up has demonstrated high rates of in-stent stenosis. The evidence is insufficient to demonstrate an improvement in the net health outcome with vertebral artery stenting or angioplasty.

Angioplasty and Stenting for Extracranial Vertebral Artery Aneurysms, Dissections, and Arteriovenous Fistulae

A smaller body of literature has addressed the use of endovascular procedures for extracranial vertebral artery aneurysms, dissections, and arteriovenous (AV) fistulae. These lesions most commonly occur after trauma or iatrogenic injury. Because aneurysms, dissections, and AV fistulae may coexist in the same vessel, studies reporting outcomes for endovascular treatment for these conditions are discussed together. The available literature consists entirely of case reports and case series, and a systematic review of case series.

Systematic Reviews

In 2011, Pham et al conducted a systematic review of studies evaluating endovascular stenting for extracranial carotid and vertebral artery dissections that included 8 studies of extracranial vertebral artery stenting with 10 patients (12 vessels). Of the 10 patients included, 70% had associated pseudoaneurysms and 20% had bilateral lesions. Most dissections (60%) were traumatic in etiology, while 20% were spontaneous and 20% were iatrogenic. The indications for stenting were failure of medical management in 40% (defined as a new ischemic event, progression of initial symptoms, or demonstration of an enlarging pseudoaneurysm despite adequate anticoagulation or antiplatelet treatment), contraindication to anticoagulation in 20%, and/or severity of dissection hemodynamics in 60%. No stent-related complications or mortalities were reported in any study. One dissection-related death was reported, although stenting was considered technically successful.

Case Series and Case Reports

Since the publication of the 2010 Pham et al systematic review, some additional case series related to the use of endovascular therapies for extracranial vertebral artery dissections have been published.

In 2014, Badve et al retrospectively compared the clinical characteristics of patients with vertebrobasilar dissections with and without aneurysmal dissection treated at a single institution from 2002 to 2010. Thirty patients were identified, 7 with aneurysmal dissections, 1 of which was 1 extracranial, and 23 with nonaneurysmal dissections, 10 of which were extracranial and 12 of which were combined intracranial/extracranial. Patients were treated with antiplatelet agents (aspirin or clopidogrel; n=8) or anticoagulation with warfarin (n=13) or neurointerventional procedures (n=6). One patient in the nonaneurysmal dissection group treated with aspirin died.

The use of endovascular therapy for extracranial vertebral artery aneurysms and AV fistulae is similarly limited to small case series and case reports. In an early report from 1996, Horowitz et al described a left-sided vertebral artery pseudoaneurysm with dissection between the vessel media and adventitia at the C7 vertebra that was treated with a balloon-expandable stent. Follow-up angiography 3 months postprocedure showed no filling of the pseudoaneurysm and normal patency of the parent artery. In 2004, Felber et al
reported outcomes from endovascular treatment with stent grafts of 11 patients with aneurysms or AV fistulae of craniocervical arteries, 2 of whom were treated for extracranial vertebral artery disorders with coronary stents (1 aneurysm, 1 traumatic AV fistula). The procedure was technically successful in both subjects, without complications. At follow-up (5 years and 14 months postprocedure in the aneurysm and fistula patients, respectively), the target vessel was patent without stenosis. In 2008, Herrera et al reported outcomes for a single-center series of 18 traumatic vertebral artery injuries, including 16 AV fistulae (7 of which had an associated pseudoaneurysm) and 2 isolated pseudoaneurysms, treated with endovascular therapy. Endovascular therapy consisted of balloon occlusion of the parent vessel and AV fistula in 12 (66.6%) patients, coil embolization in 2 (11.1%) patients, and detachable balloon and coil embolization, balloon occlusion, and stent delivery with coil and n-butyl cyanoacrylate embolization of a AV fistulae each in 1 (5.5% each) patient. Angiography immediately after endovascular treatment demonstrated complete occlusion in 16 (88.9%) patients and partial occlusion in 2 (11.1%) patients. Seventeen (94.5%) patients had complete resolution of symptoms.

Other case reports have described successful use of endovascular treatment with stenting for iatrogenic vertebral artery pseudoaneurysms, iatrogenic vertebral artery AV fistula, extracranial vertebral artery aneurysm with an unknown cause, and extracranial vertebral artery aneurysm with a cervical vertebral arteriovenous fistula.

Section Summary
The evidence on use of endovascular therapies for the treatment of extracranial vertebral artery dissections, aneurysms, and AV fistulae consists of small case series and case reports. The available case reports and case series indicate that endovascular therapy for extracranial vertebral artery disorders other than stenosis is feasible and may be associated with favorable outcomes. However, given the lack of evidence comparing endovascular therapies to alternatives, the evidence is insufficient to determine whether endovascular therapy for extracranial vertebral artery dissections, aneurysms, and AV fistulae improves the net health outcome.

Table 1: Cohort Studies of Endovascular Treatment of Extracranial Vertebral Artery Stenosis

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Type</th>
<th>Population</th>
<th>FU Period</th>
<th>Main Results</th>
</tr>
</thead>
</table>
| Kikuchi et al (2014) | Retrospective review of prospectively collected data | 404 patients from a registry treated with endovascular therapy | 30 d       | • Postprocedural morbidity: 2.0%  
• Postprocedural mortality: 0.3%  
Not reported |
| Sun et al (2015)  | Retrospective review of prospectively collected data | 188 patients with posterior circulation TIA or stroke and mRS score ≤2 | 16.5 mo^a  | • Technical success rate: 100%  
• 34 patients had recurrent TIA after 30 d  
• No cases of stroke or death occurred  
21.2% |
| Mohammadian et al (2013) | Prospective interventional study | 206 patients with clinical signs/symptoms of vertebral occlusion (239 treated lesions, 202 extracranial) | 13.15 mo^a | • Technical success rate: 100%.  
• 89.2% were balloon-expandable bare-metal stents  
• Periprocedural complication rate: 15.9% |
Endovascular Therapies for Extracranial Vertebral Artery Disease

Policy # 00466
Original Effective Date: 06/17/2015
Current Effective Date: 06/20/2016

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Type</th>
<th>Population</th>
<th>FU Period</th>
<th>Main Results</th>
<th>In-Stent Restenosis Rate</th>
</tr>
</thead>
</table>
| Hatano et al (2011) | Retrospective review of prospectively collected data | 117 patients (108 symptomatic, 9 asymptomatic) | 48 mo*    | • Technical success rate: 99%  
• During FU: 5 patients had posterior circulation ischemia; 1 patient had cerebellar infarction with ISR, 2 patients had posterior circulation strokes without ISR | 9.6% at 6 mo |

FU: follow-up; ISR: in-stent restenosis; mRS: modified Rankin Scale; TIA: transient ischemic attack.

a Mean value.

Table 2. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02197559</td>
<td>A Prospective Cohort Study of Bare-Metal Stents and Drug - Eluting Stents in the Treatment of Patients With Vertebral Artery Ostium Stenosis</td>
<td>172</td>
<td>Dec 2016</td>
</tr>
<tr>
<td>NCT02328781</td>
<td>Prospective Multi-center Single-arm Target Value Clinical Trial for Evaluating Clinical Use Safety and Efficacy of the Firehorus Vertebral Artery Rapamycin-target-eluting Stent System</td>
<td>150</td>
<td>Dec 2016</td>
</tr>
<tr>
<td>ISRCTN95212240</td>
<td>Vertebral artery Ischaemia Stenting Trial (VIST)</td>
<td>540</td>
<td>Nov 2017</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

Summary of Evidence

For individuals who have extracranial vertebral artery stenosis who receive percutaneous transluminal angioplasty with or without stent implantation, the evidence includes a phase 2 RCT. Relevant outcomes are overall survival, symptoms, morbid events, and treatment-related mortality and morbidity. The phase 2 RCT, the VAST, found no advantage for endovascular intervention compared to best medical therapy alone, with a periprocedural adverse event rate of 5% for the invasive procedures. A larger phase 3 trial comparing endovascular therapy to medical therapy for vertebral artery stenosis is ongoing, although the lack of benefit of endovascular therapy demonstrated in VAST raises questions about the need for a phase 3 trial. Evidence from noncomparative studies indicates that vertebral artery stenting can be performed with high rates of technical success and low periprocedural morbidity and mortality, and that vessel patency can be achieved in a high percentage of cases. However, long-term follow-up has demonstrated high rates of in-stent stenosis. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have extracranial vertebral artery aneurysm(s), dissection(s), and AV fistula(e) who receive percutaneous transluminal angioplasty with stent implantation, the evidence includes small case series and case reports. Relevant outcomes are overall survival, symptoms, morbid events, and treatment-
related mortality and morbidity. The available evidence indicates that endovascular therapy for extracranial vertebral artery disorders other than stenosis is feasible and may be associated with favorable outcomes. However, given the lack of data comparing endovascular therapies to alternatives, the evidence is insufficient to determine whether endovascular therapy for extracranial vertebral artery aneurysms, dissections, and AV fistulae improves the net health outcome. The evidence is insufficient to determine the effects of the technology on health outcomes.

References
Endovascular Therapies for Extracranial Vertebral Artery Disease

Policy # 00466
Original Effective Date: 06/17/2015
Current Effective Date: 06/20/2016


Policy History
Original Effective Date: 06/17/2015
Current Effective Date: 06/20/2016

06/04/2015 Medical Policy Committee review
06/17/2015 Medical Policy Implementation Committee approval. New policy.
08/03/2015 Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
06/02/2016 Medical Policy Committee review
06/20/2016 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 06/20/2017

Coding
The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®), copyright 2015 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of
Endovascular Therapies for Extracranial Vertebral Artery Disease

Policy # 00466
Original Effective Date: 06/17/2015
Current Effective Date: 06/20/2016

The information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

<table>
<thead>
<tr>
<th>Code Type</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>0075T, 0076T, 36226, 36228</td>
</tr>
<tr>
<td>HCPCS</td>
<td>No codes</td>
</tr>
<tr>
<td>ICD-9 Diagnosis</td>
<td>All related diagnoses</td>
</tr>
<tr>
<td>ICD-10 Diagnosis</td>
<td>All related diagnoses</td>
</tr>
</tbody>
</table>

*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 U.S. 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:

1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.