I. Description

Intracranial arterial disease includes thromboembolic events, vascular stenosis, and aneurysms. Endovascular techniques have been investigated for treatment of intracranial arterial disease, as an alternative to intravenous tissue plasminogen activator (tPA) and supportive care for acute stenosis and as an alternative to risk factor modification for chronic stenosis. For cerebral aneurysms, stent-assisted coiling has been evaluated as an alternative to endovascular coiling in patients whose anatomy is not amendable to simple coiling.

Cerebrovascular diseases include a range of processes affecting the cerebral vascular system, including arterial thromboembolism, arterial stenosis, and arterial aneurysms, all of which can lead to restrictions in cerebral blood flow due to ischemia or hemorrhage. Endovascular techniques, including endovascular pharmacologic thrombolysis, endovascular mechanical embolectomy; using one of several types of devices, endovascular deployment of several types of stents, and angioplasty with or without stenting, have been investigated for treatment of cerebrovascular diseases.

It is estimated that intracranial atherosclerosis causes about 8% of all ischemic strokes. Intracranial stenosis may contribute to stroke in two ways: either due to embolism or low flow ischemia in the absence of collateral circulation. Recurrent annual stroke rates are estimated at 4–12% per year with atherosclerosis of the intracranial anterior circulation and 2.5–15% per year with lesions of the posterior (vertebrobasilar) circulation. Medical treatment typically includes either anticoagulant therapy (i.e., warfarin) or antiplatelet therapy (e.g., aspirin). The “Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) trial was a randomized trial that compared the incidence of stroke brain hemorrhage or death among patients randomized to receive either aspirin or warfarin. The trial found that over a mean 1.8 years of follow-up, warfarin provided no benefit over aspirin and was associated with a significantly higher rate of complications. In addition, if symptoms could be attributed to low flow ischemia, agents to increase mean arterial blood pressure and avoidance of orthostatic hypotension may be recommended. However, medical therapy has been considered less than optimal. For example, in patients with persistent symptoms despite antithrombotic therapy, the subsequent rate of stroke or death has been extremely high, estimated in one study at
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45%, with recurrent events occurring within 1 month of the initial recurrence. Surgical approaches have met with limited success. The widely quoted extracranial-intracranial (EC/IC) bypass study randomized 1,377 patients with symptomatic atherosclerosis of the internal carotid or middle cerebral arteries to medical care or EC/IC bypass. The outcomes in the two groups were similar, suggesting that the EC/IC bypass is ineffective in preventing cerebral ischemia. Due to inaccessibility, surgical options for the posterior circulation are even more limited.

Percutaneous transluminal angioplasty (PTA) has been approached cautiously for use in the intracranial circulation, due to technical difficulties in catheter and stent design and the risk of embolism, which may result in devastating complications if occurring in the posterior fossa or brain stem. However, improvement in the ability to track catheterization, allowing catheterization of tortuous vessels, and the increased use of stents have created ongoing interest in exploring PTA as a minimally invasive treatment of this difficult-to-treat population. The majority of published studies of intracranial PTA has focused on the vertebrobasilar circulation.

Intracranial stents are also being used in the treatment of cerebral aneurysms. Stent-assisted coiling began as an approach to treat fusiform or wide-neck aneurysms in which other surgical or endovascular treatment strategies may not be feasible. As experience grew, stenting was also used in smaller berry aneurysms as an approach to decrease the rate of retreatment needed in patients who receive coiling. A randomized trial has demonstrated that treatment of ruptured intracranial aneurysms with coiling leads to improved short-term outcome compared to surgical clipping; however, patients who receive coiling have a need for more repeat/follow-up procedures.

Regulatory Status

Currently two devices have received approval for atherosclerotic disease from the U.S. Food and Drug Administration (FDA) through the humanitarian device exemption (HDE) process. This form of FDA approval is available for devices used to treat conditions with an incidence of 4,000 or less per year; the FDA only requires data showing “probable safety and effectiveness.” Devices with their labeled indications are as follows:

**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.”

**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.”

In 2011, FDA granted premarket approval to the Pipeline® Embolization Device (Covidien/eV3 Neurovascular, Irvine, CA), an intracranial aneurysm flow diverter, for the endovascular treatment of adults (≥22 years of age) with large or giant wide-necked intracranial aneurysms in the internal carotid artery from the petrous to the superior hypophyseal segments (P100018). Approval was based on the Pipeline for Uncoilable for Failed Aneurysms Study, a single-arm, open label feasibility
study that included 108 patients aged 30 to 75 years with unruptured large and giant wide-necked aneurysms.

Two stents have received FDA approval through the HDE program for treatment of intracranial aneurysms:

1. **Neuroform™ Microdelivery Stent System (Stryker, Kalamazoo, MI).** In 2002, based on a series of approximately 30 patients with 6-month follow-up, the Neuroform Microdelivery Stent System was approved (HDE) for use with embolic coils for treatment of wide-neck intracranial aneurysms that cannot be treated by surgical clipping (H020002).

2. **Enterprise™ Vascular Reconstruction Device and Delivery System (Cordis Neurovascular Inc., Miami Lakes, FL).** In 2007, based on a series of approximately 30 patients with 6-month follow-up, the Enterprise™ Vascular Reconstruction Device and Delivery was approved (HDE) for use with embolic coils for treatment of wide-neck, intracranial, saccular of fusiform aneurysms (H060001).

II. **Criteria/Guidelines**

   A. Intracranial stent placement is covered (subject to Limitations/Exclusions and Administrative Guidelines) as part of the endovascular treatment of intracranial aneurysms for patients meeting all of the following criteria:
   1. Surgical treatment is not appropriate
   2. Standard endovascular techniques do not allow for complete isolation of the aneurysm, e.g., wide-neck aneurysm (4 mm or more) or sack-to-neck ratio less than 2:1.

   B. Intracranial flow diverting stents with FDA approval for the treatment of intracranial aneurysms are covered (subject to Limitations/Exclusions and Administrative Guidelines) as part of the endovascular treatment of intracranial aneurysms for patients meeting all of the following criteria:
   1. Surgical treatment or standard endovascular therapy is not appropriate; and
   2. Flow diverting stents are indicated for the treatment of large or giant wide-necked intracranial aneurysms, with a size of 10 mm or more and a neck diameter of 4 mm or more, in the internal carotid artery from the petrous to the superior hypophyseal segments.

III. **Limitations/Exclusions**

   A. Intracranial stent placement is not covered in the treatment of intracranial aneurysms except as noted above.

   B. Intracranial percutaneous transluminal angioplasty with or without stenting is not covered in the treatment of atherosclerotic cerebrovascular disease.

IV. **Administrative Guidelines**

   A. Precertification is required for all non-emergent conditions. To pre-certify, complete HMSA’s [Precertification Request](#) and fax or mail the form with the following documentation:
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1. Clinical notes including neurosurgical and neuroradiological consultation reports (if available)
2. MRA, CTA or standard angiography brain report.

B. HMSA reserves the right to perform retrospective review using the above criteria to validate if services rendered met payment determination criteria.

C. Applicable codes:

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>61635</td>
<td>Transcatheter placement of intravascular stent(s), intracranial (e.g., atherosclerotic stenosis), including balloon angioplasty, if performed</td>
</tr>
<tr>
<td>36100</td>
<td>Introduction of needle or intracatheter, carotid or vertebral artery</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-9 Procedure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>00.65</td>
<td>Percutaneous insertion of intracranial vascular stents</td>
</tr>
</tbody>
</table>

D. Codes that do not meet payment determination criteria:

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>61630</td>
<td>Balloon angioplasty, intracranial (e.g., atherosclerotic stenosis), percutaneous</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-9 Procedure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>00.62</td>
<td>Percutaneous angioplasty or atherectomy of intracranial vessel(s)</td>
</tr>
</tbody>
</table>

E. Effective 10/01/2015 codes are only used for inpatient services:

<table>
<thead>
<tr>
<th>ICD-10-PCS</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>037G34Z,</td>
<td>Surgical, upper arteries, dilation, intracranial artery, code by approach (percutaneous or percutaneous endoscopic) and device (drug-eluting intraluminal device, intraluminal device, or no device)</td>
</tr>
<tr>
<td>037G3DZ,</td>
<td></td>
</tr>
<tr>
<td>037G3ZZ,</td>
<td></td>
</tr>
<tr>
<td>037G44Z,</td>
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<td>037G4DZ,</td>
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</tr>
</tbody>
</table>

V. Rationale

**Intracranial atherosclerotic disease**

The following discussion focuses on the U.S. Food and Drug Administration (FDA) Summary of Safety and Probable Benefit for the two devices that have received FDA approval through the humanitarian device exemption (HDE) process. The following data were presented to the FDA as part of the approval process for these devices.

**FDA submission data**

**Neurolink System.** The clinical study investigating the Neurolink device is known as the Stenting of Symptomatic Atherosclerosis Lesions in the Vertebral or Intracranial Arteries (SSYLVIA) study, a
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prospective, nonrandomized, multicenter, international study of 61 patients. Patients eligible for participation in the study were symptomatic (previous stroke or transient ischemic attack [TIA]) attributed to an angiographically demonstrated discrete stenosis (50% or greater) in an extracranial or intracranial artery. The primary endpoint was a composite endpoint of stroke or death through 30 days; four patients experienced strokes (6.6%) and there were no deaths. Mean follow-up was 216 days and lower bound for ipsilateral stroke at 12 months was estimated to be 11.5%. The FDA summary noted that in the WASID study of aspirin and warfarin therapy (see Description section), the rate of fatal or nonfatal stroke was 14.6% and total/stroke or death was 22.5% with a follow-up of 15–19 months, suggesting a potentially superior outcome with the Neurolink device. However, the short length of follow-up in the Neurolink study prevents meaningful comparisons. The FDA Summary of Safety and Probable Benefit states, “... it is reasonable to conclude that the probable benefit to health from using the Neurolink System for intracranial stenting for recurrent stroke attributable to intracranial atherosclerosis refractory to medical therapy outweighs the risk of illness or injury, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment, when used as indicated in accordance with the directions of use.”

**Wingspan™Stent System.** The Wingspan Stent System consists of a highly flexible, microcatheter-delivered self-expanding nitinol stent, which may be suitable for lesions in the distal internal carotid and middle cerebral arteries, which are difficult to access with a balloon-mounted stent, such as the Neurolink system. (2) The Wingspan was evaluated in a prospective study of 45 patients enrolled at 12 international centers. Patients were considered eligible if they presented with evidence of recurrent symptoms, refractory to medical therapy and attributed to an intracranial stenosis (50% or greater). The primary safety endpoint was similar to that of the SSYLVIA study (stroke or death through 30 days) and was reached by 2 patients (4.5%; 1 death following a hemorrhagic stroke and 1 stroke). The FDA summary provided a comparison of various outcomes of the Neurolink and Wingspan devices as follows:

<table>
<thead>
<tr>
<th>Clinical Study</th>
<th>Follow-up</th>
<th>All Stroke</th>
<th>Death</th>
<th>Stroke and Death</th>
<th>Ipsilateral Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSYLVIA (n=61)</td>
<td>Mean: 216 days (n=48 at 6 months)</td>
<td>13.1%</td>
<td>6.6%</td>
<td>13.1%</td>
<td>11.5%</td>
</tr>
<tr>
<td>Wingspan (n=45)</td>
<td>Mean: 174 days (n=42 at 6 months)</td>
<td>9.5%</td>
<td>2.4%</td>
<td>9.5%</td>
<td>7.1%</td>
</tr>
</tbody>
</table>

The FDA offered the following conclusions and appears to have based its approval in part on the favorable comparison to the Neurolink device:

“The Wingspan clinical study treated 45 patients with symptomatic atherosclerotic lesions in intracranial arteries who were refractory to medical therapy. The lesions were predilated and stented. Clinical follow-up (42 patients) and angiographic follow-up (40 patients) were performed at 6 months. The type and frequency of observed adverse events including stroke are consistent with or lower than similar neurovascular procedures. Therefore, it is reasonable to conclude that the probable benefit to health from using the Wingspan Stent System with Gateway PTA Balloon Catheter for treating transcranial stenosis outweighs the risk of illness or injury when used in
accordance with the Instructions for Use and when taking into account the probable risks and benefits of currently available alternative forms of treatment.”

**Acute stroke**

Two randomized controlled trials (RCTs) evaluating the efficacy of endovascular treatment for acute ischemic stroke were published in 2013.

The IMS III trial was an open-label RCT with a planned enrollment of 900 patients. This trial enrolled patients with acute ischemic stroke who presented within 3 hours of symptom onset and had a moderate to severe neurologic deficit on presentation. Patients were randomized to intravenous tissue plasminogen activator (tPA) alone or intravenous tPA plus endovascular intervention. Patients randomized to the endovascular group underwent immediate angiography followed by endovascular intervention if a treatable vascular occlusion was present. Endovascular intervention consisted of either endovascular delivery of tPA at the site of occlusion or mechanical thrombectomy, at the discretion of the treating physician. The primary outcome was a modified Rankin score of 2 or less at 90 days.

The trial was stopped prematurely due to futility after enrollment of 656 patients. At this point, the primary outcome had been reached by 40.8% of patients in the endovascular group compared with 38.7% of patients in the intravenous tPA group. The adjusted difference in the primary outcome was 1.5%, with a 95% confidence interval (CI) for the difference of -6.1 to 9.1. Subarachnoid hemorrhage was more frequent in the endovascular group compared to the tPA group (11.5% vs. 5.8%, p=0.02), as was asymptomatic intracerebral hemorrhage (27.4% vs. 18.9%, p=0.01). There were no significant differences between groups in other adverse events, including death and symptomatic intracerebral hemorrhage.

The second RCT, by Ciccone et al., randomized 362 patients with acute ischemic stroke presenting within 4.5 hours of symptom onset to intravenous tPA or endovascular treatment. Endovascular treatment consisted of either endovascular delivery of tPA at the site of thrombosis, mechanical thrombectomy, or both. The choice of endovascular intervention was at the discretion of the treating physician, based on results of angiography. The trial was unblinded to treatment assignment, but did include blinded endpoint assessment. The primary outcome was disability-free survival at 90 days, defined as a survival with a modified Rankin score of 0 or 1.

At 90 days of follow-up, the proportion of patients with disability-free survival was 30.4% in the endovascular group and 34.8% in the intravenous tPA group. On multivariate analysis, the odds ratio for disability-free survival with endovascular treatment was 0.71 (95% CI: 0.44-1.14, p=0.16). There were no significant differences in adverse events at 7 days, including intracerebral hemorrhage and neurologic deterioration. Subgroup analysis did not reveal any patient subgroups in which endovascular treatment was superior to tPA.

At least 2 other RCTs have been published that compare different types of mechanical thrombectomy devices for acute ischemic stroke. These trials do not offer relevant evidence
regarding the efficacy of endovascular treatment compared to standard treatment, i.e., intravenous tPA.

Numerous case series of endovascular treatment have been published. One of these was a prospective series sponsored by the U.S. Food and Drug Administration (FDA). In this study, 20 patients with acute ischemic stroke presenting within 8 hours of symptom onset, with an NIH stroke score of at least 8, and for whom thrombolysis was either contraindicated or ineffective, were treated with the Wingspan intracranial self-expanding stent. All patients were treated with aspirin and clopidogrel, and follow-up was for 6 months. Mortality at 6 months was 35% (7/20). At 6 months, 60% of patients (12/20) had an NIH stroke score of 3 or less, and 55% (11/20) had a score of 2 or less. A total of 11/13 (85%) patients who were alive at 6 months had a follow-up angiogram, and all showed patency of the stent graft with TIMI level 3 flow or greater.

Conclusions. Two RCTs have been published that evaluate the efficacy of endovascular interventions for acute ischemic stroke. Neither of these studies reported a benefit for endovascular treatment, and one of the studies reported an increase in adverse events with endovascular treatment. This evidence supports the conclusion that endovascular treatment of acute stroke does not improve outcomes compared to standard treatment, i.e., intravenous tPA.

Elective treatment of symptomatic intracranial stenosis

The evidence on this question consists of at least 2 randomized controlled trials (RCTs), a number of non-randomized comparative studies, and numerous single-arm series. The most clinically relevant studies are reviewed below.

RCTs. The stenting and aggressive medical management for preventing recurrent stroke in intracranial stenosis (SAMMPRIS) was an RCT comparing aggressive medical management alone to aggressive medical management plus stenting in patients with symptomatic cerebrovascular disease and an intracranial stenosis of between 70-99%. This trial used the Wingspan stent system implanted by experienced neurointerventionists who had been credentialed to participate in the trial. The authors had planned for an enrollment of approximately 750 patients based on power calculations. However, the trial was stopped early for futility after 451 patients had been randomized. The trial was terminated due to an excess of the primary outcome, stroke or death, at 30 days in the stenting group. In the stenting group, the rate of stroke or death at 30 days was 14.7% (95% confidence interval [CI]: 10.7-20.1) compared to a rate of 5.8% (95% CI: 3.4-9.7, p=0.002) in the medical management group. At the time of termination, the mean follow-up was 11.9 months. Kaplan-Meier estimates of the primary outcome of stroke or death at one year was 20.5% (95% CI: 15.2-26.0) in the stenting group compared to 12.2% (95% CI: 8.4-17.6, p=0.009) in the medical management group. These results represented an excess rate of early adverse events with stenting over what was expected together with a decreased rate of stroke and death in the medical management group compared to expected values.

The Carotid And Vertebral Artery Transluminal Angioplasty Study (CAVATAS) randomized 16 patients with symptomatic vertebral artery stenosis to endovascular therapy (balloon angioplasty
or stenting) or best medical treatment alone. Endovascular intervention was technically successful in all 8 patients, but 2 patients experienced TIA’s at the time of endovascular treatment. During a mean follow-up of 4.7 years, no patient in either treatment group experienced a vertebrobasilar territory stroke, but 3 patients in each arm died of myocardial infarction (MI) or carotid territory stroke, and 1 patient in the endovascular arm had a nonfatal carotid territory stroke. The investigators concluded that patients with vertebral artery stenosis were more likely to have carotid territory stroke and MI during follow-up than have recurrent vertebrobasilar stroke. While they noted the trial failed to show a benefit of endovascular treatment of vertebral artery stenosis, the small number of patients enrolled severely limits conclusions.

**Non-randomized, comparative studies.** A number of non-randomized studies have compared outcomes of endovascular procedures with medical therapy. These studies have either been retrospective, or based on registry data, and provide relatively weak evidence on the comparative efficacy of endovascular procedures compared to medical therapy. A representative sample of such studies is given below.

Tang et al. performed a retrospective comparison of 53 patients with at least 70% intracranial stenosis treated with stenting, compared with 61 patients treated with medical therapy matched for age, gender, vascular risk factors, degree of baseline stenosis, and baseline functional status. After a mean follow-up of 17.3 months, a composite outcome of stroke, TIA, or vascular death was not different for the stent group compared to medical therapy (22.6% vs. 24.6%, respectively; p=0.99). A good functional outcome, defined as a modified Rankin Score of 0-3, was more frequent in the stent group compared to medical therapy (94.3% vs. 78.7%, respectively; p=0.045).

Qureshi et al. compared outcomes of angioplasty with (n=22) or without stenting (n=22) in patients with symptomatic intracranial stenosis 50% or greater identified retrospectively from a registry (angioplasty was used preferentially in patients with more technically challenging lesions). Although, at 12 months, no differences in stroke-related outcomes or mortality were noted (stroke-free survival of 95% and 93% after stenting and angioplasty alone, respectively), the small sample, nonrandom treatment assignment, and event rates prevent valid comparisons. Further, comparison with medical therapy is required.

Samaniego et al. retrospectively reviewed outcomes at a single institution comparing study of best medical therapy to angioplasty and stenting in 111 patients with symptomatic intracranial atherosclerotic disease treated from July 2004 to September 2007. Treatment decisions were made by a multidisciplinary committee. Important baseline differences between the best medical therapy and angioplasty groups, respectively, included presenting with acute stroke (74% vs. 57%) or TIA (26% vs. 43%), emergency department (53% vs. 28%), or outpatient (19% vs. 47%) presentation, or prior TIA (19% vs. 55%). The best medical therapy group also had more diffuse disease, respectively (67% vs. 28%) rather than single lesions. In this series, 31 lesions were treated with the Wingspan system, 12 with the Neuroform stent, and 14 with various balloon-expandable stent systems. Mean follow-up was 14 months in both groups. Combined ischemic endpoints of TIA, stroke, and vascular death were similar, 24% (n=14) in the best medical therapy group and 28% (n=15) in the angioplasty and stenting group. However, inability to account for nonrandom treatment assignment and systematic differences between groups prevents conclusions.
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**Single-arm case series/Registry studies.** Numerous single arm case series have been published. These studies provide some information on the success rates and the adverse events that occur with this procedure, but offer very limited evidence on the comparative efficacy of endovascular approaches versus medical therapy. Some of these case series are reviewed below.

Marks and colleagues reported a series of 120 patients with 124 intracranial stenoses who were treated by primary angioplasty. There were 3 strokes and 4 deaths (all neurological) within 30 days of the procedure, giving a combined periprocedural stroke and death rate of 5.8%. A total of 116 patients (96.7%) were observed for a mean follow-up of 42.3 months.

Fiorella et al. reported on initial periprocedural experience with the Wingspan stent in 78 patients, average age 64 years. Eighty-one of 82 lesions were successfully stented, and percent stenosis was reduced (from 75% to 27% after stent placement). There were 5 (6.1%) major periprocedural neurologic complications with 4 patient deaths within 30 days. Long-term outcomes were not reported.

Zaidat et al. reported on the NIH registry on use of the Wingspan stent for symptomatic intracranial stenosis; 129 patients from 16 medical centers were treated with a Wingspan stent between November 2005 and October 2006. The frequency of any stroke, intracerebral hemorrhage, or death within 30 days or ipsilateral stroke beyond 30 days was 14.0% at 6 months (95% CI: 8.7% to 22.1%). The incidence of 50% or greater restenosis on follow-up angiography was 13 of 52 (25%).

**INTRASTENT** is a European 18-center registry enrolling patients with symptomatic intracranial stenoses greater than 50%. From the registry, Kurre et al. reported that in 372 patients with 388 stenoses, stenting was successful in 90.2% of patients. In-hospital death and disabling stroke rates were 2.2% and 4.8%, respectively. No subgroups with increased risk of procedure-related morbidity or mortality were discerned.

Albuquerque et al. examined angiographic patterns of in-stent restenosis with the Wingspan device. Imaging follow-up (3–15.5 months) was available for 127 intracranial stenotic lesions. Forty-one lesions (32.3%) developed either in stent restenosis (n=6, 28.3%) or complete stent occlusion (n=5, 3.9%) after treatment.

**Systematic Reviews.** The 2005 Cochrane review of angioplasty and stenting for vertebral artery stenosis identified only the CAVATAS trial for inclusion and concluded, “... there is currently insufficient evidence to support the routine use of percutaneous transluminal angioplasty (PTA) and stenting for vertebral artery stenosis. Endovascular treatment of vertebral artery stenosis should only be performed within the context of randomized controlled trials.” In addition, the authors noted, “[l]ittle is known about the natural history of vertebral artery stenosis and what constitutes best medical treatment. Future trials should concentrate on comparing different medical treatment such as antiplatelet and anticoagulant drugs as well as comparing endovascular intervention with medical treatment.”

A 2006 Cochrane Review addressed angioplasty for intracranial artery stenosis. The authors identified no RCTs but 79 publications of interest consisting of case series with 3 or more cases. The safety profile showed an overall perioperative rate of stroke of 7.9% (95% CI: 5.5% to 10.4%) and perioperative stroke or death of 9.5% (95% CI: 7.0% to 12.0%). The authors concluded the evidence insufficient to recommend angioplasty with or without stent placement in routine practice for the
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prevention of stroke in patients with intracranial artery stenosis. The descriptive studies showed the procedure was feasible, although carrying significant morbidity and mortality risks. Evidence from RCTs is needed to assess the safety of angioplasty and its effectiveness in preventing recurrent stroke.

Groschel et al. conducted a systematic review on outcomes after stenting for intracranial atherosclerosis. The authors identified 31 studies including 1,177 procedures, which had mainly been performed in patients with a symptomatic (98%) intracranial high-grade stenosis (mean: 78.7%) with high technical success rates (median: 96%; interquartile range: 90% to 100%). The periprocedural minor or major stroke and death rates ranged from 0% to 50%, with a median of 7.7%. Periprocedural complications were significantly higher in the posterior versus the anterior circulation (12.1% vs. 6.6%, \( p < 0.01 \)), but did not differ between patients treated with a balloon-mounted stent (n=906) versus those who had been treated with a self-expandable stent (n=271; 9.5% vs. 7.7%, respectively; \( p = 0.47 \)). Restenosis greater than 50% occurred more frequently after the use of a self-expandable stent (16/92; 17.4%, mean follow-up time: 5.4 months) than a balloon-mounted stent (61/443; 13.8%, mean follow-up time: 8.7 months; \( p < 0.001 \)). The authors concluded that although intracranial stenting appears to be feasible, adverse events vary widely, and thus given a high rate of restenoses and no clear impact of new stent devices on outcome, the widespread application of intracranial stenting outside the setting of randomized trials and in inexperienced centers currently does not seem to be justified.

Stent-Assisted Treatment of Intracranial Aneurysms

The literature search did not identify any trials of stent-assisted treatment of intracranial aneurysms compared to standard neurosurgical treatment. The available evidence consists of single-arm case series, registry studies, and non-randomized comparative studies.

Non-randomized comparative studies. The largest comparative series describing use of stents compared to coiling alone for treating intracranial aneurysms was described by Piotin and colleagues. They report on a series of 1,137 patients (1,325 aneurysms) treated between 2002 and 2009. In this series, 1,109 aneurysms (83.5%) were treated without stents (coiling), and 216 (16.5%) were treated with stents (15 balloon-expandable and 201 self-expandable stents). Permanent neurological procedure related complications occurred in 7.4% (16 of 216) of the procedures with stents versus 3.8% (42 of 1,109) in the procedures without stents (logistic regression \( p = 0.644 \); odds ratio: 1.289; 95% CI: 0.439–3.779). Procedure-induced mortality occurred in 4.6% (10 of 216) of the procedures with stents versus 1.2% (13 of 1,109) in the procedures without stents (logistic regression \( p = 0.006 \); odds ratio: 0.116; 95% CI: 0.025–0.531). Thus far, the authors have followed 53% (114 of 216) of aneurysms treated with stents and 70% (774 of 1,109) of aneurysms treated without stents, with angiographic recurrence in 14.9% (17 of 114) versus 33.5% (259 of 774), respectively (\( p < 0.0001 \); odds ratio: 0.3485; 95% CI: 0.2038–0.5960).

Colby et al. reported on 90 consecutive patients undergoing treatment for para-ophthalmic aneurysms, 30 of whom were treated with coil alone versus 60 who were treated with stent-assisted coils. On initial angiography following the procedure, complete occlusion of the aneurysm was achieved in 43.3% of stented patients compared to 31.7% of non-stented patients. At a mean of 14.5 months follow-up the recurrence rate was lower for the stented group at 15.4% (4/26) versus 41.5% (17/41) in the non-stented group (\( p < 0.05 \)).
A non-randomized comparative study from Korea reported on 126 aneurysms that were treated with stent-assisted coiling compared to 86 patients treated with coil alone. At 2 years of follow-up, the authors reported rates of occlusion and recurrence. Progressive occlusion was noted in 42.5% of the stent group (17/40) compared to 39.5% of the non-stented group (34/86), a difference that was not statistically significant. The rates of aneurysm recurrence were also not statistically different between groups. Recurrence occurred in 17.5% of patients in the stent group versus 21.0% in the non-stent group.

Single-arm series. There are a large number of single-arm series reporting on outcomes of stent-assisted coiling. A systematic review by Shapiro et al. identified 39 articles reporting on 1,517 patients, most of which were single-arm, retrospective series. The majority of patients treated had unruptured aneurysms, but 22% of patients had ruptured aneurysms. The authors noted a large amount of heterogeneity in reporting outcome data, particularly for adverse events. The peri-procedural mortality rate was 2.1%, and the overall complication rate was 19%. Immediately following treatment, approximately 45% of patients had occlusion of the aneurysm. At an average of 13 months post-treatment, the stroke rate in the stented area was 3.2%.

A systematic review that was restricted to ruptured aneurysms was published by Bodily et al. in 2011. This review included 17 articles that described treatment in 212 patients. Technical success was high at 93%, and 2% of patients required open surgery due to stent failure or intraoperative aneurysm rupture. A total of 63% (130/207) of aneurysms were successfully occluded. The overall mortality rate was 19%, and 14% of patients had poor clinical outcomes. There was a relatively high rate of adverse events reported, with 8% of patients having an acute intracranial bleed related to the procedure, and 6% (16/288) having a clinically significant thromboembolic event.

Mocco and colleagues reported results from a collaborative registry from 10 institutions describing initial experience in using the Enterprise stent. In this series, 141 patients with 142 aneurysms underwent 143 attempted stent deployments. The use of Enterprise assistance with aneurysm coiling was associated with a 76% rate of 90% or greater occlusion. An inability to navigate or deploy the stent was experienced in 3% of cases, as well as a 2% occurrence of inaccurate deployment. Data demonstrated a 6% temporary morbidity, 2.8% permanent morbidity, and 2% mortality (0.8% unruptured, 12% ruptured).

Wajnberg et al. reported on results for 24 patients (2005–2008) with wide-necked cerebral aneurysms who were treated with stent reconstruction of the aneurysm neck. Clinical outcome was assessed with the Glasgow Outcome Scale (GOS). In this series, the stent was easily navigated and positioned in 24 of 26 cases. However, technical difficulties occurred in 9 patients, including difficulties in crossing the stent’s interstice in 6 cases, inadvertent stent delivery in one case, and incapacity of stent delivery (n=1) and incapacity of crossing the neck (n=1). These latter 2 cases were classified as failures of the stent-assisted technique. A single procedural complication occurred, involving transient non-occlusive intra-stent thrombus formation, which was treated uneventfully. Seventeen patients experienced excellent clinical outcomes (GOS 5), with good outcomes (GOS 4) in 5 patients, and a poor outcome (GOS 3) in 2 patients. There were no treatment-related deaths or neurologic complications with mean follow-up of 12 months.

Biondi et al. reported on the midterm results of stent-assisted coil embolization in the treatment of wide-necked cerebral aneurysms. This was a retrospective review of 42 patients with 46 wide-
necked cerebral aneurysms enrolled in a prospective single-center registry of patients treated with a Neuroform stent, a flexible self-expanding nitinol stent. Twenty-seven of 46 aneurysms were unruptured aneurysms, 14 were recanalized aneurysms, and 5 were acutely ruptured. Mean aneurysm size was 9.8 mm. Stenting before coiling was performed in 13 of 45 aneurysms (29%), coiling before stenting in 27 of 45 aneurysms (60%), and stenting alone in 5 of 45 aneurysms (11%). In 40 aneurysms treated with stent-assisted coiling, angiographic results showed 14 (35%) aneurysm occlusions, 18 (45%) neck remnants, and eight (20%) residual aneurysms. At angiographic follow-up in 30 aneurysms treated with stent-assisted coiling, there were 17 (57%) aneurysm occlusions, 7 (23%) neck remnants, and 6 (20%) residual aneurysms. Procedural morbidity was observed in 2 of 42 patients (4.8%) and 1 patient died.

**Clinical Input Received through Physician Specialty Societies and Academic Medical Centers**

In response to requests, input was received from 3 physician specialty societies and 3 academic medical centers while this policy was under review in 2011. While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

For treatment of intracranial stenosis, the majority of those providing input would consider use of this technology in selected patients who remained symptomatic from intracranial atherosclerotic disease despite maximum medical therapy. There was unanimous support for use of this technology in selected patients with intracranial aneurysms; i.e., in those patients for whom surgical treatment is not possible and for whom endovascular treatment (coils) does not completely isolate the aneurysm.

**Summary**

For elective treatment of symptomatic intracranial stenosis, endovascular procedures with or without stenting have not been shown to be superior to best medical care. One very small RCT did not report benefit and a larger RCT was terminated prematurely due to an excess of the primary outcome of death or stroke in the endovascular group. This evidence suggests that the adverse event rate with endovascular procedures is relatively high and may outweigh the benefit in preventing recurrent ischemic events. As a result, endovascular procedures with or without stenting are considered investigational for the elective treatment of symptomatic intracranial stenosis.

For acute stroke, the evidence is very limited, consisting of only small case series. This evidence is insufficient to form conclusions about the effect of endovascular interventions in acute stroke, and as a result, endovascular interventions are considered investigational for the treatment of acute stroke.

For the treatment of intracranial aneurysms, there are no RCTs of stent-assisted coiling with coiling alone. Non-randomized comparative studies report occlusion rates that are similar to coiling alone, and recurrence rates that may be lower than for coiling alone. Results of clinical vetting indicated strong support for treatment of aneurysms that are not amenable to surgery or simple coiling. Comparative trials with and without stenting for this clinical situation are unlikely. As a result, use
of stent-assisted coiling for the treatment of intracranial aneurysms may be considered medically necessary when surgical treatment is not appropriate and standard endovascular techniques do not allow for complete isolation of the aneurysm.

**Practice Guidelines and Position Statements**

In 2005, The American Society of Interventional and Therapeutic Neuroradiology (ASITN), the Society of Interventional Radiology (SIR), and the American Society of Neuroradiology (ASNR) jointly published a position paper regarding angioplasty and stenting for cerebral atherosclerosis. This position statement reviewed a number of case series and also the SSYLVIA and Wingspan multi-institutional studies. The following position statement was offered, although the underlying rationale and process for development for the position statement was not provided:

“The ASITN, SIR, and ASNR concur that sufficient evidence now exists to recommend that intracranial angioplasty with or without stenting should be offered to symptomatic patients with intracranial stenoses who have failed medical therapy. Endovascular interventions are intensive services provided to patients who are at very high risk for strokes and typically have multiple comorbidities. Similar to revascularization for extracranial carotid artery stenosis, patient benefit from revascularization for symptomatic intracranial arterial stenosis is critically dependent on a low per procedural stroke and death rate and should thus be performed by experienced neurointerventionists. We recommend reimbursement by third party insurers so that these patients may have access to such interventions. Continued attempts to improve the benefits of endovascular therapy are warranted.”

In April 2009, the American Heart Association (AHA), along with several other organizations, published an AHA scientific statement on indications for intracranial endovascular neurointerventional procedures. The recommendation related to endovascular treatment of symptomatic intracranial stenoses was noted as Class IIb, Level of Evidence C (usefulness/effectiveness is unknown/unclear). The level of evidence was the same for use of angioplasty and stenting in the treatment of acute ischemic stroke.

**Medicare National Coverage Determinations**

A Medicare National Coverage Determination (NCD) on intracranial angioplasty and stenting was released by the Centers for Medicare and Medicaid Services (CMS) in January 2007. This decision was based on a review of available studies at that time, which consisted of several uncontrolled case series. The CMS review indicated that this evidence was promising and that, while further well-designed RCTs were needed to confirm whether outcomes were improved, coverage should be allowed. The NCD contained the following coverage determinations:

1. "Medicare coverage for angioplasty and or stenting for symptomatic patients with greater than 70 percent intracranial arterial stenosis; and
2. Medicare coverage for intracranial angioplasty and stenting for other patients within the context of Category B investigational device exemption (IDE) trials under coverage with evidence development (CED) within a registry."
VI. Important Reminder

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA’s determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

VII. References


