MEDICAL POLICY

SUBJECT: ENDOVASCULAR TREATMENT OF ACUTE ISCHEMIC STROKE (e.g., MECHANICAL EMBOLECTOMY)

POLICY NUMBER: 7.01.82
CATEGORY: Technology Assessment

EFFECTIVE DATE: 12/18/08
REVISED DATE: 11/19/09, 11/18/10, 10/20/11, 09/20/12, 10/17/13, 09/18/14, 09/17/15, 08/18/16
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• If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.
• If a commercial product, including an Essential Plan product, covers a specific service, medical policy criteria apply to the benefit.
• If a Medicare product covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.

POLICY STATEMENT:

Based upon our criteria and review of the peer-reviewed literature;

I. Endovascular treatment of acute ischemic stroke (e.g., mechanical embolectomy, microcatheter/microwire clot maceration, percutaneous angioplasty [PTA], or stent deployment) may be considered a medically appropriate treatment option only for selected patients with angiographically documented occlusion and profound neurological deficits who have failed or are not candidates for thrombolysis and only when performed in an institution with a multidisciplinary stroke team (See policy guideline II).

II. Endovascular treatment of acute ischemic stroke for all other patients is considered investigational.

Refer to Corporate Medical Policy # 7.01.60 regarding Carotid Artery Stents.
Refer to Corporate Medical Policy # 7.01.70 regarding Angioplasty of Intracranial Atherosclerotic Stenoses with or without Stenting
Refer to Corporate Medical Policy #11.01.03 regarding Experimental and Investigational Services.
Refer to Corporate Medical Policy #11.01.10 regarding Clinical Trials.

POLICY GUIDELINES:

I. The Federal Employee Health Benefit Program (FEHBP/FEP) requires that procedures, devices or laboratory tests approved by the U.S. Food and Drug Administration (FDA) may not be considered investigational and thus these procedures, devices or laboratory tests may be assessed only on the basis of their medical necessity.

II. Covered procedures must be performed at a facility:
   A. Recognized by the New York State Department of Health or the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) as a designated stroke center, and
   B. Have 24 hour/day 7 days/week availability of a multidisciplinary stroke team that includes a neuroendovascular interventionalist.

DESCRIPTION:

Approximately 750,000 strokes occur in the US annually. Some strokes are caused by emboli and frequently present as acute neurologic emergencies. Intravenous tissue plasminogen activator (tPA) given within 3 hours of symptom onset is currently the only FDA approved treatment for acute ischemic stroke. However, many patients fail or are not candidates for tPA due to time of presentation for treatment or contraindications to thrombolytic therapy. Several endovascular treatments, including mechanical clot disruption via microcatheter/microwire clot maceration, percutaneous angioplasty (PTA), stent deployment, or use of a snare device have been proposed as treatments for this population. The most studied of these procedures is mechanical embolectomy using the Merci Retriever.

RATIONALE:

The Merci Retriever was cleared by the FDA in August 2004 through the 510(k) process. The FDA clearance indicated that the MERCI Clinical Study established that no new issues of safety and effectiveness exist when the Merci Retriever is used for thrombus removal versus foreign body removal from the neurovasculature. A modified Merci Retriever, also manufactured by Concentric Medical, Inc., received 510(k) clearance from the FDA in May 2006. The clearance notes
Support for the use of the Merci Retrieval System comes from the MERCI (Mechanical Embolus Removal in Cerebral Ischemia) trial. This was a prospective, nonrandomized, multicenter trial for patients with symptoms of acute stroke for less than 8 hours who were not candidates for thrombolytic therapy, either because of contraindications (approximately 25%) or because symptoms were present for more than 3 hours. Of the 151 patients enrolled in the trial, 141 had the device deployed. Recanalization was achieved in 46% (69/151) of patients on intention to treat analysis, and in 48% (68/141) of patients in whom the device was deployed. Clinically significant procedural complications occurred in 10 of 141 (7.1%) patients and symptomatic intracranial hemorrhages were observed in 11 (7.8%). Good neurological outcomes were more frequent at 90 days in those with successful recanalization compared to those with unsuccessful recanalization (46% vs. 10%, p less than 0.0001) and mortality was less (32% vs. 54%, p equal to 0.01). This rate is significantly higher than that expected using a historical control (PROACT II trial) of 18% (P less than 0.0001). Of note, in the study up to 6 passes could be made to remove the clot, and at least 2 devices were used in each patient in the MERCI trial. Overall mortality in the MERCI trial was 44%. The study fails to confirm that the flow restoration is due to thrombus removal (embolectomy), as opposed to clot disruption with proximal recanalization and distal embolization.

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 (Broderick, et al.). 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 and colleagues 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.

The primary results of the MR RESCUE trial (Randomized Trial of Neuroradiology Selection for mechanical embolectomy versus standard care for acute ischemic stroke) was presented at the February 2013 International Stroke Conference by CS Kidwell. In this phase 2b, multicenter, controlled, blinded outcome study, the researchers randomly assigned 118 eligible patients within 8 hours of the onset of large-vessel, anterior circulation strokes to undergo...
mechanical embolectomy with the Merci Retriever or the Penumbra System or to receive standard care. All patients underwent multimodal CT or MRI before treatment, and randomization was stratified by whether they had a favorable penumbral pattern or a nonpenumbral pattern (a large infarct core with a small or no penumbra). Patients who had received intravenous thrombolysis were allowed into the trial if vessel imaging after treatment showed a persistent target occlusion. Clinical outcomes were assessed by using the modified Rankin Scale (mRS). The mean age of patients was 65.5 years, mean time to enrollment was 5.5 hours, and 58% of patients had a favorable penumbral pattern.

Revascularization in the embolectomy group was achieved in 67% of patients. At 90 days, mortality was 21% in the overall group, the rate of symptomatic intracranial hemorrhage was 4%, and neither outcome differed between groups.

"For the primary hypothesis, there was no significant interaction between treatment assignment and penumbral pattern by shift analysis of the day 90 modified Rankin score. As such, MR RESCUE failed to demonstrate that penumbral imaging identifies patients who will differentially benefit from endovascular therapy for acute ischemic stroke."

The 2007 Guidelines for the early management of adults with ischemic stroke from the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups include the following Class II Recommendations:

I. Although the MERCI device is a reasonable intervention for extraction of intra-arterial thrombi in carefully selected patients, the panel also recognizes that the utility of the device in improving outcomes after stroke is unclear (Class IIb, Level of Evidence B). The panel also recommends that the device be studied in additional clinical trials that will define its role in the emergency management of stroke.

II. The usefulness of other mechanical endovascular treatments is not established (Class IIb, Level of Evidence C). These devices should be used in the setting of clinical trials.

Because intravenous (IV) recombinant tissue plasminogen activator (rtPA) does not always lead to a good outcome in a considerable proportion of patients, combined IV rtPA and rescue endovascular therapy (ET) have been performed in several recent studies. Other studies have evaluated mechanical endovascular treatments for patients who are not candidates for rtPA. Based on the acute nature of these neurologic emergencies most studies reported are relatively small, retrospective case series. Some have compared outcomes to matched historical controls.

A review by Lutsep (2008) compares recent trials using mechanical endovascular therapies to treat acute stroke. The Multi Mechanical Embolus Removal in Cerebral Ischemia trial showed that good revascularization success could be obtained using the Merci retrievers within 8 h of symptom onset. In patients with persistent vascular occlusions despite intravenous tissue plasminogen activator, mechanical embolectomy appeared to be safe.

In September 2007, the FDA granted 510(k) marketing clearance to the Penumbra System™. Penumbra System (Penumbra Inc., San Leandro, California, USA) first aspirates clot and then employs clot extraction if needed. A feasibility study and a single-arm trial were recently completed. In the feasibility study, the first 20 patients treated with the device had occlusions located in the MCA, internal carotid and basilar arteries. The primary occlusion was recanalized in 100% of cases. Intra-arterial tPA or urokinase was used to treat occlusions distal to the primary occlusion in 35% of (7/20) cases. Good outcomes (4-point improvement on the NIHSS) were observed in 42% of patients and 45% died. A single-arm study of 125 patients at 35 centers in Europe and the USA included patients aged between 18 and 79 years with an NIHSS score of 8 or more presenting within 8 hours of symptom onset. Patients refractory to intravenous tPA were eligible. Success criteria included a 48% or more revascularization rate and device related serious adverse event rate of 15% or less. R Tarr and colleagues (2009) assessed the post-market experience of the Penumbra System in a retrospective case review of 139 patients at seven international centers. After use of the Penumbra System, 84% of the treated vessels to TIMI 2 or 3. At discharge, 34% of patients had a NIHSS score of 0-1 or an improvement of at least 10 points. Eight procedural serious adverse events were reported in 139 patients; there were a total of 10 symptomatic intracerebral hemorrhage reported at 24 hours. To date, all-cause mortality is 23%. Of the 110 patients who have died or reached 90-day follow-up, 40% had a modified Rankin Scale score less than 2. Patients who were successfully revascularized by the Penumbra System had significantly better outcomes than those who were not.
A systematic review and meta-analysis by Stead, et al. (2008) of mechanical thrombectomy in the treatment of ischemic stroke and assessed factors for technical and clinical success and survival. The pooled cohort was compared with a historical cohort matched for sex, age, and National Institutes of Health Stroke Survey score. The search yielded 114 publications. Mean preprocedure National Institutes of Health Stroke Survey (NIHSS) score was 20.4. The middle cerebral artery (36%) and the posterior circulation (38%) were the most frequently occluded areas. The clot was accessible in 85% of the patients. Hemorrhage occurred in 22% of the patients. Of 81 patients with concurrent thrombolysis, 18.5% had hemorrhage compared with 27.3% of 66 patients without thrombolysis (P = .21). Of the 126 patients with accessible clots, 36% had a good modified Rankin score (less than or equal to 2) and 29% died; in patients with inaccessible clots, 24% had a good modified Rankin score and 38% died. Factors associated with clinical success were younger age (P = .001) and lower NIHSS score at admission to the hospital (P = .001). Compared with a matched cohort, patients who received mechanical intervention were 14.8 times more likely to have a good modified Rankin score (95% confidence interval, 4.4-50.0; p less than .001).

Qureshi, et al. (2007) prospectively evaluated the safety of aggressive mechanical disruption of thrombus following full-dose intravenous (IV) recombinant tissue plasminogen activator (rt-PA) to treat ischemic stroke in 24 patients with an initial National Institutes of Health stroke scale (NIHSS) score of greater than or equal to 10. Methods: Clinical evaluations were performed at presentation and 24 hours, 7 to 10 days, and 1 to 3 months (using modified Rankin scale) after treatment. These end points were compared to matched historical controls treated with IV rt-PA alone. Of the 24 patients, mechanical disruption was undertaken in 17 patients with persistent angiographic occlusion using microcatheter exploration (n = 3), angioplasty (n = 5), snare maneuvers (n = 7), and combination of both (n = 2). Partial or complete recanalization was observed in 10 of the 17 patients. Neurological improvement at 24 hours (greater than or equal to 4 point reduction in NIHSS score) was observed in 11 of 17 patients. Comparisons with matched controls suggest potential equivalence for symptomatic ICH (0% vs 12%), asymptomatic ICH (18% vs 15%), and early neurological improvement (65% vs 53%). The authors concluded that aggressive mechanical thrombus disruption in large artery occlusion in the setting of acute ischemic stroke is safe with acceptable rates of ICH and promotes angiographic recanalization.

Mokin et al. published a systematic review in 2012 that evaluated clinical outcomes from endovascular therapy compared to thrombolysis. The authors selected studies that used either thrombolysis or endovascular therapy for patients with acute ischemic stroke due to internal carotid artery occlusion. Included studies reported on functional outcomes past 30 days, mortality rates beyond 30 days, and rates of symptomatic intracerebral hemorrhage. A total of 28 studies were reviewed, including 385 patients treated with thrombolysis and 584 patients treated with endovascular therapy. There were no differences in mortality between the thrombolysis and endovascular groups (27.3% vs. 32.0%, p=0.12). A favorable clinical outcome, defined as a Rankin scale of less than 2 or a Barthel index of 90-100, was attained by a greater percentage of patients in the endovascular group compared to the thrombolysis group (33.6% vs. 24.9%, p=0.004). Symptomatic intracranial hemorrhage was also more common in the endovascular group compared to thrombolysis (11.1% vs. 4.9%, p=0.001).

Almekhlafi et al. published a systematic review of observational studies of endovascular treatment in 2012. The authors identified 16 eligible studies and classified them according the type of device used. There were 4 studies (n=357) that used the Merci device, 8 studies (n=455) that used the Penumbra system, and 4 studies (n=113) that used a retrievable stent. Mean procedural time was 120 minutes for the Merci device, compared to 65 and 55 minutes for the Penumbra and retrievable stents. The successful recanalization rate was 59.1% for the Merci group, 86.6% for the Penumbra system, and 92.9% for the retrievable stent group.

The Solitaire™ FR Revascularization Device (Covidien plc) received FDA 510(k) clearance in February 2012. It is intended to restore blood flow by removing thrombus from a large intracranial vessel in patients experiencing ischemic stroke within 8 hours of symptom onset. Patients who are ineligible for IV-t-PA or have failed IB t-PA therapy are candidates for treatment. The device is intended for use in the neurovasculature such as the internal carotid artery, middle cerebral artery, vertebral and basilar arteries. It is a nitinol self-expanding, fully retrievable stent based design that allows for clot retrieval when deployed in occluded target vessels after acute ischemic stroke. The FDA approval was based on results from the SWIFT trial, an active-comparator, non-inferiority study (n=144) where patients with
Acute ischemic stroke (NIHSS greater than 8 and less than 30) were randomized to receive treatment with either the Merci retriever or the Solitaire device. The primary and secondary efficacy endpoints included successful recanalization with no symptomatic intracerebral hemorrhage (ICH), and neurological assessments at 90-day (+ 15 days) follow-up. Analysis of the primary efficacy endpoint showed statistically significant evidence that Solitaire FR was non inferior to the Merci device in the arterial recanalization of the occluded target vessels without any presence of symptomatic intracranial hemorrhage. The Solitaire FR group success rate was 60.7% (34/56) compared to 24.1% (13/54) for the merci group. The criterion for non-inferiority was met with an associated p less than 0.0001. At 30 days, the good neurological outcome (GNO) for the Solitaire FR was 50.9% compared to 33.3% for Merci; 90- day GNO was 58.2% and 33.3 % respectively. Mortality rates for subjects randomized to the Merci group was 38.2% compared to 17.2 for the Solitaire FR group. The rate of symptomatic intracranial hemorrhage was 10.9% in the Merci group and 1.7% in the Solitaire FR group; and the rate of all intracranial hemorrhage was 38.2% and 17.2% respectively. The nominal overall device and/or procedure-related serious adverse event rate for the Solitaire was observed to be lower also (22.4% vs 40.0%).

The FDA issued 510(k) marketing approval for the Trevo® Pro Retrieval System by device maker Stryker in August 2012. TREVO 2 trial results presented in May at the 2012 European Stroke Conference. The trial randomized 178 individuals for treatment with either the Trevo Pro or the Merci Retriever following acute ischemic stroke. Results demonstrated significantly greater revascularization rates for the Trevo Pro compared to the Merci (86.4% vs. 60%). Functional outcomes were also improved with Trevo Pro, with 40% of patients having a modified Rankin score of two or less in the Trevo Pro arm of the study, compared to 21.8% in the Merci arm. Other measures that favored the Trevo Pro included National Institutes of Health Stroke Scale scores and hospital length of stay.

Based on review of published literature, endovascular treatment of angiographically documented intracranial arterial occlusions has demonstrated sufficient safety and efficacy to consider the procedures appropriate for a select group of acute ischemic stroke patients with profound neurological deficits who have failed or are not candidates for thrombolysis. Patients with vessels revascularized by devices have consistently exhibited better outcomes than those without revascularization. When performed in an institution with a multidisciplinary stroke team, recanalization rates have approached 75% and the greater than 50% favorable outcomes achieved are clearly different from the natural history of the disease in this narrowly defined subgroup.

**CODES:**

**Number** | **Description**
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Eligibility for reimbursement is based upon the benefits set forth in the member’s subscriber contract.

CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

**CPT:**

There are no specific CPT codes for these procedures. Components of the procedure would include the following:

36215-36218 | Selective catheter placement, arterial system, thoracic or brachiocephalic family (code range)

36221 | Non-selective catheter placement, thoracic aorta, with angiography of the external carotid, vertebral, and/or intracranial vessels, unilateral or bilateral, and all associated radiological supervision and interpretation, includes angiography of the cervicocerebral arch, when performed

36223 | Selective catheter placement, common carotid or innominate artery, unilateral, any approach, with angiography of the ipsilateral intracranial carotid circulation and all associated radiological supervision and interpretation, includes angiography of the cervicocerebral arch, when performed
Selective catheter placement, internal carotid artery, unilateral, with angiography of the ipsilateral intracranial carotid circulation and all associated radiological supervision and interpretation, includes angiography of the external carotid and cervicocerebral arch, when performed

Selective catheter placement, each intracranial branch of the internal carotid or vertebral arteries, unilateral, with angiography of the selective vessel circulation and all associated radiological supervision and interpretation (e.g., middle cerebral artery, posterior inferior cerebellar artery)

Primary percutaneous transluminal mechanical thrombectomy, noncoronary, arterial or arterial bypass graft, including fluoroscopic guidance and intraprocedural pharmacological thrombolytic injection(s); initial vessel second and all subsequent vessels(s) within the same vascular family

Percutaneous arterial transluminal mechanical thrombectomy and/or infusion for thrombolysis, intracranial, any method, including diagnostic angiography, fluoroscopic guidance, catheter placement, and intraprocedural pharmacological thrombolytic injection(s)

HCPCS: No codes

ICD9: 433.20-433.21 Occlusion and stenosis of vertebral artery with or without mention of cerebral infarction (code range)
434.00-434.91 Occlusion of cerebral arteries (code range)
435.0-437.9 Transient cerebral ischemia, acute, but ill-defined, cerebrovascular disease, and other and ill-defined cerebrovascular disease (code range)

ICD10: G45.0-G46.8 Vascular syndromes of brain (code range)
163.011-163.119 Cerebral infarction due to thrombus/embolism of vertebral artery (code range)
163.211-163.219 Cerebral infarction due to unspecified occlusion or stenosis vertebral artery (code range)
163.30-163.49 Cerebral infarction due to thrombosis/embolism of cerebral artery (code range)
163.50-163.9 Cerebral infarction due to unspecified occlusion or stenosis of cerebral artery (code range)
165.01-165.09 Occlusion and stenosis of vertebral artery (code range)
166.01-166.9 Occlusion and stenosis of cerebral artery (code range)
167.1 Cerebral aneurysm
167.2 Cerebral atherosclerosis
167.4-168.8 Cerebrovascular diseases (code range)

REFERENCES:

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* key article

KEY WORDS:
Angioplasty, Intracranial Circulation, Percutaneous Transluminal Angioplasty, Merci Retriever, Mechanical Embolectomy, Penumbra, Solitaire®, Trevo®.

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**CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS**

Based on our review, mechanical retrieval of clots following an ischemic stroke is not addressed in National or Regional Medicare coverage determinations or policies.

There is currently a National Coverage Determination (NCD) for percutaneous transluminal angioplasty (PTA) and a CMS decision memo related to percutaneous transluminal angioplasty (PTA) with intracranial stent placement. Please
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