June 7, 2012

John Whitney, MD
Office of Medical Policy, Technology, Assessment and Credentialing
WellPoint, Inc.
233 South Wacker Dr., Ste 3900
Chicago, IL 60606
(518) 367-5422
John.whitney@wellpoint.com

Subject: Anthem Policy Mechanical Embolectomy for Treatment of Acute Stroke

Dear Dr. Whitney,

On behalf of the American Association of Neurological Surgeons (AANS), the American Society of Neuroradiology, the Congress of Neurological Surgeons (CNS), the Society of NeuroInterventional Surgery, and the Society of Vascular and Interventional Neurologists, we would like to thank WellPoint and Anthem for the opportunity to comment on the Anthem medical policy SURG.00098 (Effective Date: 4/11/2012) on the subject of "Mechanical Embolectomy for Treatment of Acute Stroke." We appreciate the efforts of your team in developing a review of the published literature reporting on the use of mechanical embolectomy in the treatment of acute stroke, but **disagree** that such intervention is investigational and not medically necessary.

We believe that for acute ischemic stroke, mechanical embolectomy is a medically necessary option in appropriate in patients with medical indications as determined by their treating physician. Our assessment of the literature would indicate that mechanical embolectomy is an appropriate option in patients:

- Presenting outside the 3-4.5 hour window for intravenous tissue plasminogen activator (IV tPA).
- Patients in whom IV tPA was not effective at recanalizing the vessel.
- Patients who have calcified clots or calcified deposits.
- Patients who have large vessel occlusion of their internal carotid artery (ICA) or basilar artery (BA)

We are concerned that the medical policy compounds the omission of the grave natural history and the state of the literature. Specifically, the policy states:

- "Overall, controversy exists regarding the clinical implications of the MERCI study (Becker, 2005; Davis, 2006; Saver, 2006; Weschler, 2006). A number of commentators feel that recanalization rates represent an intermediate outcome, and that data on clinical outcomes is needed. Additionally comparison to historical controls is not adequate to validate the safety and effectiveness of mechanical embolectomy; randomized, controlled trials are needed."

The devices utilized for mechanical embolectomy have been approved by the Food and Drug Administration (FDA). The study designs in our field reflect the internal control offered by stroke pathophysiology. In the absence of meaningful intervention, pre-procedural National Institutes of Health Stroke Scale (NIHSS) offers a preview of long-term functional status were the stroke to proceed to completion. Moreover, once the seminal connection between technical success and clinical outcomes was proven, device trials began to emphasize the technical success and efficiency of flow restoration for occlusions at various levels of the cerebrovasculature. We disagree with the implication that the efficiency of neurovascular thrombectomy in practice matches established efficacy in the literature, which is a non-trivial policy point.

In addition, IV tPA and neurovascular thrombectomy do not represent mutually exclusive therapies. Thrombolytic reperfusion therapy (IV rTPA is viable in less than five percent of patients with acute stroke (AHRQ Draft Technical Brief on Neurothrombectomy Devices for Treatment of Acute Ischemic Stroke, 2010) and the natural history of stroke represents a more reasonable baseline for the assessment of neurothrombectomy devices. It is clear that long-term dependency or mortality awaited these patients who did not respond to IV tPA in the absence of meaningful intervention. The stark and costly reality of moribund dependence is the true alternative to neurothrombectomy devices; these gravely stricken patients are the population of interest. The difficulty in comparing studies for devices is that most include patients that have presented between 0 - 8 hours, in comparison to studies looking at intraarterial (IA) tPA or combined IV and IA tPA which only included patients within a 3 or 6 hour window, reducing the average number of patients that have a benefit.

Many studies including the Interventional Management of Stroke (IMS II) Trial determined that recanalization of cranial vessels is important for treatment of stroke:

- The faster a vessel is opened the better the patient outcome.
- tPA cannot always be used or is known to not be effective in some instances
- In patients with calcified plaques or very organized clot
- Clot obstructing large vessels like the ICA
- People with contraindications to tPA

In many instances, if IV and IA tPA fail to re-canalize a vessel, then the patient typically is treated with mechanical embolectomy within an 8 hour window. IA and IV tPA studies continue to presume the improved outcome is due to recanalization, and one would assume that patients who do poorly either had a hemorrhage or failed to have recanalization. Unfortunately, there has never been a study that looks at the patients treated with IA or IV therapy that failed and then randomized those patients to a mechanical device. But based on the best available evidence currently, it would seem that improved outcomes are related to recanalization within the 8 hour window.

Conclusion

We appreciate the opportunity to review and comment on the Anthem medical policy SURG.00098 (Effective Date: 4/11/2012) on the subject of “Mechanical Embolectomy for Treatment of Acute Stroke”. Thank you for considering our comments. We recognize that mechanical embolectomy is a costly technology and is not appropriate for all patients with acute stroke. However, we believe that for acute

ischemic stroke, mechanical embolectomy may be a beneficial and necessary option for many patients and should not be considered "investigational and not medically necessary". After review of the current literature, the AANS and CNS believe mechanical embolectomy remains an important treatment alternative for clinically appropriate cases, as chosen by treating physicians.

Again, thank you for this opportunity to comment and we hope you will reconsider your medical policy regarding mechanical embolectomy in acute stroke. If you have any questions, please feel free to contact Joseph Cheng, MD (joseph.cheng@vanderbilt.edu), Committee for Payor and Policy Responses, or Catherine Hill, Senior Manager, Regulatory Affair AANS/CNS (chill@neurosurgery.org).

Sincerely,

Mitchel S. Berger, MD, President
American Association of Neurological Surgeons

Joshua Hirsh, MD, President
Society of NeuroInterventional Surgery

Christopher E. Wolfla, MD, President
Congress of Neurological Surgeons

Dileep R. Yavagal, MD, President
Society of Vascular and Interventional Neurologists

Pamela W. Shaefer, MD, President
American Society of Neuroradiology

References

1. Mocco J, Hanel RA, Sharma J, et al. Use of a vascular reconstruction device to salvage acute ischemic occlusions refractory to traditional endovascular recanalization methods. J Neurosurg 2010;112:557-62.
2. Levy EI, Siddiqui AH, Crumlish A, et al. First Food and Drug Administration-approved prospective trial of primary intracranial stenting for acute stroke: SARIS (stent-assisted recanalization in acute ischemic stroke). Stroke 2009;40:3552-6.
3. Broderick JP. William M. Feinberg Lecture: stroke therapy in the year 2025: burden, breakthroughs, and barriers to progress. Stroke 2004;35:205-211.

4. Wolpert SM, Bruckmann H, Greenlee R, Wechsler L, Pessin MS, del Zoppo GJ. Neuroradiologic evaluation of patients with acute stroke treated with recombinant tissue plasminogen activator. The rt-PA Acute Stroke Study Group. AJNR Am J Neuroradiol 1993;14:3-13.
5. Smith WS, Tsao JW, Billings ME, et al. Prognostic significance of angiographically confirmed large vessel intracranial occlusion in patients presenting with acute brain ischemia. Neurocrit Care 2006;4:14-7.
6. Smith WS, Lev MH, English JD, et al. Significance of large vessel intracranial occlusion causing acute ischemic stroke and TIA. Stroke 2009;40:3834-40.
7. Zeumer H, Freitag HJ, Grzyska U, Neunzig HP. Local intraarterial fibrinolysis in acute vertebrobasilar occlusion. Technical developments and recent results. Neuroradiology 1989;31:336-340.
8. Archer CR, Horenstein S. Basilar artery occlusion: clinical and radiological correlation. Stroke 1977;8:383-390.
9. Hacke W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med 2008;359:1317-29.
10. del Zoppo GJ, Saver JL, Jauch EC, Adams HP, Jr. Expansion of the time window for treatment of acute ischemic stroke with intravenous tissue plasminogen activator. A Science Advisory From the American Heart Association/American Stroke Association (doi 10.1161/STROKEAHA.109.192535). Stroke 2009;epub May 28.
11. Fink JN, Kumar S, Horkan C, et al. The stroke patient who woke up: clinical and radiological features, including diffusion and perfusion MRI. Stroke 2002;33:988-993.
12. Serena J, Davalos A, Segura T, Mostacero E, Castillo J. Stroke on awakening: looking for a more rational management. Cerebrovasc Dis 2003;16:128-133.
13. Barreto AD, Martin-Schild S, Hallevi H, et al. Thrombolytic therapy for patients who wake-up with stroke. Stroke 2009;40:827-832.
14. Natarajan SK, Snyder KV, Siddiqui AH, Ionita CC, Hopkins LN, Levy EI. Safety and effectiveness of endovascular therapy after 8 hours of acute ischemic stroke onset and wake-up strokes. Stroke 2009;40:3269-74.
15. Patil CG, Long EF, Lansberg MG. Cost-effectiveness analysis of mechanical thrombectomy in acute ischemic stroke. J Neurosurg 2009;110:508-13.
16. Haley EC, Jr., Levy DE, Brott TG, et al. Urgent therapy for stroke. Part II. Pilot study of tissue plasminogen activator administered 91-180 minutes from onset. Stroke 1992;23:641-5.
17. Brott TG, Haley EC, Jr., Levy DE, et al. Urgent therapy for stroke. Part I. Pilot study of tissue plasminogen activator administered within 90 minutes. Stroke 1992;23:632-40.
18. Tissue plasminogen activator for acute ischemic stroke. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. N Engl J Med 1995;333:1581-7.
19. Qureshi AI, Siddiqui AM, Kim SH, et al. Reocclusion of recanalized arteries during intra-arterial thrombolysis for acute ischemic stroke. AJNR Am J Neuroradiol 2004;25:322-328.
20. Rha JH, Saver JL. The impact of recanalization on ischemic stroke outcome: a meta-analysis. Stroke 2007;38:967-973.
21. Ginsberg MD. Current status of neuroprotection for cerebral ischemia: synoptic overview. Stroke 2009;40:S111-4.
22. Albers GW, Thijs VN, Wechsler L, Kemp S, Schlaug G, Skalabrin E, Bammer R, Kakuda W, Lansberg MG, Shuaib A, Coplin W, Hamilton S, Moseley M, Marks MP. Magnetic resonance

imaging profiles predict clinical response to early reperfusion: The diffusion and perfusion imaging evaluation for understanding stroke evolution (defuse) study. Ann Neurol. 2006;60:508-517

23. Davis SM, Donnan GA, Parsons MW, Levi C, Butcher KS, Peeters A, Barber PA, Bladin C, De Silva DA, Byrnes G, Chalk JB, Fink JN, Kimber TE, Schultz D, Hand PJ, Frayne J, Hankey G, Muir K, Gerraty R, Tress BM, Desmond PM. Effects of alteplase beyond 3 h after stroke in the echoplanar imaging thrombolytic evaluation trial (epithet): A placebo-controlled randomised trial. Lancet Neurol. 2008;7:299-309
24. Hacke W, Albers G, Al-Rawi Y, Bogousslavsky J, Davalos A, Eliasziw M, Fischer M, Furlan A, Kaste M, Lees KR, Soehngen M, Warach S. The desmoteplase in acute ischemic stroke trial (dias): A phase ii mri-based 9-hour window acute stroke thrombolysis trial with intravenous desmoteplase. Stroke. 2005;36:66-73
25. Furlan AJ, Eyding D, Albers GW, Al-Rawi Y, Lees KR, Rowley HA, Sachara C, Soehngen M, Warach S, Hacke W. Dose escalation of desmoteplase for acute ischemic stroke (dedas): Evidence of safety and efficacy 3 to 9 hours after stroke onset. Stroke. 2006;37:1227-1231
26. Hacke W, Furlan AJ, Al-Rawi Y, Davalos A, Fiebach JB, Gruber F, Kaste M, Lipka LJ, Pedraza S, Ringleb PA, Rowley HA, Schneider D, Schwamm LH, Leal JS, Sohngen M, Teal PA, Wilhelm-Ogunbiyi K, Wintermark M, Warach S. Intravenous desmoteplase in patients with acute ischaemic stroke selected by mri perfusion-diffusion weighted imaging or perfusion ct (dias-2): A prospective, randomised, double-blind, placebo-controlled study. Lancet Neurol. 2009;8:141-150