AMERICAN ASSOCIATION OF
NEUROLOGICAL SURGEONS
KATHLEEN T. CRAIG, *Executive Director*
5550 Meadowbrook Drive
Rolling Meadows, IL 60008
Phone: 888-566-AANS
Fax: 847-378-0600
info@aans.org

President
CHRISTOPHER I. SHAFFREY, MD
Durham, North Carolina

CONGRESS OF
NEUROLOGICAL SURGEONS
REGINA SHUPAK, *CEO*
10 North Martingale Road, Suite 190
Schaumburg, IL 60173
Phone: 877-517-1CNS
FAX: 847-240-0804
info@cns.org

President
STEVEN N KALKANIS, MD
Detroit, Michigan

February 8, 2020

Debra L. Patterson, MD, Vice President, Clinical Affairs
and Chief Medical Officer
Novitas Solutions, Inc.
ATTN: Medical Policy Unit
2020 Technology Parkway, Suite 100
Mechanicsburg, PA 17050
Submitted electronically via LCDComments@novitas-solutions.com

SUBJECT: Support for Coverage for Magnetic Resonance Image Guided High Intensity Focused Ultrasound (MRgFUS) for Essential Tremor (ET) DL 38495

Dear Dr. Patterson:

On behalf of the American Association of Neurological Surgeons (AANS), the Congress of Neurological Surgeons (CNS) and the American Society for Stereotactic and Functional Neurosurgery (ASSFN), we appreciate the opportunity to express our support for the recent draft local coverage determination (LCD) DL38495 posted by Novitas for Magnetic Resonance Image Guided High Intensity Focused Ultrasound (MRgFUS) for Essential Tremor (ET).

We are pleased that Novitas proposes to cover MRgFUS for ET. As you may recall from our previous conference call and letters, we stongly support coverage for this important procedure. We appreciate your time and consideration over the last year and the specific mention of the ASSFN's thorough review of published literature on MRgFUS for ET and guidance on the optimal expertise for the treating neurosurgeon.

Below are some specific comments on the indications and limitations. With the exception of the items mentioned, we feel the policy is reasonable.

Indications

1) Medication refractory ET (defined as refractory to at least two trials of medical therapy, including at least one first-line agent)

   AANS/CNS/ASSFN Response: Not all patients treated since FDA approval have taken, want to take, or can take two medications as a prelude to treatment. While most patients will have tried propranolol or other beta-blocker, which has either failed to alleviate their symptoms adequately or required such a high dose that side effects became limiting, and many have also tried primidone, and a few have tried topiramate or gabapentin or a benzodiazepine, patients should not be forced to go through a trial of two medications. Many patients, such as those with bradycardia or asthma, are not candidates for a beta blocker. If they fail primidone, the likelihood of adequate tremor control with one of the other medications is unlikely. Certain industries, e.g.,

airlines and heavy manufacturing, prohibit the use of many of these medications by their employees.

While for a pivotal study, it was reasonable to limit the treatment to a patient who was refractory to many medications, it is now reasonable to allow treatment of patients refractory to a standard medication, given the confidence we gained through the trial of the safety profile and efficacy of the procedure. We recommend that Novitas change the language for this criterion to: "A confirmed diagnosis of Essential Tremor refractory to medication such as propranolol, primidone, topiramate, gabapentin or benzodiazepines."

2) Moderate to severe postural or intention tremor of the dominant hand (defined by a score of ≥2 on the Clinical Rating Scale for Tremor (CRST)

AANS/CNS/ASSFN Response: We note that tremor can be more disabling in the non-dominant hand. Also, neurosurgeons do not routinely use the CRST and believe that other scales may be more relevant for some patients. We recommend that Novitas change the language for this criterion to: "Moderate to severe postural or intentional tremor of the hand to be treated."

3) Disabling ET (defined by a score of ≥2 on any of the eight items in the disability subsection of the CRST)

AANS/CNS/AASFN Response: As noted above, many clinicians do not routinely use the CRST as a clinical assessment. This tool was used in the clinical trials as an attempt to quantify the outcomes. We recommend that Novitas change the language for this criterion to: "tremor that is sufficiently disabling with home or work activities."

4) Not a surgical candidate for DBS (e.g., advanced age, anticoagulant therapy, or surgical comorbidities)

AANS/CNS/ASSFN Response: We strongly disagree with this requirement. We believe that some patients and surgeons may have valid reasons for choosing MRgFUS over DBS. For example, ET patients may prefer MRgFUS over DBS due to professional reasons (e.g., MRI technologists or arc welders; or due to risks of implanted hardware near high strength magnetic fields). In addition, individual patients with ET may prefer not to have implanted hardware with its associated maintenance and/or complication risks, or due to lack of proximity to a center capable of programming a DBS. We recommend that this criterion be deleted. It was not a component of the inclusion/exclusion criteria from any of the clinical trials and is not part of the FDA label. MRgFUS is an alternative option to DBS with its own set of merits/limitations based on class 1 evidence.

<u>Limitations (not covered)</u>:

1) A neurodegenerative condition (other than ET)

AANS/CNS/ASSFN Response: This seems reasonable, but the degree to which neurodegenerative condition is a contraindication should be a case-by-case decision between the surgeon and patient. We suggest this condition be retitled as "An advanced neurodegenerative condition."

2) Unstable cardiac disease

AANS/CNS/ASSFN Response: This seems reasonable, but the degree to which cardiac disease is a contraindication should be a case-by-case decision between the surgeon and patient.

3) Severe depression (defined by a score ≥20 on Patient Health Questionnaire 9 (PHQ-9)

AANS/CNS/ASSFN Response: This should be reviewed on a case-by-case basis between the surgeon and patient. There is no evidence that depression leads to worsened outcomes or higher risk from this procedure. Note that patients with depression and on stable antidepressant medications for at least three months were able to enroll in the study.

4) Cognitive impairment (defined by a score of <24 on the Mini-Mental State Examination)

AANS/CNS/ASSFN Response: This should be reviewed on a case-by-case basis between the surgeon and patient.

5) Previous brain procedure (transcranial magnetic stimulation, DBS, stereotactic lesioning, or electroconvulsive therapy)

AANS/CNS/ASSFN Response: This seems reasonable for patients with an existing DBS system or contralateral lesion. However, MRgFUS could be considered in a patient that has had the DBS implants removed, allowing for visualization of the thalamus on MRI and ablation with focused ultrasound. Furthermore, for patients who have previously undergone Transcranial Magnetic Stimulation or electroconvulsive therapy, the decision regarding MRgFUS should be reviewed on a case-by-case basis between the surgeon and patient. We suggest removal of "TMS" and "Electroconvulsive therapy" as there is no data to suggest that these procedures should preclude MRgFUS ablation of the thalamus. These two items were included in the trial protocol specifically as metrics to exclude patients with severe, medically refractory depression from the pivotal study. Note that patients with depression and on stable antidepressant medications for at least three months were able to enroll in the study.

6) A skull density ratio (the ratio of cortical to cancellous bone) <0.45

AANS/CNS/ASSFN Response: We advise caution on the application of this criterion. SDR is an indicator of the acoustic transparency of the skull to the ultrasound beam. For the FDA trial and the subsequent label, this criterion was <0.45 +/- 0.05. The need for a range rather than a set threshold is based in part on the fact that the actual SDR number can vary based on the acquisition parameters of the CT scan. Parameters such as slice thickness, matrix, photon energy, reconstruction methods, kernel, collimation and field of view can cause variation in the SDR by 0.01 - 0.1. Also, while in general, the lower the SDR, the higher the energies needed to reach ablative temperature, the prediction is not perfect, and some SDRs less than 0.45 are hard to treat, and some are easier to treat. Indeed, treatment has frequently proven to be beneficial for some patients with skull density ratio (SDR) of less than 0.45. Referring to the cohort of 189 ET patients treated with MRgFUS as part of clinical trials, 42 patients (22%) had SDR between 0.40 – 0.45. An improvement of CRST of at least 50% at one year compared to baseline was achieved in over 70% of patients within this range of SDRs. Therefore, at a minimum, we recommend that this exclusion condition read: "a skull density ratio (the ratio of cortical to cancellous bone) of 0.45 ± 0.05 or less, as calculated from the screening CT."

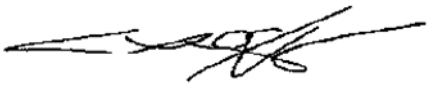
However, consideration should be given to not having any criterion, or lowering the criterion further. In Japan and Korea, for example, the average SDR for patients that have been treated is

lower than in patients treated in the United States, Canada and Europe, due to differences in skull shape and thickness. Even applying a criterion of SDR < 0.45 ± 0.05 would exclude many Asian patients and does not take into consideration racial differences in average SDR. Also, there is preliminary evidence that the use of DTI tractography, improved anatomic imaging and/or fMRI will facilitate the use of overall lower treatment energies in the future to achieve similar functional outcomes, allowing a wider "treatable" range of SDR. We thus request that consideration be given to eliminating the criterion for treatment eligibility based on SDR.

The AANS, the CNS and the ASSFN appreciate the opportunity to support the proposed LCD. We thank you for your attention to the ASSFN recommendations and for allowing Medicare beneficiaries and their neurosurgeons in your jurisdiction access to MRgFUS when clinically appropriate.

Thank you for considering our comments.

Sincerely,



Christopher I. Shaffrey, MD, President
American Association of Neurological Surgeons

Steven N. Kalkanis, MD, President
Congress of Neurological Surgeons

Robert Gross, MD, President
American Society for Stereotactic and Functional Neurosurgery

Staff Contact:
Catherine Jeakle Hill
Senior Manager, Regulatory Affairs
AANS/CNS Washington Office
25 Massachusetts Ave., NW
Washington, DC 20005
Phone: 202-446-2026
E-mail: chill@neurosurgery.org