DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Healthcare
Research and Quality

5600 Fishers Lane
Rockville, MD 20857
www.ahrq.gov

FEB - 8 2016

Tamara Syrek Jensen, JD
Director, Coverage and Analysis Group
Center for Clinical Standards and Quality
Centers for Medicare and Medicaid Services
7500 Security Blvd.
Baltimore, MD 21244

Dear Ms. Jensen,

The Agency for Healthcare Research and Quality understands that the Centers for Medicare and Medicaid Services (CMS) is issuing a National Coverage Determination (NCD) that will cover percutaneous left atrial appendage closure (LAAC) for non-valvular atrial fibrillation (NVAF) through Coverage with Evidence Development (CED) under 1862(a)(1)(E) of the Social Security Act with the following conditions:

A. Left Atrial Appendage Closure devices are covered when the device has received Food and Drug Administration (FDA) Premarket Approval (PMA) for that device's FDA-approved indication and meet all of the conditions specified below:

- *The patient must have:*
  - *A CHADS2 score ≥ 2 (Congestive heart failure, Hypertension, Age >75, Diabetes, Stroke/transient ischemia attack/thromboembolism) or CHA2DS2-VASc score ≥ 3 (Congestive heart failure, Hypertension, Age ≥ 65, Diabetes, Stroke/transient ischemia attack/thromboembolism, Vascular disease, Sex category)*
  - *A formal shared decision making interaction with an independent non-interventional physician using an evidence-based decision tool on oral anticoagulation in patients with NVAF prior to LAAC. Additionally, the shared decision making interaction must be documented in the medical record.*
  - *A suitability for short-term warfarin but deemed unable to take long term oral anticoagulation following the conclusion of shared decision making, as LAAC is only covered as a second line therapy to oral anticoagulants. The patient (preoperatively and postoperatively) is under the care of a cohesive, multidisciplinary team (MDT) of medical professionals. The procedure must be furnished in a hospital with an established structural heart disease (SHD) and/or electrophysiology (EP) program.*
  - *The procedure must be performed by an interventional cardiologist(s), electrophysiologst(s) or cardiovascular surgeon(s) that meet the following criteria:*

- *Has received training prescribed by the manufacturer on the safe and effective use of the device prior to performing LAAC; and*
- *Has performed ≥ 25 interventional cardiac procedures that involve transeptal puncture through an intact septum; and*
- *Continues to perform ≥ 25 interventional cardiac procedures that involve transeptal puncture through an intact septum, of which at least 12 are LAAC, over a two year period.*

- *The patient is enrolled in, and the MDT and hospital must participate in a prospective, national, audited registry that: 1) consecutively enrolls LAAC patients and 2) tracks the following annual outcomes for each patient for a period of at least four years from the time of the LAAC:*
  - *Operator-specific complications*
  - *Device-specific complications including device thrombosis*
  - *Stroke, adjudicated, by type*
  - *Transient Ischemic Attack (TIA)*
  - *Systemic embolism*
  - *Death*
  - *Major bleeding, by site and severity*

The registry must be designed to permit identification and analysis of patient, practitioner and facility level factors that predict patient risk for these outcomes. The registry must collect all data necessary to conduct analyses adjusted for relevant confounders and have a written executable analysis plan in place to address the following questions:

- *How do the outcomes listed above compare to outcomes in the pivotal clinical trials in the short term (≤12 months) and in the long term (≥ 4 years)?*
- *What is the long term (≥ 4 year) durability of the device?*
- *What are the short term (≤12 months) and the long term (≥4 years) device-specific complications including device thromboses?*

To appropriately address some of these questions, Medicare claims or other outside data may be necessary.

Registries must be reviewed and approved by CMS. Potential registry sponsors must submit all registry documentation to CMS for approval including the written executable analysis plan and auditing plan. CMS will review the qualifications of candidate registries to ensure that the approved registry follows standard data collection practices and collects data necessary to evaluate the patient outcomes specified above. The registry's NCT number must be recorded on the claim.

All approved registries will be posted on the CED website located at https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/index.html. Consistent with section 1142 of the Act, the Agency for Healthcare Research and Quality (AHRQ) supports clinical research studies that CMS determines address the above-listed research questions and the a-m criteria listed in Section C of this decision.

B. LAAC is covered for NVAF patients not included in Section A of this decision when performed within an FDA-approved randomized controlled trial (RCT) if such trials meet the criteria established below:

As a fully-described written part of its protocol, the RCT must critically answer, in comparison to optimal medical therapy, the following questions:

- *As a primary endpoint, what is the true incidence of ischemic stroke and systemic embolism?*
- *As a secondary endpoint, what is cardiovascular mortality and all-cause mortality?*

FDA-approved RCTs must be reviewed and approved by CMS. Consistent with section 1142 of the Act, the Agency for Healthcare Research and Quality (AHRQ) supports clinical research studies that CMS determines address the above-listed research questions and the a-m criteria listed in Section C of this decision.

The principal investigator must submit the complete study protocol, identify the relevant CMS research question(s) that will be addressed and cite the location of the detailed analysis plan for those questions in the protocol, plus provide a statement addressing how the study satisfies each of the standards of scientific integrity a through m listed in section C of this decision, as well as the investigator's contact information, to the address below.

Director, Coverage and Analysis Group
Re: LAAC CED
Centers for Medicare & Medicaid Services (CMS)
7500 Security Blvd., Mail Stop S3-02-01
Baltimore, MD 21244-1850

All approved registries will be posted on the CED website located at https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/index.html.

C. All clinical studies, RCTs and registries submitted for review must adhere to the following standards of scientific integrity and relevance to the Medicare population.

a. The principal purpose of the study is to test whether the item or service meaningfully improves health outcomes of affected beneficiaries who are represented by the enrolled subjects.
b. The rationale for the study is well supported by available scientific and medical evidence.
c. The study results are not anticipated to unjustifiably duplicate existing knowledge.
d. The study design is methodologically appropriate and the anticipated number of enrolled subjects is sufficient to answer the research question(s) being asked in the National Coverage Determination.
e. The study is sponsored by an organization or individual capable of completing it successfully.
f. The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found in the Code of Federal Regulations (CFR) at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration (FDA), it is also in compliance with 21 CFR Parts 50 and 56. In addition, to further enhance the protection of human subjects in studies conducted under CED, the study must provide and obtain meaningful informed consent from patients regarding the risks associated with the study items and/or services, and the use and eventual disposition of the collected data.

g. All aspects of the study are conducted according to appropriate standards of scientific integrity.
h. The study has a written protocol that clearly demonstrates adherence to the standards listed here as Medicare requirements.
i. The study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Such studies may meet this requirement only if the disease or condition being studied is life threatening as defined in 21 CFR §312.81(a) and the patient has no other viable treatment options.
j. The clinical research studies and registries are registered on the www.ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject. Registries are also registered in the Agency for Healthcare Quality (AHRQ) Registry of Patient Registries (RoPR).
k. The research study protocol specifies the method and timing of public release of all prespecified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 12 months of the study's primary completion date, which is the date the final subject had final data collection for the primary endpoint, even if the trial does not achieve its primary aim. The results must include number started/completed, summary results for primary and secondary outcome measures, statistical analyses, and adverse events. Final results must be reported in a publicly accessibly manner; either in a peer-reviewed scientific journal (in print or on-line), in an on-line publicly accessible registry dedicated to the dissemination of clinical trial information such as ClinicalTrials.gov, or in journals willing to publish in abbreviated format (e.g., for studies with negative or incomplete results).
l. The study protocol must explicitly discuss beneficiary subpopulations affected by the item or service under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria effect enrollment of these populations, and a plan for the retention and reporting of said populations in the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.
m. The study protocol explicitly discusses how the results are or are not expected to be generalizable to affected beneficiary subpopulations. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

D. LAAC is non-covered for the treatment of NVAF when not furnished under CED according to the above-noted criteria.

Sincerely,

Arlene Bierman, MD, MS
Director
Center for Evidence and Practice Improvement