DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Healthcare
Research and Quality

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Rockville, MD 20850
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May 8, 2014

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

Dear Ms. Jensen,

The Agency for Healthcare Research and Quality understands that the Centers for Medicare &Medicaid Services (CMS) will cover transcatheter mitral valve repair (TMVR) only when these procedures are performed under Coverage with Evidence Development (CED) and when the following specific conditions are met:

The Centers for Medicare & Medicaid Services (CMS) proposes to cover transcatheter mitral valve repair (TMVR) under Coverage with Evidence Development (CED) with the following conditions:

A. TMVR is covered for the treatment of significant symptomatic mitral regurgitation when furnished according to an FDA approved indication and when all of the following conditions are met.

1. The procedure is furnished with a complete transcatheter mitral valve repair system that has received FDA premarket approval (PMA) for that system's FDA approved indication.

2. Both a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease have independently examined the patient face-to-face and evaluated the patient's suitability for mitral valve surgery and determination of prohibitive risk; and both physicians have documented the rationale for their clinical judgment and the rationale is available to the heart team.

3. The patient (preoperatively and postoperatively) is under the care of a heart team: a cohesive, multi-disciplinary, team of medical professionals. The heart team concept embodies collaboration and dedication across medical specialties to offer optimal patient-centered care.

TMVR must be furnished in a hospital with the appropriate infrastructure that includes but is not limited to:

a. On-site heart valve surgery program,
b. Cardiac catheterization lab or hybrid operating room/catheterization lab equipped with a fixed radiographic imaging system with flat-panel fluoroscopy offering catheterization laboratory-quality imaging,
c. Non-invasive imaging including expertise in transthoracic and transesophageal echocardiography,
d. Sufficient space, in a sterile environment, to accommodate necessary equipment for cases with and without complications,
e. Post-procedure intensive care facility with personnel experienced in managing patients who have undergone open-heart valve procedures,
f. Appropriate volume requirements per the applicable qualifications below.

Outlined below are qualification requirements for hospital surgical programs wishing to perform TMVR procedures.

The hospital surgical program must have the following:

a. ≥ 25 total mitral valve procedures in the previous year of which at least 10 must be mitral valve repairs, and;
b. ≥1000 catheterizations per year, including ≥ 400 percutaneous coronary interventions (PCIs) per year;
c. Interventionalist with: ≥ 50 structural procedures per year including atrial septal defects (ASD) and patent foramen ovale (PFO); and
d. Additional members of the heart team including echocardiographers, other imaging specialists, heart valve and heart failure specialists, electrophysiologists, cardiac anesthesiologists, intensive care and cardiac imaging departments, congenital heart disease specialists and surgeons, nurse practitioners, data/research coordinators and a dedicated administrator, and; Device-specific training as required by the manufacturer.

4. The heart team's interventional cardiologist(s) and cardiac surgeon(s) must jointly participate in the intra-operative technical aspects of TMVR.

5. The heart team and hospital are participating in a prospective, national, audited registry that: 1) consecutively enrolls TMVR patients; 2) accepts all manufactured devices; 3) follows the patient for at least one year; and 4) complies with relevant regulations relating to protecting human research subjects, including 45 CFR Part 46 and 21 CFR Parts 50 & 56. The following outcomes must be tracked by the registry; and the registry must be designed to permit identification and analysis of patient, practitioner and facility level variables that predict each of these outcomes:

i. Quality of Life (QoL);
ii. Functional capacity
iii. Stroke;
ii. All-cause mortality;

iii. Transient ischemic events (TIAs);
iv. Major vascular events;
v. Renal complications;
vi. Repeat mitral valve surgery or other mitral procedures;
vii. Worsening mitral regurgitation.

The registry should collect all data necessary and have a written executable analysis plan in place to address the following questions (to appropriately address some questions, Medicare claims or other outside data may be necessary):

- When performed outside a controlled clinical study, how do outcomes and adverse events compare to the pivotal clinical studies?
- How do outcomes and adverse events in subpopulations compare to patients in the pivotal clinical studies?
- What is the long term (≥ 5 year) durability of the device?
- What are the long term (≥ 5 year) outcomes and adverse events?
- How do the demographics of registry patients compare to the pivotal studies?

Consistent with section 1142 of the Act, the Agency for Healthcare Research and Quality (AHRQ) supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

B. TMVR is covered for uses that are not expressly listed as an FDA approved indication when performed within an FDA-approved randomized controlled clinical trial that fulfills all of the following.

1. The heart team's interventional cardiologist(s) and cardiac surgeon(s) must jointly participate in the intra-operative technical aspects of TMVR.

2. As a fully-described, written part of its protocol, the clinical research study must critically evaluate the following questions:
   - What is the patient's post-TMVR quality of life (compared to pre-TMVR) at one year?
   - What is the patient's post-TMVR functional capacity (compared to pre-TMVR) at one year?

3. In addition, the clinical research study must address all of the following questions at one year post procedure:
   - What is the incidence of stroke?
   - What is the rate of all-cause mortality?
   - What is the incidence of transient ischemic attacks (TIAs)?
   - What is the incidence of major vascular events?
   - What is the incidence of renal complications?

- What is the incidence of subsequent mitral valve surgery or other mitral valve procedures?
- What is the incidence of worsening mitral regurgitation?

C. All CMS-approved clinical studies and registries must adhere to the following standards of scientific integrity and relevance to the Medicare population:

a. The principal purpose of the research study is to test whether a particular intervention potentially improves the participants' health outcomes.
b. The research study is well supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use.
c. The research study does not unjustifiably duplicate existing studies.
d. The research study design is appropriate to answer the research question being asked in the study.
e. The research study is sponsored by an organization or individual capable of executing the proposed study 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 also must be in compliance with 21 CFR Parts 50 and 56.
g. All aspects of the research study are conducted according to appropriate standards of scientific integrity.
h. The research study has a written protocol that clearly addresses, or incorporates by reference; the standards listed as Medicare coverage requirements.
i. The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard 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

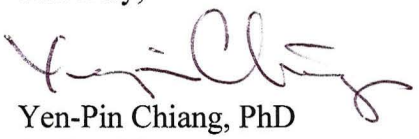
ClinicalTrials.gov, or in journals willing to publish in abbreviated format (e.g., for studies with negative or incomplete results).

l. The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria affect enrollment of these populations, and a plan for the retention and reporting of said populations on 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 research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

Consistent with section 1142 of the Act, the Agency for Healthcare Research and Quality (AHRQ) supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

Sincerely,



Yen-Pin Chiang, PhD
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