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Centers for Medicare & Medicaid Services  
7500 Security Blvd.  
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JUL 24 2014

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:

A. TMVR is covered for the treatment of significant symptomatic degenerative 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 cardiothoracic 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 active valvular heart disease surgical program with  $\geq 2$  hospital-based cardiothoracic surgeons experienced in valvular surgery;
- b. Cardiac catheterization laboratory or hybrid operating room/catheterization laboratory equipped with a fixed radiographic imaging system with flat-panel fluoroscopy offering catheterization laboratory-quality imaging;
- c. Non-invasive imaging expertise including transthoracic/ transesophageal/3D echocardiography, vascular studies and cardiac CT studies;

- 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. Adequate outpatient clinical care facilities; and
- g. Appropriate volume requirements per the applicable qualifications below.

Outlined below are institutional and operator requirements for performing TMVR.

The hospital must have the following:

- a. A surgical program that performs  $\geq 25$  total mitral valve surgical procedures for severe mitral regurgitation (MR) per year of which at least 10 must be mitral valve repairs;
  - b. An interventional cardiology program that performs  $\geq 1000$  catheterizations per year, including  $\geq 400$  percutaneous coronary interventions (PCIs) per year, with acceptable outcomes for conventional procedures compared to National Cardiovascular Data Registry (NCDR) benchmarks;
  - c. Each interventional cardiologist performs  $\geq 50$  structural procedures per year including atrial septal defects (ASD), patent foramen ovale (PFO) and trans-septal punctures; and
  - d. Additional members of the heart team including cardiac echocardiographers, other cardiac imaging specialists, heart valve and heart failure specialists, electrophysiologists, cardiac anesthesiologists, intensivists, nurses, nurse practitioners, physician assistants, data/research coordinators and a dedicated administrator;
  - e. Interventional cardiologist(s) must receive prior suitable training on the devices to be used;
  - f. All cases must be submitted to a single national database;
  - g. Ongoing continuing medical education (or the nursing/technologist equivalent) of 10 hours per year of relevant material;
  - h. The interventional cardiologist(s) must be board-certified in interventional cardiology or board-certified/eligible in pediatric cardiology or similar boards from outside the United States;
  - i. The cardiothoracic surgeon(s) must be board-certified in thoracic surgery or similar foreign equivalent.
4. TMVR must be performed by an interventional cardiologist or a cardiothoracic surgeon. Interventional cardiologist(s) and cardiothoracic surgeon(s) may jointly participate in the intra-operative technical aspects of TMVR as appropriate.
  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. All-cause mortality;
- ii. Stroke;
- iii. Repeat mitral valve surgery or other mitral procedures;
- iv. Worsening mitral regurgitation;
- v. Transient ischemic events (TIAs);
- vi. Major vascular events;
- vii. Renal complications;
- viii. Functional capacity;
- ix. Quality of Life (QoL).

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 ( $\geq 5$  year) durability of the device?
- What are the long term ( $\geq 5$  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 a FDA-approved randomized controlled trial that fulfills all of the following:

1. TMVR must be performed by an interventional cardiologist or a cardiac surgeon. Interventional cardiologist(s) and cardiothoracic surgeon(s) may jointly participate in the intra-operative technical aspects of TMVR as appropriate.
2. As a fully-described, written part of its protocol, the clinical research trial must critically evaluate the following questions at 12 months or longer follow-up:
  - What is the rate of all-cause mortality in the group randomized to TMVR compared to the patients randomized to control (surgical repair, optimal medical therapy or other specified control group)?
  - What is the rate of re-operations (open surgical or transcatheter) of the mitral valve in the group randomized to TMVR compared to the patients randomized to control (surgical repair or other specified control group)?

- What is the rate of severe mitral regurgitation in the group randomized to TMVR compared to the patients randomized to control (surgical repair or other specified control group)?

3. In addition, the randomized controlled trial must address all of the following questions at one year post procedure:

- What is the incidence of stroke?
- 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 worsening mitral regurgitation?
- What is the patient's post TMVR quality of life?
- What is the patient's post TMVR functional capacity?

C. All CMS-approved clinical trials 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](http://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 Research and 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 accessible 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](http://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  
Acting Deputy Director  
Center for Evidence and Practice Improvement