

(20230)

Medical Benefit		Effective Date: 04/01/16	Next Review Date: 01/20
Preauthorization	No	Review Dates: 01/16, 01/17, 01/18, 01/19	

Preauthorization is not required.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none"> With symptomatic primary or secondary mitral regurgitation and are at prohibitive risk for open surgery 	Interventions of interest are: <ul style="list-style-type: none"> Transcatheter mitral valve repair using MitraClip 	Comparators of interest are: <ul style="list-style-type: none"> Medical management 	Relevant outcomes include: <ul style="list-style-type: none"> Overall survival Morbid events Functional outcomes Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> With symptomatic primary or secondary mitral regurgitation and are surgical candidates 	Interventions of interest are: <ul style="list-style-type: none"> Transcatheter mitral valve repair using MitraClip 	Comparators of interest are: <ul style="list-style-type: none"> Open mitral valve repair Open mitral valve 	Relevant outcomes include: <ul style="list-style-type: none"> Overall survival Morbid events Functional outcomes Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> With symptomatic primary or secondary mitral regurgitation 	Interventions of interest are: <ul style="list-style-type: none"> Transcatheter mitral valve repair using devices other than MitraClip 	Comparators of interest are: <ul style="list-style-type: none"> Open mitral valve repair Open mitral valve 	Relevant outcomes include: <ul style="list-style-type: none"> Overall survival Morbid events Functional outcomes Treatment-related morbidity

DESCRIPTION

Transcatheter mitral valve repair (TMVR) is an alternative to surgical therapy for mitral regurgitation (MR). MR is a common valvular heart disease that can result from a primary structural abnormality of the mitral valve (MV), complex or a secondary dilatation of an anatomically normal MV due to a dilated left ventricle caused by ischemic or dilated cardiomyopathy. Surgical therapy may be underutilized, particularly in patients with multiple comorbidities, suggesting that there is an unmet need for less invasive procedures for MV repair. One device, MitraClip, has approval from the U.S. Food and Drug Administration for the treatment of severe symptomatic MR due to a primary abnormality of the MV (primary MR) in patients considered at prohibitive risk for surgery.

SUMMARY OF EVIDENCE

MITRACLIP

Primary MR at Prohibitive Risk for Surgery

For individuals who have symptomatic primary MR and are at prohibitive risk for open surgery who receive TMVR using MitraClip, the evidence includes a single-arm prospective cohort with historical cohort and registry studies. Relevant outcomes are overall survival, morbid events, functional outcomes, and treatment-related morbidity. The primary evidence includes the pivotal EVEREST II HRR and EVEREST II REALISM studies and Transcatheter Valve Therapy Registry studies. These studies have demonstrated that MitraClip implantation is feasible with a procedural success rate greater than 90%, 30-day mortality ranging from 2.3% to 6.4% (less than predicted Society of Thoracic Surgeons (STS) mortality risk score for MR repair or replacement; range, 9.5%-13.2%), postimplantation MR severity grade of 2+ or less in 82% to 93% of patients, and a clinically meaningful gain in quality of life (five- to six-point gains in 36-Item Short-Form Health Survey scores). At one year, freedom from death and MR more than 2+ was achieved in 61% of patients but the one-year mortality or heart failure hospitalization rates remain considerably high (38%). Conclusions related to the treatment effect on mortality based on historical controls cannot be made because the control groups did not provide unbiased or precise estimates of the natural history of patients eligible to receive MitraClip. Given that primary MR is a mechanical problem and there is no effective medical therapy, a randomized controlled trial (RCT) comparing MitraClip with medical management is not feasible or ethical. The postmarketing data from the United States is supportive that MitraClip surgery is being performed with short-term effectiveness and safety in select patient population. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Secondary MR at Prohibitive Risk for Surgery

For individuals who have symptomatic secondary MR and at prohibitive risk for open surgery who receive TMVR using MitraClip, the evidence includes multiple observational studies. Relevant outcomes are overall survival, morbid events, functional outcomes, and treatment-related morbidity. Multiple observational studies from Europe have suggested that MitraClip reduces the severity of MR and improves functional class in patients with secondary MR. However, recommendations from major societies regarding mitral valve surgery (conventional or percutaneous) are weak because the current evidence is inconsistent on whether mitral valve surgery produces a clinical benefit in patients with secondary MR. An RCT comparing the safety and effectiveness of MitraClip (COAPT trial) in patients with secondary MR is currently underway and is expected to be completed in 2024. The evidence is insufficient to determine the effects of the technology on health outcomes.

Primary or Secondary MR Not at Risk for Surgery

For individuals who have symptomatic primary or secondary MR and are surgical candidates who receive TMVR using MitraClip, the evidence includes a systematic review and an RCT. Relevant outcomes are overall survival, morbid events, functional outcomes, and treatment-related morbidity. The RCT found that MitraClip did not reduce MR as often or as completely as the surgical control, although it could be safely implanted and was associated with fewer adverse events at one year. Long-term follow-up from the RCT showed that significantly more MitraClip patients required surgery for MV dysfunction than conventional surgery patients. For these reasons, this single trial is not definitive in demonstrating improved clinical outcomes with MitraClip compared with surgery. Additional RCTs are needed to corroborate these results. The evidence is insufficient to determine the effects of the technology on health outcomes.

Devices Other Than MitraClip

For individuals who have symptomatic primary or secondary MR who receive TMVR using devices other than MitraClip, the evidence includes primarily noncomparative feasibility studies. Relevant outcomes are overall survival, morbid events, functional outcomes, and treatment-related morbidity. The body of evidence consists only of very small case series and case reports. Controlled studies, preferably RCTs, are needed to draw conclusions about the net health benefit. The evidence is insufficient to determine the effects of the technology on health outcomes.

POLICY

Transcatheter mitral valve repair with a device approved by the U.S. Food and Drug Administration for use in mitral valve repair may be considered **medically necessary** for patients with symptomatic, primary mitral regurgitation who are considered at prohibitive risk for open surgery (see Policy Guidelines).

Transcatheter mitral valve repair is considered **investigational** in all other situations.

POLICY GUIDELINES

“Prohibitive risk” for open surgery may be determined based on:

- Presence of a Society for Thoracic Surgeons predicted mortality risk of 12% or greater and/or
- Presence of a logistic EuroSCORE of 20% or greater.

MEDICARE ADVANTAGE

For Medicare Advantage TMVR for MR is considered **medically necessary** under Coverage with Evidence Development (CED), with the following conditions (not an inclusive list):

Treatment of significant symptomatic degenerative MR 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 TMVR 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 surgeons have documented the rationale for their clinical judgment and the rationale is available to the heart team.
3. The patient (pre-operatively and post-operatively) is under the care of a heart team: a cohesive, multidisciplinary, team of medical professionals. The heart team concept embodies collaboration and dedication across medical specialties to offer optimal patient-centered care.

TMVR is considered **investigational** for the treatment of MR when not furnished under CED according to the above-noted criteria.

TMVR used for the treatment of any non-MR indications are considered **investigational**.

TMVR may be eligible for uses that are not expressly listed as an FDA-approved indication when performed within an eligible clinical trial.

BACKGROUND

MITRAL REGURGITATION

Epidemiology and Classification

Mitral regurgitation (MR) is the second most common valvular heart disease, occurring in 7% of people older than age 75 years and accounting for 24% of all patients with valvular heart disease.^{1,2} Patients with MR generally fall into two categories—primary (also called degenerative) and secondary (also called functional) MR. Primary MR results from a primary structural abnormality in the valve, which causes it to leak. This leak may result from a floppy leaflet (called prolapse) or a ruptured cord that caused the leaflet to detach partially (called flail).³

Because the primary cause is a structural abnormality, most cases of primary MR are surgically corrected. In contrast, secondary MR results from left ventricular dilatation due to ischemic or dilated cardiomyopathy. This causes the MV leaflets not to coapt or meet in the center.⁴ Because the valves are structurally normal in secondary MR, correcting the dilated left ventricular using medical therapy is the primary treatment strategy used in the United States.

MR severity is classified as mild, moderate, or severe disease on the basis of echocardiographic and/or angiographic findings (1+, 2+, and 3-4+ angiographic grade, respectively). MR with accompanying valvular incompetence leads to left ventricular volume overload with secondary ventricular remodeling, myocardial dysfunction, and left heart failure. Clinical signs and symptoms of dyspnea and orthopnea may also present in patients with valvular dysfunction.⁴

Standard Management

Medical Management

Medical management has a primary role in secondary MR. Patients with chronic secondary MR should receive standard therapy for heart failure with reduced ejection fraction; standard management includes angiotensin converting enzyme inhibitor (or angiotensin II receptor blocker or angiotensin receptor-neprilysin inhibitor), β -blocker and mineralocorticoid receptor antagonist, and diuretic therapy as needed to treat volume overload.^{3,4}

Surgical Management

In symptomatic patients with primary MR, surgery is the main therapy. In most cases, MV repair is preferred over replacement, as long as the valve is suitable for repair and personnel with appropriate surgical expertise are available. The American College of Cardiology and the American Heart Association have issued joint guidelines on the surgical management of MV, which are outlined in Table 1.³

Table 1. Guidelines on Mitral Value Surgery

Recommendation	COR	LOE
MV surgery is recommended for the symptomatic patient with acute severe MR.	I	B
MV surgery is beneficial for patients with chronic severe MR and NYHA functional class II, III, or IV symptoms in the absence of severe LV dysfunction (severe LV dysfunction is defined as ejection fraction less than 0.30) and/or end-systolic dimension greater than 55 mm.	I	B
MV surgery is beneficial for asymptomatic patients with chronic severe MR and mild-to-moderate LV dysfunction, ejection fraction 0.30 to 0.60, and/or end systolic dimension greater than or equal to 40 mm.	I	B
MV repair is recommended over MV replacement in the majority of patients with severe chronic MR who require surgery, and patients should be referred to surgical centers experienced in MV repair.	I	C
MV repair is also reasonable for asymptomatic patients with chronic severe MR with preserved LV function ... in whom the high likelihood of successful MV repair without residual MR is greater than 90%.	Ia	B
MV surgery is reasonable for asymptomatic patients with chronic severe MR, preserved LV function, and new onset of atrial fibrillation.	Ia	C
MV surgery is reasonable for asymptomatic patients with chronic severe MR,* preserved LV function, and pulmonary hypertension.	Ia	C
MV surgery is reasonable for patients with chronic severe MR due to a primary abnormality of the mitral apparatus and NYHA functional class III-IV symptoms and severe LV dysfunction ... in whom MV repair is highly likely.	Ia	C

COR: class of recommendation; LOE: level of evidence; LV: left ventricular; MR: mitral regurgitation; MV: mitral valve; NYHA: New York Heart Association.

The use of standard open MV repair is limited by the requirement for thoracotomy and cardiopulmonary bypass, which may not be tolerated by elderly or debilitated patients due to their underlying cardiac disease or other conditions. In a single-center evaluation of 5737 patients with severe MR in the United States, Goel et al (2014) found that 53% of patients did not have MV surgery performed, suggesting an unmet need for such patients.⁵

Transcatheter MV Repair

Transcatheter approaches have been investigated to address the unmet need for less invasive MV repair, particularly among inoperable patients who face prohibitively high surgical risks due to age or comorbidities. MV repair devices under development address various components of the MV complex and generally are performed on the beating heart without the need for cardiopulmonary bypass.^{1,6} Approaches to MV repair include direct leaflet repair, repair of the mitral annulus via direct annuloplasty, or indirect repair based on the annulus's proximity to the coronary sinus. There are also devices in development to counteract ventricular remodeling, and systems designed for complete MV replacement via catheter.

Direct Leaflet Approximation

One device that undertakes direct leaflet repair, the MitraClip Clip Delivery System (Abbott Vascular), has been approved through the premarket approval process by the U.S. Food and Drug Administration (FDA) for use in certain patients with symptomatic primary MR (see Regulatory Status section). Of the transcatheter MV repair devices under investigation, MitraClip has the largest body of evidence evaluating its use; it has been in use in Europe since 2008.⁷ The MitraClip system is deployed percutaneously and approximates the open Alfieri edge-to-edge repair approach to treating MR. The delivery system consists of a catheter, a steerable sleeve, and the MitraClip device, which is a four-mm wide clip fabricated from a cobalt-chromium alloy and polypropylene fabric. MitraClip is deployed via a transfemoral approach, with transseptal puncture used to access the left side of the heart and the MV. Placement of MitraClip leads to coapting of the mitral leaflets, thus creating a double-orifice valve.

Other MV Repair Devices

Devices for transcatheter MV repair that use different approaches are in development. Techniques to repair the mitral annulus include those that target the annulus itself (direct annuloplasty) and those that tighten the mitral annulus via manipulation of the adjacent coronary sinus (indirect annuloplasty). Indirect annuloplasty devices include the Carillon[®] Mitral Contour System (Cardiac Dimension) and the Monarc[™] device (Edwards Lifesciences). The CE-marked Carillon Mitral Contour System is comprised of self-expanding proximal and distal anchors connected with a nitinol bridge, with the proximal end coronary sinus ostium and the distal anchor in the great cardiac vein. The size of the connection is controlled by manual pullback on the catheter (CE-marked). The Carillon system was evaluated in the Carillon Mitral Annuloplasty Device European Union Study (AMADEUS) and the follow-up Tighten the Annulus Now study, with further studies planned.⁸ The Monarc system also involves two self-expanding stents connected by a nitinol bridge, with one end implanted in the coronary sinus via internal jugular vein and the other in the great cardiac vein. Several weeks after implantation, the biologically degradable coating over the nitinol bridge degrades, allowing the bridge to shrink and the system to shorten. It has been evaluated in the Clinical Evaluation of the Edwards Lifesciences Percutaneous Mitral Annuloplasty System for the Treatment of Mitral Regurgitation (EVOLUTION I) trial.⁹

Direct annuloplasty devices include the Mitralign Percutaneous Annuloplasty System (Mitralign) and the AccuCinch[®] System (Guided Delivery Systems), both of which involve transcatheter placement of anchors in the MV; they are cinched or connected to narrow the mitral annulus. Other transcatheter direct annuloplasty devices under investigation include the enCorTC[™] device (MiCardia), which involves a percutaneously insertable annuloplasty ring that is adjustable using radiofrequency energy, a variation on its CE-marked enCorSQ[™] Mitral Valve Repair System, and the Cardioband[™] Annuloplasty System (Valtech Cardio), an implantable annuloplasty band with a transfemoral venous delivery system.

Transcatheter MV Replacement

Permavalve™ (MicroInterventional Devices), under investigation in the United States, is a transcatheter MV replacement device that is delivered via the transapical approach. On June 5, 2017, the SAPIEN 3 Transcatheter Heart Valve (Edwards Lifesciences) was approved by FDA as MV replacement device. These replacement valves are outside the scope of this protocol.

REGULATORY STATUS

In October 2013, the MitraClip® Clip Delivery System (Abbott Vascular) was approved by the FDA through the premarket approval process for treatment of “significant symptomatic mitral regurgitation (MR \geq 3+) due to primary abnormality of the mitral apparatus (degenerative MR) in patients who have been determined to be at a prohibitive risk for mitral valve surgery by a heart team.”¹⁰ FDA product code: NKM

RELATED PROTOCOLS

Transcatheter Aortic Valve Implantation for Aortic Stenosis

Transcatheter Pulmonary Valve Implantation

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

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We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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