**Preauthorization is 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.

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals: • With symptomatic degenerative or functional mitral regurgitation and are at prohibitive risk for open surgery</td>
<td>Interventions of interest are: • Transcatheter mitral valve repair using MitraClip</td>
<td>Comparators of interest are: • Medical management</td>
<td>Relevant outcomes include: • Overall survival • Morbid events • Functional outcomes • Treatment-related morbidity</td>
</tr>
<tr>
<td>Individuals: • With symptomatic degenerative or functional mitral regurgitation and are surgical candidates</td>
<td>Interventions of interest are: • Transcatheter mitral valve repair using MitraClip</td>
<td>Comparators of interest are: • Open mitral valve repair • Open mitral valve replacement</td>
<td>Relevant outcomes include: • Overall survival • Morbid events • Functional outcomes • Treatment-related morbidity</td>
</tr>
<tr>
<td>Individuals: • With degenerative or functional mitral regurgitation</td>
<td>Interventions of interest are: • Transcatheter mitral valve repair using devices other than MitraClip</td>
<td>Comparators of interest are: • Open mitral valve repair • Open mitral valve replacement</td>
<td>Relevant outcomes include: • Overall survival • Morbid events • Functional outcomes • Treatment-related morbidity</td>
</tr>
</tbody>
</table>

**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 (FDA) for the treatment of severe symptomatic MR due to a primary abnormality of the MV (degenerative mitral regurgitation [DMR]) in patients considered at prohibitive risk for surgery.

**Summary of Evidence**

For individuals who have symptomatic DMR or functional mitral regurgitation (FMR) and are at prohibitive risk for open surgery who receive TMVR using MitraClip, the evidence includes primarily single-arm cohort studies.
Relevant outcomes are overall survival, morbid events, functional outcomes, and treatment-related morbidity. Several single-arm studies have demonstrated that MitraClip implantation is feasible, with high rates (at least 70% to 90%) of short-term reductions in MR grade 2+ or less, and a reasonable safety profile. A nonrandomized analysis matching patients in the EVEREST registries to similar non-surgically-treated patients found significantly lower one-year mortality rates in MitraClip-treated patients. However, the lack of concurrent control groups, especially in randomized trials, makes it difficult to draw conclusions on whether there is a net health benefit compared with alternative therapies in this population. There are no strong barriers to conducting controlled trials, including randomized controlled trials (RCTs) comparing MitraClip to continued medical management. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have symptomatic DMR or FMR and are surgical candidates who receive TMVR using MitraClip, the evidence includes a systematic review, an RCT, and several comparative and noncomparative cohort studies. Relevant outcomes are overall survival, morbid events, functional outcomes, and treatment-related morbidity. The RCT found that MitraClip was noninferior to open surgery in terms of safety and effectiveness at one-year follow-up. At five-year follow-up, efficacy, assessed using a composite outcome, was significantly higher in the surgery group than in the MitraClip group. The RCT had some methodologic limitations, including a wide noninferiority margin and permissibility of crossing over to surgery and still considered to have a positive outcome. This single trial does not definitively demonstrate improved clinical outcomes with MitraClip compared with surgery. Additional RCTs are needed to corroborate these results. A subsequent nonrandomized controlled trial, which attempted to verify the findings of the RCT, did not find the same low rates of long-term MR control in MitraClip patients with an initially positive response to treatment. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have DMR or FMR 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, degenerative 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

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. MR can result from a heterogeneous set of disease processes that may affect one or more parts of the MV complex. The functional anatomy of the MV complex includes the left ventricular (LV) myocardium, the subvalvular apparatus including the papillary muscles and chordae tendineae, the mitral annulus, the MV leaflets, and the left atrium. The underlying cause of MR and the portion of the MV complex involved determine the underlying treatment strategy.

MR is classified into degenerative and functional MV disease. In degenerative DMR, disease results from a primary structural abnormality of the MV complex. Common causes of DMR include MV prolapse syndrome with subsequent myxomatous degeneration, rheumatic heart disease, coronary artery disease, infective endocarditis, and collagen vascular disease. In contrast, in FMR, the primary abnormality is a dilated LV due to ischemic or dilated cardiomyopathy, which leads to secondary dilatation of an anatomically normal MV. 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 LV 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. MR can be acute or chronic. Acute MR can result from conditions such as ruptured chordae tendineae or infectious endocarditis; and when severe, it can present with simultaneous shock and pulmonary congestion. Chronic MR may remain asymptomatic over a long period of time due to compensatory LV hypertrophy secondary to the LV overload. This leads to increased LV end-diastolic volume and, in turn, increased stroke volume (to restore forward cardiac output) and increased LV and left atrial size (to accommodate the regurgitant volume at lower filling pressure). Eventually, prolonged volume overload leads to contractile dysfunction, with increased end-systolic volume, further LV dilatation, and increased LV filling.
pressure. These changes ultimately lead to reduced forward cardiac output and signs and symptoms of pulmonary congestion.3

Standard Management

MEDICAL MANAGEMENT

Medical management has a role in a subset of MR cases. Among patients with chronic DMR, there is no generally accepted medical management. In FMR, medical management plays a much greater role because the underlying pathophysiology is related to LV dysfunction and dilatation. Primary treatment of the LV systolic dysfunction with angiotensin-converting enzyme inhibitors, β-blockers, and biventricular pacing can reduce LV pressures, decrease LV dilatation, improve cardiac output, and thus ameliorate clinical symptoms.3, 4

SURGICAL MANAGEMENT

In patients with symptoms of MR with preserved LV function (DMR), surgery is the main therapy. In most cases, repair of the MV 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 for the surgical management of MV, which are outlined in Table 1.3

Table 1. Guidelines on Mitral Valve Surgery

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>MV surgery is recommended for the symptomatic patient with acute severe MR.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>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.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>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.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>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.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>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%.</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>MV surgery is reasonable for asymptomatic patients with chronic severe MR, preserved LV function, and new onset of atrial fibrillation</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>MV surgery is reasonable for asymptomatic patients with chronic severe MR,* preserved LV function, and pulmonary hypertension....</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>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</td>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>

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

Standard open MV repair includes quadrangular leaf resection (if MV prolapse is present), transposition of normal valve chords to other areas of prolapsing leaflet, and a remodeling annuloplasty with a ring prosthesis. Multiple types of annuloplasty rings and bands specific to the underlying cause of the MR are commercially available.2 Introduced in the 1990s, the edge-to-edge approximation technique (Alfieri repair), typically combined with an annuloplasty, involves suturing the anterior and posterior MV leaflets together at their midpoint, creating a double-orifice MV.2, 5

However, there are limitations to the open surgical approaches for MV repair. While surgical MV repair is durable, its use is limited by the requirement for thoracotomy and cardiopulmonary bypass, which may not be tolerated by patients who are elderly or debilitated due to their underlying cardiac disease or other conditions.
In a 2007 study of 396 patients in Europe with severe, symptomatic MR, Mirabel et al found that about half of patients did not undergo surgical repair, specifically 56% of patients with DMR and 32% with FMR did not. Older age, impaired LV ejection fraction, and presence of comorbidities were all associated with the decision not to operate. 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. Compared with those who received surgery, patients who did not had lower ejection fractions (27% vs. 42%, \( p < 0.001 \)) and were at higher surgical risk, as judged by a higher Society of Thoracic Surgeons score (median, 5.8 vs. 4.0, \( p < 0.001 \)). These findings suggest that there is an unmet need for less invasive procedures for MV repair.

Transcatheter MV Repair

Transcatheter approaches have been investigated to address the unmet need for less invasive MV repair, particularly among 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. 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, Menlo Park, CA), has been approved through the premarket approval process by the U.S. Food and Drug Administration (FDA) for use in certain patients with symptomatic MR (see Regulatory Status section). Of the transcatheter MV repair devices under investigation, MitraClip has the largest body of evidence evaluating its use and has been in use in Europe since 2008. 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**

Additional 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, Kirkland, WA) and the Monarc™ device (Edwards Lifesciences, Irvine, CA). 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 (TITAN) study, with further studies planned. 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 following implantation, a 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. Direct annuloplasty devices include the Mitralign Percutaneous Annuloplasty System (Mitralign, Tewksbury, MA) and the AccuCinch® System (Guided Delivery Systems, Santa Clara, CA), both of which involve transcatheter
placement of anchors in the MV, which are cinched or connected to narrow the mitral annulus. Other transcuta-
neous direct annuloplasty devices under investigation include the enCorTC™ device (MiCardia, Irvine, CA), which
involves a percutaneously insertable annuloplasty ring that is adjustable using radiofrequency energy, a vari-
tion on its CE-marked enCorSQ™ Mitral Valve Repair System, and the Cardioband™ Annuloplasty System
(Valtech Cardio, Or-Yehuda, Israel), an implantable annuloplasty band with a transfemoral venous delivery
system.

**TRANSCATHETER MV REPLACEMENT**

Several devices are under development for transcatheter MV replacement, including the Endovalve™ (Micro-
Interventional Devices, Langhorne, PA), the CardiAQ™ (CardiAQ Valve Technologies, Irvine, CA) valve, the
Cardiovalve (Valtech Cardio, Or-Yehuda, Israel), and the Fortis Transcatheter Mitral Valve (Edwards Lifesciences,
Irvine, CA).

**Regulatory Status**

In October 2013, the MitraClip® Clip Delivery System (Abbott Vascular, Menlo Park, CA) was approved by the
FDA through the premarket approval process for treatment of “significant symptomatic mitral regurgitation (MR
≥ 3+) due to primary abnormality of the mitral apparatus (degenerative MR) in patients who have been deter-
mined to be at a prohibitive risk for mitral valve surgery by a heart team.”12 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.*

**References**

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

1. Chiam PT, Ruiz CE. Percutaneous transcatheter mitral valve repair: a classification of the technology. JACC
Feb 19 2008; 117(7):963-974. PMID 18285577


