Molina Clinical Policy
Transcatheter Mitral Valve Implantation: Policy No. 437

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DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

The mitral valve is the bicuspid valve that connects the left atrium of the heart to the left ventricle. When the valve is functioning properly, it opens allowing the left atrium to pump freshly oxygenated blood into to the left ventricle and closes preventing regurgitation, or backflow, into the left atrium when the left ventricle pumps fresh blood to the rest of the body. Over time, wear or structural changes to the heart can result in the valve not closing properly, allowing blood to flow from the left ventricle back into the left atrium. This condition is known as mitral regurgitation (MR). Primary MR results from structural failure of the valve, whereas secondary MR results from left ventricular dysfunction. MR results in the heart having to work harder to oxygenate the body, which leads to an enlarged left ventricle and ultimately can lead to heart failure. The first treatment for MR is guideline directed medical therapy. For patients with severe symptomatic MR after maximally tolerated guideline directed medical therapy, mitral valve repair or replacement may be warranted, with repair being preferable to replacement when feasible (AHA 2020, Pislaru 2020).

Transcatheter mitral valve replacement (TMVR), or transcatheter mitral valve implantation (TMVI), is a minimally invasive intervention aimed to treat MR that would normally require open surgical intervention. During the procedure, a prosthetic valve is delivered via a transeptally or transapically inserted catheter and then deployed over the diseased mitral valve. This type of transcatheter procedure has also been used to place a new valve inside an existing prosthetic valve that is no longer functioning properly in what is referred to as mitral valve-in-valve replacement (MViV). Less commonly, a transcatheter replacement procedure may be used to treat a calcified mitral valve, and this procedure involves significantly more risk of complication. At this time, TMVI and MViV are intended for patients who are at high risk for conventional open mitral valve repair or replacement.

Currently there is no device approved by the United States Food and Drug Association (FDA) for TMVI over a native valve. There are numerous interventional trials currently active or recruiting, including the APOLLO Study (NCT03242642) to evaluate the Medtronic Intrepid™ TMVR System in patients with severe symptomatic MR and the MISCEND Study (NCT02718001) to evaluate the safety and performance of the Edwards EVOQUE Eos mitral valve replacement system (www.clinicaltrials.gov). The SAPIEN 3 THV System and SAPIEN 3 Ultra THV System (Edwards Lifesciences) received expanded FDA approval in 2021 for use in individuals with symptomatic heart disease due to failure of a surgical bioprosthetic mitral valve who are at high risk or greater for open surgical treatment (FDA 2020).

RELATED POLICIES

MCP-184: Experimental and Investigational Services
For Transcatheter Mitral Valve Repair, please refer to MCG Guidelines.

COVERAGE POLICY

Transcatheter mitral valve implantation for native mitral valve disease is considered experimental, investigational,

and unproven due to insufficient published evidence to assess the safety and/or impact on health outcomes of transcatheter mitral valve implantation in patients with diseased mitral valves.

Transcatheter mitral valve-in-valve implantation using an FDA approved device (e.g., Edwards SAPIEN 3 Transcatheter Heart Valve System or Edwards SAPIEN 3 Ultra Transcatheter Heart Valve System) is considered medically necessary when **ALL** the following are met:

1. Symptomatic heart disease due to failing (i.e., stenosed, insufficient, or combined) surgical bioprosthetic mitral valve; **AND**

2. There is high or greater risk for open surgical therapy (e.g., predicted 30-day risk of surgical mortality ≥8%, based on Society of Thoracic Surgeons [STS] risk score and other clinical co-morbidities unmeasured by the STS risk calculator) as determined by a heart team including a cardiothoracic surgeon.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

Transcatheter Mitral Valve Implantation (TMVI)

There are currently no FDA approved devices for TMVI over a native valve and existing evidence is comprised of observational or retrospective studies of patients who have undergone TMVI for experimental or compassionate use. Further studies with larger numbers of participants are needed to determine safety, appropriate candidate selection, and long-term device durability.

Muller et al. (2017) examined short-term and 30-day outcomes in a prospective cohort early feasibility study comprised of 30 patients who underwent TMVR with the Tendyne Mitral Valve System (Abbott) to for treatment of symptomatic grade 3 (6.9%) or 4 (93.1%) MR (NCT02321514). Device implantation was successful in 28 of the 30 patients and of those, 1 death occurred 13 days following the procedure which was attributable to hospital-acquired pneumonia and 1 incidence of leaflet thrombus requiring increased anticoagulation dosage. During the 30-day follow up period, 4 patients were re-hospitalized requiring treatment for heart failure. Transthoracic echocardiography showed positive results at 30 days with 26 patients showing no MR and the remaining patient showing mild MR, resulting in an overall successful device rate of 83.3%. The primary safety endpoint was freedom from major adverse events which was achieved in 83.3% of participants. Additional participants were enrolled as an expansion of this study, and 1-year outcomes (Sorajja et al. 2019) and 2-year outcomes (Muller et al. 2021) of the first 100 patients were reported. Device implantation was successful in 97 of the 100 patients. At two years, there were 39 deaths among the participants of 34 were cardiovascular in origin, with 17 deaths occurring within the first 90 days post-TMVI. The predominant causes of death were refractory heart failure (n = 14) and fatal arrhythmias (n = 8). At 2 years, 93.2% of the 44 patients available for evaluation had no MR on transthoracic echocardiograph and the remaining 6.8% had mild MR.

Regueiro et al. (2017) reported on two-year outcomes of 13 patients who underwent TMVI as part of a compassionate use program that took place in centers in Europe and Canada. All 13 patients had severe symptomatic MR, New York Heart Association (NYHA) functional class III or greater heart failure and were deemed to be at very high or prohibitive risk for open cardiac surgery. Outcomes were assessed at 30 days, 6 months, 1 year, and 2 years following the procedure. There were 3 periprocedural deaths and 2 additional patients died within 30 days of successful valve placement resulting in a 30-day all-cause mortality rate of 38.5%. The two deaths were attributed to sudden cardiac death and multiorgan failure. All-cause mortality rates were 46% and 54% at two years respectively. Of the 2 patients who died after the first 30 days post placement the cause of death was attributed to terminal heart failure, however there was no evidence of mitral valve dysfunction on echocardiography. Of the remaining 6 patients, evaluation at 2 years showed no valve dysfunction, all but 1 patient in NYHA class II, and no rehospitalizations due to heart failure since the procedure.

Webb et al. (2017) conducted a first-in-human study of a transseptal TMVI system comprised of 10 patients with severe MR and NYHA functional class II or greater heart failure at high surgical risk. Patients with a left ventricular ejection fraction (LVEF) < 30% were excluded. Device implantation was successful in 9 of the 10 patients, all of which showed a post-procedure reduction in MR to trivial or less. Median length of stay was 1.5 days. At 30 days, subjects with successful implantation were free from mortality, stroke, rehospitalization and device dysfunction. One patient developed paravalvular regurgitation at 1 month related to a leaflet or chordal tear which was treated with a vascular plug and MR reduced to moderate. In the remaining 8 patients, MR was graded mild or less. The results were judged as promising in terms of transseptal delivery, which is less invasive and with a shorter recovery time than an apical approach.

Bapat et al. (2018) reported on an international study investigating the feasibility of the Twelve Intrepid TMVR system (Medtronic, Inc.) in 50 patients with severe MR, NYHA class III or IV, and LVEF of at least 20% at high or extreme surgical risk (NCT02322840). Transapical device implantation was successful in 48 patients. Seven deaths (14%) occurred within the first 30 days; with 3 deaths related to apical access site bleeding, 1 after device malpositioning during the procedure, and 3 due to refractory heart failure. Four additional patients died between 30 days and 4 months post TMVR, with 3 of these deaths due to sudden cardiac arrest and 1 due to non-cardiac causes. At 1 year, survival rate was 76.5%. At the point of last follow up (median 173 days), NYHA was class II or less in 79% of subjects and all subjects MR reduced to mild or trace.

Cheung et al. (2018) performed a retrospective analysis of TMVR for patients with MR and preexisting aortic valve prosthesis at high surgical risk. Previously, patients with existing bioprosthetic aortic valves had been excluded from TMVR trials due to potentially increased risk of left ventricular outflow tract (LVOT) obstruction. Twelve patients were selected and had the Tiara TMVR device (Neovasc, Inc.) placed via a transapical approach with success. No death, myocardial infarction, stroke, major bleeding, or access site complications occurred within the first 30 days.

A systematic review conducted by Alperi et al. (2023) included outcomes of 347 patients who underwent TMVR and summarized 30-day outcomes for 12 included studies and mid-term (data after 30 days) outcomes for 8 studies. Of the 8 studies with mid-term outcomes, the mean follow-up time was 17.5 months. Findings noted high technical success rates (95.4%). Thirty-day mortality rate was 8.4% (n = 29). The most common adverse effect in the initial 30 days was life-threatening or major bleeding (15.6%; n = 54). Rate of stroke in the first 30 days was 2.6% (n = 9). Despite a rather high mortality and major bleeding rate, mid-term outcomes showed a statistically significant reduction in both in grade 3+ or greater MR and number of patients with continued NYHA class III or greater after intervention.

Transcatheter Mitral Valve-In-Valve

Whisenant et al. (2020) reported on a prospective cohort study to investigate the SAPIEN 3 transcatheter heart valve (Edwards Lifesciences) as a mitral valve-in-valve (MViV) replacement for an existing bioprosthetic mitral valve that has failed. A total of 1529 patients who underwent transeptal (n = 1326; 86.7%) or transapical (n = 203; 13.3%) MViV implantation were included in the analysis. Of the patients, mitral stenosis was the most common cause of prosthetic valve failure (n= 784; 55.4%), followed by mitral regurgitation (n = 351; 24.8%), and mixed disease (n = 280; 19.8%). Procedural technical success, the primary safety end point, was achieved in 1480 patients (96.8%; 97.1% TS vs 94.6% TA; P = .08). Procedure complications included stroke (n = 10; 0.7%), device embolization (0.3%), LVOT obstruction (0.9%), and cardiac perforation (1.1%). In- hospital deaths attributed to cardiovascular cause were observed in 33 of 1529 patients and occurred more frequently in the transapical access group (4.4% vs. 1.8%; P = .03). The primary efficacy end point, one-year all-cause mortality, was 16.7% and transseptal access was associated with lower rates than transapical (15.8% vs. 21.7%; P = .03). NYHA class, a secondary outcome, also improved to class I or II in 90.3% (n = 1318) of patients. Another secondary outcome, quality of life measured by the Kansas City Cardiomyopathy Questionnaire, improved an average of 29.4 points from baseline.

Hu et al. (2018) performed a systematic review and meta-analysis on data from 245 patients (from 101 studies) who underwent MViV (n = 172) and valve-in-ring implantation (n = 73) for degenerated bioprosthetic valves and failed annuloplasty rings. Technical success rate in the MViV group was 97.1%. In-hospital death occurred in 9 patients (5.2%) with 5 deaths (2.9%) determined to be cardiovascular related. MR was reduced to mild or less in 95.5% of patients post-procedure. At the time of last follow up, 92% of patients were NYHA class 2 or lower. Limitations include lack of long-term follow-up data (only 40% of patients completed 6-month follow up and few studies reported 1-year

follow up), heterogeneous patient population, heterogenicity in the device used and approach (transapical vs. venous transseptal access).

Khan et al. (2021) conducted a retrospective registry analysis comprised of registry data from the National Inpatient Sample database. Patients identified as undergoing redo mitral valve replacement were identified using ICD-10 codes. Exclusions included age < 50 years, presence of infective endocarditis, or those also undergoing coronary artery bypass graft surgery. A total of 2,745 cases were identified with 495 treated with MViV and 2,250 treated with SMVR. The propensity approach was used to reduce dimensions to 1:1. The primary outcomes were in-hospital mortality and periprocedureal complications, while the secondary end points were resource use and tends over time. In the matched cohort, in-hospital mortality was higher in the SMVR group (7.6% vs. 2.8%) and a higher-percentage of patients undergoing MViV were discharged directly to home. Rates of blood transfusion (38% vs. 7.6%), acute kidney injury (36.7% vs. 13.9%) and pneumonia (10.1% vs. <2.8%) were higher in the SMVR group.

National and Specifical Organizations

The American College of Cardiology and American Heart Association 2020 Guidelines for the Management of Patients with Valvular Heart Disease (Otto 2020) does not address TMVI for treatment of MR in a native valve. Preferred treatments of native MR requiring intervention are surgical and transcatheter edge-to-edge repair, and selection between the two depends on various factors. Authors note that in patients with severe symptomatic bioprosthetic valve regurgitation, surgical replacement is preferred unless the member is at high or prohibitive surgical risk, in which case a transcatheter valve-in-valve procedure is reasonable when performed at a Comprehensive Valve Center.

The National Institute for Health and Care Excellence (NICE) published a guideline on Transapical transcatheter mitral valve-in-valve implantation for a failed surgically implanted mitral valve bioprosthesis (NICE 2021) including the following recommendations:

- Evidence on the safety of transapical transcatheter mitral valve-in-valve implantation for a failed surgically implanted mitral valve bioprosthesis is adequate and shows some serious but well-recognized complications. Evidence on its efficacy is limited in quality. So, this procedure should only be used with special arrangements for clinical governance, consent, and audit or research.
- Patient selection should be done by a multidisciplinary team which must include interventional cardiologists experienced in the procedure, cardiac surgeons, an expert in cardiac imaging, and where appropriate, a cardiac anesthetist and a specialist in medicine for older people. The multidisciplinary team should determine the risk level for each patient and the device most suitable for them.
- The procedure is technically challenging and should only be done in specialized centers, and only by clinical teams with special training and experience in complex endovascular cardiac interventions, including regular experience in transcatheter valve implantation procedures.
- NICE encourages further research into transapical transcatheter mitral valve-in-valve implantation for a failed surgically implanted mitral valve bioprosthesis. Studies should include details on patient selection, type and size of valve used, functional outcomes, quality of life, patient-reported outcome measures, survival, and complications. Studies should report long-term follow up of clinical outcomes and valve durability.

In 2019, The American Association for Thoracic Surgery (AATS), The American College of Cardiology (ACC), The Society for Cardiovascular Angiography and Interventions (SCAI), and The Society for Thoracic Surgeons (STS) published a joint report outlining operator and institutional recommendations and requirements for transcatheter interventions for treatment of MV disease ([1]Bonow et al. 2020). The guideline underscores the importance of a multidisciplinary team, typically led by interventional cardiology and surgical codirectors, in determining the most appropriate treatment options for each individual patient. Patients are part of the decision-making process and should be well informed of various treatment options, their availability, expected outcomes, and the risks and benefits. The recommendations also note that these procedures should only be performed at centers experienced in both transcatheter and surgical MV intervention.

The ACC published a 2020 update to the 2017 Expert Consensus Decision Pathway on the Management of Mitral Regurgitation ([2]Bonow et al. 2020) to provide guidance on patient evaluation, treatment options, and treatment goals. The consensus statement does not address TMVI other than to note that devices for TMVI are currently under investigation at the time of publication.

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology) Codes

CPT	Description
0483T	Transcatheter mitral valve implantation/replacement (TMVI) with prosthetic valve; percutaneous approach, including transseptal puncture, when performed
0484T	Transcatheter mitral valve implantation/replacement (TMVI) with prosthetic valve; transthoracic exposure (e.g., thoracotomy, transapical)

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

08/09/2023 New policy. Independent Review Organization Peer Review on July 19, 2023 by a practicing, board-certified physician specializing in Cardiology and Interventional Cardiology.

REFERENCES

1. Alperi A, Avanzas P, Leon V, et al. Current status of transcatheter mitral valve replacement: systematic review and meta-analysis. Front Cardiovasc Med. 2023 May 10;10:1130212. doi: 10.3389/fcvm.2023.1130212. PMID: 37234369; PMCID: PMC10206247.
2. Bapat V, Rajagopal V, Meduri C, et al. Early Experience With New Transcatheter Mitral Valve Replacement. J Am Coll Cardiol. 2018 Jan 2;71(1):12-21. doi: 10.1016/j.jacc.2017.10.061. Epub 2017 Nov 16. PMID: 29102689.
3. [1]Bonow RO, O'Gara PT, Adams DH, et al. 2019 AATS/ACC/SCAI/STS Expert Consensus Systems of Care Document: Operator and Institutional Recommendations and Requirements for Transcatheter Mitral Valve Intervention: A Joint Report of the American Association for Thoracic Surgery, the American College of Cardiology, the Society for Cardiovascular Angiography and Interventions, and The Society of Thoracic Surgeons. J Am Coll Cardiol. 2020 Jul 7;76(1):96-117. doi: 10.1016/j.jacc.2019.12.002. Epub 2019 Dec 16. Erratum in: J Am Coll Cardiol. 2020 Jul 7;76(1):130. PMID: 31857196.
4. [2]Bonow RO, O'Gara PT, Adams DH, et al. 2020 Focused Update of the 2017 ACC Expert Consensus Decision Pathway on the Management of Mitral Regurgitation: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2020 May 5;75(17):2236-2270. doi: 10.1016/j.jacc.2020.02.005. Epub 2020 Feb 14. Erratum in: J Am Coll Cardiol. 2020 Jun 16;75(23):3000. PMID: 32068084
5. Centers for Medicare and Medicaid Services (CMS). Medicare coverage database. https://www.cms.gov/medicare-coverage-database/search.aspx.
6. Hayes. Transcatheter mitral valve replacement for mitral regurgitation. Published January 11, 2021. Annual review May 3, 2023. https://evidence.hayesinc.com/.
7. Muller DWM, Farivar RS, Jansz P, et al. Transcatheter Mitral Valve Replacement for Patients With Symptomatic Mitral Regurgitation: A Global Feasibility Trial. J Am Coll Cardiol. 2017 Jan 31;69(4):381-391. doi: 10.1016/j.jacc.2016.10.068. Epub 2016 Dec 28. Erratum in: J Am Coll Cardiol. 2017 Mar 7;69(9):1213. PMID: 28040318.
8. Muller DWM, Sorajja P, Duncan A, et al. 2-Year Outcomes of Transcatheter Mitral Valve Replacement in Patients With Severe Symptomatic Mitral Regurgitation. J Am Coll Cardiol. 2021 Nov 9;78(19):1847-1859. doi: 10.1016/j.jacc.2021.08.060. PMID: 34736561.
9. Otto CM, Nishimura RA, Bonow RO. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2021 Feb 2;143(5):e72-e227. doi: 10.1161/CIR.0000000000000923. Epub 2020 Dec 17. Erratum in: Circulation. 2021 Feb 2;143(5):e229. PMID: 33332150.
10. Pislaru S. Surgical procedures for severe chronic mitral regurgitation. Updated November 23, 2020. Reviewed June 2023. http://www.uptodate.com
11. Regueiro A, Ye J, Fam N, et al. 2-Year Outcomes After Transcatheter Mitral Valve Replacement. JACC Cardiovasc Interv. 2017 Aug 28;10(16):1671-1678. doi: 10.1016/j.jcin.2017.05.032. PMID: 28838478.
12. Sorajja P, Moat N, Badhwar V, et al. Initial Feasibility Study of a New Transcatheter Mitral Prosthesis: The First 100 Patients. J Am Coll Cardiol. 2019 Mar 26;73(11):1250-1260. doi: 10.1016/j.jacc.2018.12.066. PMID: 30898200.
13. United States Food and Drug Administration (FDA). SAPIEN 3 and SAPIEN 3 Ultra Transcatheter Heart Valve System. Premarket approval no. P140031. Received November 18, 2020. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P140031S125
14. United States National Library of Medicine. http://clinicaltrials.gov
15. Webb JG, Murdoch DJ, Boone RH, et al. Percutaneous Transcatheter Mitral Valve Replacement: First-in-Human Experience With a New

Transseptal System. J Am Coll Cardiol. 2019 Mar 26;73(11):1239-1246. doi: 10.1016/j.jacc.2018.12.065. PMID: 30898198.
16. Whisenant B, Kapadia SR, Eleid MF, et al. One-Year Outcomes of Mitral Valve-in-Valve Using the SAPIEN 3 Transcatheter Heart Valve. JAMA Cardiol. 2020 Nov 1;5(11):1245-1252. doi: 10.1001/jamacardio.2020.2974. PMID: 32745164; PMCID: PMC7391176.
17. Zia Khan M, Zahid S, Khan MU, et al. Redo Surgical Mitral Valve Replacement Versus Transcatheter Mitral Valve in Valve From the National Inpatient Sample. J Am Heart Assoc. 2021 Sep 7;10(17):e020948. doi: 10.1161/JAHA.121.020948. Epub 2021 Aug 28. PMID: 34459226; PMCID: PMC8649266.