Original Effective Date: 08/01/2022
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Last P&T Approval/Version: 01/29/2025
Next Review Due By: 01/2026
Policy Number: C23723-A

Camzyos (mavacamten)

PRODUCTS AFFECTED

Camzyos (mavacamten)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

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.

DIAGNOSIS:
Obstructive hypertrophic cardiomyopathy

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. OBSTRUCTIVE HYPERTROPHIC CARDIOMYOPATHY:
   1. Documented diagnosis of New York Heart Association (NYHA) class II-III obstructive hypertrophic cardiomyopathy
      AND
   2. Documentation member's left ventricular ejection fraction (LVEF) is ≥55% [DOCUMENTATION

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REQUIRED]
AND

3. Documentation member has had prior therapy or labeled contraindication or serious side effect to beta blockers (e.g., metoprolol, propranolol, atenolol) and/or calcium channel blockers (e.g., verapamil, diltiazem)
AND
4. Prescriber attests that female members of reproductive potential have been counseled to use effective contraception until 4 months after the last dose of Camzyos (mavacamten). Contraception containing a combination of ethinyl estradiol and norethindrone may be used with mavacamten. Use a contraceptive not affected by CYP450 enzyme induction or add nonhormonal contraception.
AND
5. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Camzyos (mavacamten) include: Concomitant use of moderate to strong CYP2C19 inhibitors or strong CYP3A4 inhibitors, concomitant use of moderate to strong CYP2C19 inducers or moderate to strong CYP3A4 inducers, pregnancy, avoid concomitant use with a combined hormonal contraceptive that contains a progestin other than norethindrone, avoid use in combination with disopyramide, ranolazine, verapamil with a beta blocker, or diltiazem with a beta blocker.]

CONTINUATION OF THERAPY:

A. OBSTRUCTIVE HYPERTROPHIC CARDIOMYOPATHY:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
AND
3. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms
AND
4. Documentation member's most recent (within the last 30 days) left ventricular ejection fraction (LVEF) is ≥50% [DOCUMENTATION REQUIRED]

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified cardiologist [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:

Maximum of 1 tablet every day of any strength
Maximum Quantity Limits – 15mg daily

PLACE OF ADMINISTRATION:

The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

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DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Cardiac Myosin Inhibitors

FDA-APPROVED USES:
Indicated for the treatment of adults with symptomatic New York Heart Association (NYHA) class II-III obstructive hypertrophic cardiomyopathy (HCM) to improve functional capacity and symptoms.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Camzyos is an oral, selective allosteric and reversible inhibitor of cardiac myosin. It reduces cardiac muscle contractility by inhibiting excessive myosin actin cross-bridge formation and dysregulation that result in hypercontractility, left ventricular hypertrophy and reduced compliance.
The approval was based on data from the randomized, multicenter, double-blind, placebo- controlled, parallel-group phase 3 EXPLORER-HCM trial which assessed the efficacy and safety of mavacamten in 251 adults with symptomatic, obstructive HCM. Patients were randomly assigned 1:1 to receive a starting dose of mavacamten 5mg orally once daily or placebo for 30 weeks. The mavacamten dose was periodically adjusted to optimize patient response (decrease in LVOT gradient with Valsalva maneuver) and maintain LVEF of 50% or greater.
Results showed that 37% of patients treated with mavacamten met the primary endpoint at week 30 compared with 17% of patients who received placebo (treatment difference, 19%; 95% CI, 9-30; P =.0005). Additionally, mavacamten was associated with statistically significant and clinically meaningful improvements in the change from baseline through week 30 in the following key secondary endpoints vs placebo, respectively:

- Mean change in post exercise left ventricular outflow tract (LVOT) peak gradient: -47mmHg vs -10mmHg (treatment difference, -35; 95% CI: -43, -28; P <.0001);
- Mean change in pVO2: 1.4mL/kg/min vs -0.1 (treatment difference, 1.4; 95% CI, 0.6-2.1; P <.0006);
- Number (%) of patients with an improvement of at least 1 NYHA class: 80 (65%) vs 40 (31%) (treatment difference, 34%; 95% CI, 22-45; P <.0001);
- Mean change in Kansas City Cardiomyopathy Clinical Summary Score (KCCQ-CSS): 14 vs 4 (treatment difference, 9; 95% CI, 5-13; P <.0001);
- Mean change in HCM Symptom Questionnaire Shortness of Breath Domain Score: -3 vs - 1 (treatment difference, -2; 95% CI: -2, -1; P <.0001).
- In the mavacamten arm, at the end of the treatment period, 49% of patients were receiving the 5mg dose, 33% were receiving the 10mg dose, and 11% were receiving the 15mg dose.

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Camzyos carries a Boxed Warning associated with a risk of heart failure due to systolic dysfunction. Echocardiogram assessments of left ventricular ejection fraction (LVEF) are required prior to and during treatment. Initiation of Camzyos in patients with LVEF less than 55% is not recommended.
Due to the risk of heart failure, Camzyos is available only through a restricted program called the Camzyos REMS Program.

Camzyos is contraindicated with the concomitant use of moderate to strong CYP2C19 inhibitors or strong CYP3A4 inhibitors and moderate to strong CYP2C19 inducers or moderate to strong CYP3A4 inducers. Concomitant use of Camzyos and drugs that interact with these enzymes may lead to life-threatening drug interactions such as heart failure or loss of effectiveness.

On June 15, 2023, Bristol Myers Squibb (BMS) announced that the FDA approved the sNDA for Camzyos (mavacamten) to add positive data from the Phase 3 VALOR-HCM trial to the drug's prescribing information. There was no change to the approved indication for Camzyos with the approval of the sNDA. The data from the VALOR-HCM trial (N = 112) demonstrated that treatment with Camzyos significantly reduced the composite endpoint of guideline-based eligibility for SRT at Week 16 or patient decision to proceed with SRT prior to or at Week 16. In the VALOR-HCM trial, 18% of Camzyos-treated patients decided to proceed with SRT or were eligible for SRT, versus 77% of patients who received placebo. The primary endpoint was driven by guideline eligibility rather than patient-clinician decision to proceed with SRT. Camzyos also met the secondary endpoints of the VALOR-HCM trial at Week 16 vs placebo, including change from baseline in mean post-exercise left ventricular outflow tract (LVOT), proportion of patients with at least one class improvement from baseline in NYHA class, and change from baseline in Kansas City Cardiomyopathy Questionnaire-23 Clinical Summary Score (KCCQ-23, CSS). No new adverse reactions to Camzyos were identified in the trial. The FDA's approval of the inclusion of positive data from the VALOR-HCM trial reinforces the value of Camzyos to improve symptoms and significantly reduce eligibility for SRT in patients with oHCM.

CAMZYOS REMS-
What is the CAMZYOS REMS?
A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential risks associated with a drug product and is required by the Food and Drug Administration (FDA) to ensure the benefits of a drug outweigh its risks.
Because of the serious risk of heart failure due to systolic dysfunction, CAMZYOS is available only through a restricted program called the CAMZYOS REMS.
CAMZYOS may increase the risk of heart failure due to systolic dysfunction; patients may experience heart failure at any time during treatment with CAMZYOS.
What are the requirements of the CAMZYOS REMS?
In order for patients to receive CAMZYOS, healthcare providers, pharmacies, and patients must comply with the requirements of the CAMZYOS REMS.

Before starting each patient on CAMZYOS Healthcare providers MUST:
1. Counsel the patient, using the Patient Brochure, on the:
   • Risk of heart failure due to systolic dysfunction, including how to recognize and respond to the symptoms of heart failure due to systolic dysfunction
   • Risk of drug-drug interactions with CYP2C19 or CYP3A4 inhibitors and inducers and the need to inform healthcare providers of all the prescription and nonprescription medications they take
2. Provide the patient with the Patient Brochure
3. Assess the patient's cardiovascular status and the appropriateness of initiating treatment by obtaining an echocardiogram
4. Assess the patient's prescription and nonprescription medications and supplements for drug- drug interactions

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5. Enroll the patient by completing the Patient Enrollment Form together with the patient and documenting and submitting the confirmation of the echocardiogram, screening for drug-drug interactions, and authorization for treatment to the REMS

Once the patient is on CAMZYOS Healthcare providers MUST:

1. Counsel the patient on the risk of heart failure due to systolic dysfunction and drug-drug interactions with CYP2C19 and CYP3A4 inhibitors and inducers, and the related safe-use requirements using the Patient Brochure
2. Assess the patient's cardiovascular status, including obtaining echocardiograms at the frequency described in the Prescribing Information:
   i. 4, 8, and 12 weeks after treatment initiation, then every 12 weeks thereafter
   ii. 4 weeks after interruption of treatment
   iii. 4 and 12 weeks after any dose change (including restart of treatment)
   iv. 4 and 12 weeks after initiating a weak CYP2C19 inhibitor or a moderate CYP3A4 inhibitor
3. Assess the patient's current prescription and nonprescription medications and supplements for drug-drug interactions
4. Complete, sign, and submit a Patient Status Form to the CAMZYOS REMS, documenting that the patient has been counseled, the echocardiogram for the required time interval based on the Prescribing Information has been performed, assessment of drug-drug interactions has been performed, and it is appropriate for the patient to continue treatment
5. Report adverse events of heart failure due to systolic dysfunction to Bristol Myers Squibb at 833- 628-7367

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Camzyos (mavacamten) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Camzyos (mavacamten) include: Concomitant use of moderate to strong CYP2C19 inhibitors or strong CYP3A4 inhibitors, concomitant use of moderate to strong CYP2C19 inducers or moderate to strong CYP3A4 inducers, pregnancy, avoid concomitant use with a combined hormonal contraceptive that contains a progestin other than norethindrone, avoid use in combination with disopyramide, ranolazine, verapamil with a beta blocker, or diltiazem with a beta blocker.

OTHER SPECIAL CONSIDERATIONS:

Dosage must be individualized based on clinical status and echocardiographic assessment of patient response. Refer to the Full Prescribing Information for instructions.

Camzyos (mavacamten) has a Black Box Warning for risk of heart failure.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. 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. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION

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NA	

AVAILABLE DOSAGE FORMS:
Camzyos CAPS 2.5MG, 5MG, 10MG, 15MG

REFERENCES

1. Camzyos (mavacamten) capsules for oral use [prescribing information]. Brisbane, CA: MyoKardia Inc; April 2024.
2. Olivotto I, Oreziak A, Barriales-Villa R, et al; EXPLORER-HCM study investigators. Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy (EXPLORER-HCM): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2020;396(10253):759-769. doi:10.1016/S0140-6736(20)31792-X [PubMed 32871100]
3. Ommen, S. R., Mital, S., Burke, M. A., Day, S. M., Deswal, A., Elliott, P., Sorajja, P. (2020). 2020 AHA/ACC guideline for the diagnosis and treatment of patients with hypertrophic cardiomyopathy. Circulation, 142(25). doi:10.1161/cir.0000000000000937
4. Ommen, S, Ho, C. et al. 2024 AHA/ACC/AMSSM/HRS/PACES/SCMR Guideline for the Management of Hypertrophic Cardiomyopathy: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. JACC. 2024 Jun, 83 (23) 2324–2405. https://doi.org/10.1016/j.jacc.2024.02.014

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Quantity Contraindications/Exclusions/ Discontinuation References	Q1 2025
REVISION- Notable revisions: Required Medical Information Background Contraindications/Exclusions/Discontinuation References	Q1 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Contraindications/Exclusions/Discontinuation Other Special Considerations References	Q1 2023
NEW POLICY	Q3 2022

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