Clinical Policy: Mavacamten (Camzyos)

Reference Number: CP.PMN.272
Effective Date: 04.28.22
Last Review Date: 02.23
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Mavacamten (Camzyos®) is a cardiac myosin inhibitor.

FDA Approved Indication(s)

Camzyos is 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.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Camzyos is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Obstructive Hypertrophic Cardiomyopathy (must meet all)**:**

1. Diagnosis of obstructive HCM;
2. Member exhibits NYHA Class II to III symptoms, including but not limited to: effort-related dyspnea or chest pain, or syncope or near syncope attributed to left ventricular outflow tract obstruction;
3. Prescribed by or in consultation with a cardiologist;
4. Age ≥ 18 years;
5. Member has left ventricular hypertrophy with maximal left ventricular wall thickness of one of the following (a or b):
   a. ≥ 15 mm;
   b. ≥ 13 mm to < 15 mm if member has familial hypertrophic cardiomyopathy or in conjunction with a positive genetic test;
6. Member has a left ventricular ejection fraction (LVEF) ≥ 55%;
7. Member has a peak left ventricular outflow tract (LVOT) gradient ≥ 50 mmHg at rest or with provocation;
8. Failure of all of the following at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated (a, b, and c):
   a. Non-vasodilating beta-blocker (e.g., atenolol, metoprolol, bisoprolol, propranolol);
   b. Non-dihydropyridine calcium channel blocker (e.g., verapamil, diltiazem);

c. Add-on disopyramide therapy after failure of beta-blocker or calcium channel blocker monotherapy;

9. Dose does not exceed 15 mg per day.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Obstructive Hypertrophic Cardiomyopathy (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by improvement in obstructive HCM symptoms;
3. Member has not undergone a septal reduction procedure within the last 6 months;
4. If request is for a dose increase, new dose does not exceed 15 mg per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ER: extended release
FDA: Food and Drug Administration
HCM: hypertrophic cardiomyopathy
IR: immediate release
LVEF: left ventricular ejection fraction
LVOT: left ventricular outflow tract
NYHA: New York Heart Association
REMS: Risk Evaluation and Mitigation Strategy

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
atenolol	50-100 mg PO QD	200 mg/day
metoprolol	50-100 mg PO QD	400 mg/day
bisoprolol	5-20 mg PO QD	20 mg/day
propranolol	80-320 mg PO QD or divided into 2-4 doses/day	320 mg/day
nadolol	40-80 mg PO QD	240 mg/day
verapamil	80-120 mg PO TID	480 mg/day
diltiazem	Immediate-release (IR): 30 mg PO QID Extended-release (ER): 120-180 mg PO QD	IR: 360 mg/day ER: 360-540 mg/day
disopyramide	200-250 mg PO BID	600 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): concomitant use of moderate to strong CYP2C19 inhibitors/inducers or strong CYP3A4 inhibitors of moderate to strong CYP3A4 inducers
- Boxed warning(s): risk of heart failure due to systolic dysfunction

- Echocardiogram assessments of LVEF are required prior to and during treatment with Camzyos; initiation of Camzyos in patients with LVEF < 55% is not recommended; interrupt Camzyos if LVEF is < 50% at any visit or if the patient experiences heart failure symptoms or worsening clinical status; because of the risk of heart failure due to systolic dysfunction, Camzyos is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called Camzyos REMS Program

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Obstructive HCM	Initiation: 5 mg PO QD x 4 weeks Week 4: • If Valsalva LVOT gradient is < 20 mmHg, down-titrate to 2.5 mg PO QD • If Valsalva LVOT gradient is ≥ 20 mmHg, maintain 5 mg daily dose Week 8: • If Valsalva LVOT gradient is ≥ 20 mmHg, maintain current dose x 4 weeks and then begin Maintenance therapy at Week 12 • If Valsalva LVOT gradient is < 20 mmHg and previous dose was 2.5 mg daily: withhold drug and return at Week 12 o At Week 12, restart on 2.5 mg daily dose if LVEF ≥ 50% and recheck clinical status and echocardiogram in 4 weeks o Maintain same dose x 8 weeks, consistent with Maintenance dosing, unless LVEF is < 50% • If Valsalva LVOT gradient is < 20 mmHg and previous dose was 5 mg daily: down-titrate to 2.5 mg PO QD x 4 weeks and then begin Maintenance therapy Maintenance: • If LVEF is < 50%: interrupt Camzyos treatment (see instructions for dose interruption below) • If LVEF is 50-55%, regardless of Valsalva LVOT gradient OR LVEF is > 55% and Valsalva LVOT gradient is < 30 mmHg: maintain on the same dose and follow-up 12 weeks later • If LVEF ≥ 55% and Valsalva LVOT gradient ≥ 30 mmHg: Up-titration to next	15 mg/day

Indication	Dosing Regimen	Maximum Dose
	higher daily (mg) dose level (2.5 → 5; 5 → 10; 10 → 15); recheck clinical status and echocardiogram in 4 weeks and maintain the same dose for the next 8 weeks unless LVEF is < 50%; further up-titration is allowed after 12 weeks of treatment on the same dose level <u>Dose interruption at any clinic visit if LVEF is < 50%:</u> • After dose interruption, recheck echocardiogram parameters every 4 weeks until LVEF ≥ 50%; once LVEF ≥ 50%: o Restart treatment at next lower daily (mg) dose level (5 → 2.5; 10 → 5; 15 → 10; if interrupted at 2.5 mg, restart at 2.5 mg) o Recheck clinical status and echocardiogram in 4 weeks and maintain the same dose for the next 8 weeks unless LVEF < 50%; o Next follow instructions above for Maintenance dosing • Permanently discontinue Camzyos treatment if LVEF is < 50% twice on 2.5 mg daily dose.	

VI. Product Availability

Capsules: 2.5 mg, 5 mg, 10 mg, 15 mg

VII. References

1. Camzyos Prescribing Information. Brisbane, CA: Bristol Myers Squibb; April 2022. Available at: www.camzyos.com. Accessed May 23, 2022.
2. ClinicalTrials.gov. NCT03470545. Clinical study to evaluate mavacamten (MYK-461) in adults with symptomatic obstructive hypertrophic cardiomyopathy (EXPLORER-HCM). Available at www.clinicaltrials.gov. Accessed November 29, 2021.
3. Olivotto I, Oreziak A, Barriales-Villa R, et al. Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy (EXPLORER-HCM): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet.* September 2020;396:759–69.
4. Ommen SR, Mital S, Burke MA, et al. 2020 AHA/ACC guideline for the diagnosis and treatment of patients with hypertrophic cardiomyopathy: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2020;76:e159–240.
5. Mavacamten Drug Monograph. Clinical Pharmacology. Accessed May 30, 2022. https://www.clinicalkey.com/pharmacology/.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	11.30.21	02.22
Drug is now FDA approved - criteria updated per FDA labeling: removed requirement for maximal left ventricular wall thickness and this is not a requirement per the FDA label, changed "Member exhibits NYHA Class II or III symptoms" to "Member exhibits NYHA Class II to III symptoms", changed wording of "or after Valsalva maneuver or exercise" to "or with provocation" for alignment with label language; references reviewed and updated.	05.10.22	05.22
RT1: no significant changes; references reviewed and updated.	06.07.22	08.22
Criteria updated per P&T feedback: added requirement for maximal left ventricular wall thickness. Template changes applied to other diagnoses/indications and continued therapy section.	08.23.22	11.22
For familial hypertrophic cardiomyopathy, updated maximal left ventricular wall thickness range to ≥ 13 mm to < 15 mm and added option for positive genetic test per AHA/ACC hypertrophic cardiomyopathy guidelines; clarified disopyramide's place in therapy as add-on therapy to beta blocker or calcium channel blockers.	01.06.23	02.23

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a

discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.