Clinical Policy: Mavacamten (Camzyos)

Reference Number: CP.PMN.272
Effective Date: 05/2022
Last Review Date: 07/2024

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 PA Health & Wellness® 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 if member has familial hypertrophic cardiomyopathy or in conjunction with a positive genetic test (*see Appendix D*);
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 two of the following at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated:
   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

1. Refer to the off-label use policy PA.CP.PMN.53

II. Continued Therapy

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
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. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy PA.CP.PMN.53

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 – PA.CP.PMN.53

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 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

Appendix D: General Information

- The 2 most common genes associated with familial HCM are beta myosin heavy chain 7 (MYH7) and myosin-binding protein C3 (MYBPC3). Other genes include TNNI3, TNNT2, TPM1, MYL2, MYL3, and ACTC1.

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	15 mg/day

	• 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 <u>Maintenance:</u> • 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 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%;	

	○ 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 2024. Available at: www.Camzyos.com. Accessed May 9, 2024.
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 May 14, 2024.
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. Desai M, Owens A, Geske JB, et al. Dose-blinded myosin inhibition in patients with obstructive hypertrophic cardiomyopathy referred for septal reduction therapy: outcomes through 32 weeks. Circulation. March 14, 2023;147(11):850-63. Available at: https://doi.org/10.1161/CIRCULATIONAHA.122.062534.
5. Ommen SR, Ho CY, Asif IM, 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. J Am Coll Cardiol. May 08, 2024. Epublished DOI: 10.1016/j.jacc.2024.02.014.

Reviews, Revisions, and Approvals	Date
Policy created	06/2022
Criteria updated per P&T feedback: added requirement for maximal left ventricular wall thickness.	10/2022
3Q 2023 annual review: 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; references reviewed and updated.	07/2023
3Q 2024 annual review: no significant changes; added Appendix D with examples of genes that can cause familial HCM; references reviewed and updated.	07/2024