Clinical Policy Title:	mavacamten
Policy Number:	RxA.770
Drug(s) Applied:	Camzyos™
Original Policy Date:	07/18/2022
Last Review Date:	07/13/2023
Line of Business Policy Applies to:	All lines of business

Background

Camzyos™ is a cardiac myosin inhibitor 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
mavacamten (Camzyos™)	Obstructive hypertrophic cardiomyopathy	**Initiation:** 5 mg orally once daily if left ventricular ejection fraction (LVEF) ≥ 55%. May adjust dose every 4 weeks. <u>At Week 4</u>: • If Valsalva left ventricular outflow tract (LVOT) gradient is < 20 mmHg, down-titrate to 2.5 mg orally once daily. • If Valsalva LVOT gradient is ≥ 20 mmHg, maintain 5 mg daily dose. <u>At Week 8:</u> • If Valsalva LVOT gradient is ≥ 20 mmHg, maintain current dose until Week 12. • If Valsalva LVOT gradient is < 20 mmHg and current dose is 2.5 mg daily, withhold drug and re-evaluate at Week 12. • If Valsalva LVOT gradient is < 20 mmHg and current dose is 5 mg daily, down-titrate to 2.5 mg daily until Week 12. **Maintenance (at Week 12 + every 12 weeks):** • If LVEF is < 50%, discontinue. Recheck clinical status and echocardiogram (ECHO) every 4 weeks until LVEF ≥ 50%. ○ *Permanently discontinue if LVEF < 50% twice on 2.5mg daily.*	15 mg/day

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose

		• If had dose withheld, restart on 2.5 mg daily if LVEF ≥ 50% and recheck clinical status and ECHO in 4 weeks.
		  ○ At Week 16, if LVEF ≥ 50%, continue with same dose x 8 weeks.
		• 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 mg to 5 mg; 5 mg to 10 mg; 10 mg to 15 mg); recheck clinical status and ECHO 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. Interrupt dose if LVEF is < 50% at any clinic visit.
		• After dose interruption, recheck echocardiogram parameters every 4 weeks until LVEF ≥ 50%; once LVEF ≥ 50%:
		  ○ Restart treatment at next lower daily (mg) dose level (5 mg to 2.5 mg; 10 mg to 5 mg; 15 mg 10 mg; if interrupted at 2.5 mg, restart at 2.5 mg)
		  ○ 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 treatment if LVEF is < 50% twice on 2.5 mg daily.*	

Dosage Forms

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

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

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

1. Diagnosis of obstructive HCM;
2. Member has New York Heart Association (NYHA) Class II to III symptoms;
3. Prescribed by or in consultation with a cardiologist;
4. Age ≥ 18 years;
5. Member has a left ventricular ejection fraction (LVEF) ≥ 55%;
6. Member has Valsalva left ventricular outflow teact (LVOT) ≥ 50 mmHg at rest or with provocation;
7. Trial and failure of all of the following at up to maximally indicated doses, unless clinically significant adverse effects are experienced, or all are contraindicated (a or b):
   a. Beta-blocker (e.g., atenolol, nadolol);
   b. Calcium channel blocker (e.g., verapamil, diltiazem);
8. Member is not currently treated or planning to be treated with disopyramide, ranolazine, or a combination of beta blockers and calcium channel blockers;
9. Dose does not exceed 15 mg per day.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Obstructive Hypertrophic Cardiomyopathy (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member has a left ventricular ejection fraction (LVEF) ≥ 55%;
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose does not exceed 15 mg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
ECHO: echocardiogram
HCM: Hypertrophic Cardiomyopathy
LVOT: left ventricular outflow tract
LVEF: left ventricular ejection fraction
FDA: Food and Drug Administration
NYHA: New York Heart Association

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
atenolol (Tenormin®)	50-100 mg orally once daily	100 mg/day
nadolol (Corgard®)	10-240 mg orally once daily	240 mg/day
verapamil (Calan SR®, Verelan®, Verelan® PM)	80 to 120 mg orally every 8 hours	Calan®, Calan SR®, Verelan®: 480 mg/day Verelan® PM: 540 mg/day orally
diltiazem (Cardizem®; Cardizem® CD; Cardizem® LA; Cartia XT®; Dilt-XR; Matzim® LA; Taztia XT®; Tiadylt® ER; Tiazac®)	Immediate release: 30 mg orally 4 times daily Extended release: 120-180 mg orally once daily	Immediate release: 360 mg/day Extended release: 360-540 mg/day

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s)*:
  - Moderate to strong CYP2C19 inhibitors or strong CYP3A4 inhibitors;
  - Moderate to strong CYP2C19 inducers or moderate to strong CYP3A4 inducers.

  *Contraindications listed reflect direct statements made in the manufacturer's package insert; for additional uses, warnings, and precautions, please refer to clinical guidelines.

- Boxed Warning(s):
  - Camzyos™ can cause heart failure due to systolic dysfunction;
  - Echocardiogram assessments of LVEF required before and during Camzyos™ use;
  - Initiation in patients with LVEF <55% not recommended. Interrupt if LVEF < 50% or if worsening clinical status;
  - Certain CYP450 inhibitors and inducers are contraindicated in patients taking Camzyos™ because of an increased risk of heart failure;
  - Camzyos™ is available only through a restricted program called the Camzyos™ REMS Program.

APPENDIX D: General Information

- Drug interactions leading to heart failure or loss of effectiveness: Advise patients of the potential for drug interactions including with over-the-counter medications.
- Embryo-Fetal Toxicity: May cause fetal harm. Advise females of reproductive potential to use effective contraception until 4 months after the last dose. Use a contraceptive not affected by CYP450 enzyme induction or add nonhormonal contraception.

References

1. Camzyos™ Prescribing Information. Brisbane, CA: MyoKardia, Inc. (a subsidiary of Bristol Myers Squibb); September 2022. Available at: https://packageinserts.bms.com/pi/pi_camzyos.pdf. Accessed June 2, 2023
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3. Clinical Pharmacology. Tampa, FL: Elsevier, 2023. Available at: https://www.clinicalkey.com. Accessed June 2, 2023.
4. Camzyos. Lexi-Drugs. Lexicomp. Wolters Kluwer. Hudson, OH. Available at: https://online.lexi.com/lco/action/home.

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5. 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. Circulation. 2020 Dec 22;142(25):e558-e631. Doi: 10.1161/CIR.0000000000000937. Epub 2020 Nov 20. Erratum in: Circulation. 2020 Dec 22;142(25):e633. PMID: 33215931. Accessed June 29, 2023.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	06/20/2022	07/18/2022
Policy was reviewed: 1. Dosing information, dosing regimen updated to simplify wording. 2. Initial approval criteria I.A.6 was updated from "resting oxygen saturation ≥ 90%" to "LVOT ≥ 50 mmHg at rest or with provocation". 3. Continued approval criteria II.A.2 was updated from "Documents supporting improvement of mixed peakVO_2 by ≥1.5 mL/kg/min plus at least one NYHA class reduction or a ≥3.0 mL/kg/min peakVO_2 increase without NYHA class worsening" to "Member has a left ventricular ejection fraction (LVEF) ≥ 55%". 4. Appendix A was updated to add ECHO. 5. References were reviewed and updated.	06/29/2023	07/13/2023