

PHARMACY COVERAGE GUIDELINE

CAMZYOS™ (mavacamten) oral Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):

- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively “Service”) is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider’s judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member’s benefit plan; and
- Is subject to change as new information becomes available.

Scope

- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance

- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The “Criteria” section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member’s benefit plan.
- The “Description” section describes the Service.
- The “Definition” section defines certain words, terms or items within the policy and may include tables and charts.
- The “Resources” section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the [request form](#) and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for CAMZYOS (mavacamten)

Criteria for Initial Therapy:

Prescriber Qualifications

- Prescribed by or in consultation with a Cardiologist

Indication

- Symptomatic New York Heart Association (NYHA) Class II–III obstructive hypertrophic cardiomyopathy (HCM)

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Age Requirement

- 18 years or older

Baseline Clinical Evaluation

- Echocardiogram shows left ventricular ejection fraction (LVEF) is at least 55%
- Left ventricular outflow tract (LVOT) peak gradient is at least 50 mmHg at rest or with exertion
- Unexplained left ventricular hypertrophy present with maximal left ventricular wall thickness of at least 15 mm (or at least 13 mm if there is a history of familial HCM)
- Negative pregnancy test in a woman of childbearing potential

Alternative Therapies

- Failure (trial for at least three months duration), contraindication, intolerance for
 - **ONE** of the following beta-blockers: bisoprolol, carvedilol, or metoprolol
 - **ONE** of the following calcium channel blockers: verapamil or diltiazem
- Disopyramide combined with either:
 - **ONE** beta-blocker (from above)
 - **ONE** calcium channel blocker (from above)

Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. Note: Any failure, contraindication, or intolerance to the generic drugs should be reported to the U.S. Food and Drug Administration (FDA)

Safety

- No FDA-label contraindications such as:
 - Moderate to strong CYP2C19 inhibitors
 - Moderate to strong CYP2C19 inducers
 - Strong CYP3A4 inhibitors
 - Moderate to strong CYP3A4 inducers
- No concomitant use with any of the following:
 - Disopyramide
 - Ranolazine
 - Verapamil with a beta blocker
 - Diltiazem with a beta blocker
- Does not have any of the following:
 - NYHA Class IV
 - Amyloidosis
 - Fabry disease
 - Noonan syndrome with left ventricular hypertrophy
 - Severe hepatic impairment (Child-Pugh Class C)

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- Severe renal impairment (estimated glomerular filtration rate: 15 to 30 mL/min/1.73m²) and kidney failure (estimated glomerular filtration rate: less than 15 mL/min/1.73m²; including dialysis)

Documentation Requirements

- A completed request form must be submitted, including:
 - Chart notes
 - Lab results (LVEF, pregnancy test)
 - Supporting clinical documentation

Initial approval duration:

- 6 months OR end of plan year
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Criteria for Continuation of Therapy (renewal therapy)

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualifications

- Continues to be seen by or in consultation with a Cardiologist

Clinical Response

- Positive clinical response defined as **THREE** of the following:
 - Decrease in LVOT gradient of at least 30 mmHg with valsalva maneuvers
 - Maintains LVEF of at least 50%
 - Improvement in at least one NYHA class or no worsening in NYHA class
 - Improvement of peak oxygen consumption (pVO₂) by at least 1.5 mL/kg/min plus improvement in NYHA class of one
 - Improvement of peak oxygen consumption (pVO₂) by at least 3 mL/kg/min plus no worsening in NYHA class

Adherence

- Adherence to the prescribed therapy regimen has been documented and is enrolled in the CAMZYOS REMS PROGRAM

Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- No development of contraindications or significant adverse drug effects including:
 - LVEF less than 50%
 - Heart failure symptoms or worsening clinical status
 - Moderate to strong CYP2C19 inhibitors

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- Moderate to strong CYP2C19 inducers
- Strong CYP3A4 inhibitors
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- No concomitant use with any of the following:
 - Disopyramide
 - Ranolazine
 - Verapamil with a beta blocker
 - Diltiazem with a beta blocker
- Does not have any of the following:
 - NYHA Class IV
 - Amyloidosis
 - Fabry disease
 - Noonan syndrome with left ventricular hypertrophy
 - Severe hepatic impairment (Child-Pugh Class C)
 - Severe renal impairment (estimated glomerular filtration rate: 15 to 30 mL/min/1.73m²) and kidney failure (estimated glomerular filtration rate: less than 15 mL/min/1.73m²; including dialysis)

Additional Requirements

- Has not had two LVEF determinations of less than 50% while on a dose of 2.5 mg daily

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications
2. Off-Label Use of Cancer Medications

Description:

Camzyos (mavacamten) 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.

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Camzyos (mavacamten) is an allosteric and reversible inhibitor selective for cardiac myosin. Mavacamten modulates the number of myosin heads that can enter “on actin” (power-generating) states, thus reducing the probability of force-producing (systolic) and residual (diastolic) cross-bridge formation. Excess myosin actin cross-bridge formation and dysregulation of the super-relaxed state are mechanistic hallmarks of HCM. Mavacamten shifts the overall myosin population towards an energy-sparing, recruitable, super-relaxed state. In HCM individuals, myosin inhibition with mavacamten reduces dynamic left ventricular outflow tract (LVOT) obstruction and improves cardiac filling pressures.

HCM is a genetically determined cardiomyopathy that typically manifests as left ventricular hypertrophy (LVH). LVH results in structural and functional abnormalities that can produce a variety of symptoms that include dyspnea, chest discomfort, palpitations, and syncope.

Echocardiographic evidence of an LVOT gradient ≥ 30 mmHg at rest or with exertion caused by systolic anterior motion of the mitral valve defines the presence of obstructive HCM. Symptoms of LVOT obstruction occur when the LVOT gradient is ≥ 50 mmHg at rest or with provocation. Individuals with HCM who have symptoms that may be due to obstruction but have an LVOT gradient <50 mmHg at rest, should have exercise echocardiography (or other provocative maneuvers) performed to assess for a provokable gradient. Despite the presence of LVOT obstruction, there is no predictable correlation between the degree of LVOT obstruction and symptoms.

Mavacamten should only be use in individuals with an LVEF $\geq 55\%$ who do not have NYHA class IV heart failure symptoms. Symptoms of HCM are those that are related to heart failure (HF), chest pain, or arrhythmias. A clinical diagnosis of HCM is confirmed when unexplained increased left ventricular (LV) wall thickness of ≥ 15 mm is imaged. However, a wall thickness of ≥ 13 mm may also be considered diagnostic of HCM, when discovered in an individual who has a family member with HCM.

In 2020, the American Heart Association (AHA) and the American College of Cardiology (ACC) published guidelines for the diagnosis and treatment of individuals with HCM. For symptomatic individuals with obstructive HCM attributable to LVOT obstruction, non-vasodilating beta blockers (e.g., atenolol, bisoprolol, metoprolol, nadolol, propranolol) are recommended titrated to effectiveness or maximally tolerated doses. In individuals for whom beta blockers are not effective or not tolerated, a switch to non-dihydropyridine calcium channel blockers (CCBs e.g., verapamil, diltiazem) is recommended. If the individual continues to have persistent severe symptoms despite beta blocker therapy or CCBs, either adding disopyramide in combination with one of the other drugs is recommended or septal reduction therapy (surgical myectomy or alcohol septal ablation). The guideline also recommends discontinuing medications that may promote outflow tract obstruction such as pure vasodilators (e.g., dihydropyridine CCBs, angiotensin converting enzyme inhibitors, angiotensin receptor blockers) and high-dose diuretics. However, use of low-dose diuretics added to other first-line medications, may be useful for individuals with persistent dyspnea or congestive symptoms.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
[MedWatch Forms for FDA Safety Reporting | FDA](#)

Some examples of Cytochrome P450 Interactions: (Not a complete list)

CYP2C19			
Strong Inducer	Moderate Inducer	Strong Inhibitor	Moderate Inhibitor

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rifampin	carbamazepine, dabrafenib, enzalutamide, letermovir, phenytoin derivatives, Saint John's wort, tipranavir/ritonavir	delavirdine, fluconazole, fluvoxamine, ticlopidine	armodafinil, cimetidine, eslicarbazepine, esomeprazole, felbamate, fluoxetine, isoniazid, modafinil, omeprazole, oxcarbazepine, voriconazole
CYP3A4			
Strong Inducer	Moderate Inducer	Strong Inhibitor	Moderate Inhibitor
carbamazepine, phenobarbital, phenytoin derivatives, primidone, rifabutin, rifampin, rifapentine, rufinamide, Saint John's wort	armodafinil, bexarotene, bosentan, dabrafenib, deferasirox, dexamethasone, efavirenz, modafinil, nafcillin, nevirapine, oxcarbazepine	clarithromycin, isoniazid, itraconazole, ketoconazole, nefazodone, nelfinavir, posaconazole, ritonavir, telaprevir, telithromycin, tipranavir/ritonavir, voriconazole	amiodarone, aprepitant, cyclosporine, diltiazem, dronedarone, erythromycin, fluconazole, fluvoxamine, grapefruit juice, isavuconazonium, netupitant, verapamil, zafirlukast

Resources:

Camzyos (mavacamten) product information, revised by Myokardia, Inc. 04-2024. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed February 18, 2025.

Maron MS. Hypertrophic cardiomyopathy: Clinical manifestations, diagnosis, and evaluation. In: UpToDate, McKenna WJ, Dardas TF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Literature current through January 2025. Topic last updated October 04, 2022. Accessed February 28, 2025.

Maron MS. Hypertrophic cardiomyopathy: Management of patients without outflow tract obstruction. In: UpToDate, McKenna WJ, Dardas TF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Literature current through January 2025. Topic last updated May 20, 2024. Accessed February 28, 2025.

Maron MS. Hypertrophic cardiomyopathy: Management of patients with outflow tract obstruction. In: UpToDate, McKenna WJ, Dardas TF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Literature current through January 2025. Topic last updated July 31, 2024. Accessed February 28, 2025.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT03470545: A Randomized, Double Blind, Placebo Controlled Clinical Study to Evaluate Mavacamten (MYK-461) in adults with Symptomatic Obstructive Hypertrophic Cardiomyopathy. Available from: <http://clinicaltrials.gov>. Last update posted October 04, 2021. Last verified May 2020. Accessed February 22, 2024.

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;142:e558–e631. Accessed February 28, 2025.