BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

**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 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.

## Criteria:

➢ **Criteria for initial therapy:** Camzyos (mavacamten) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Cardiologist
2. Individual is 18 years of age or older
3. Individual has a confirmed diagnosis of symptomatic New York Heart Association (NYHA) Class II–III obstructive hypertrophic cardiomyopathy (HCM)
4. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
    a. Echocardiogram shows left ventricular ejection fraction (LVEF) is at least 55%

ORIGINAL EFFECTIVE DATE: 05/19/2022 | ARCHIVE DATE: | LAST REVIEW DATE: 05/15/2025 | LAST CRITERIA REVISION DATE: 05/15/2025

b. Left ventricular outflow tract (LVOT) peak gradient is at least 50 mmHg at rest or with exertion
c. Unexplained left ventricular hypertrophy present with maximal left ventricular wall thickness of ≥ 15 mm (or ≥ 13 mm if there is a history of familial hypertrophic cardiomyopathy)
d. Negative pregnancy test in a woman of childbearing potential

5. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate for a drug from **EACH** of the following:
   a. **ONE** of the following beta-blockers: bisoprolol, carvedilol, or metoprolol
   b. **ONE** of the following calcium channel blockers: verapamil or diltiazem
   c. Disopyramide combined with **either:**
      i. **ONE** beta-blocker (from "a")
      ii. **ONE** calcium channel blocker (from "b")

7. There are **NO** FDA-label contraindications such as:
   a. Concurrent use of moderate to strong CYP2C19 inhibitors (see Definitions section)
   b. Concurrent use of moderate to strong CYP2C19 inducers (see Definitions section)
   c. Concurrent use of strong CYP3A4 inhibitors (see Definitions section)
   d. Concurrent use of moderate to strong CYP3A4 inducers (see Definitions section)

8. Requested agent will not be used in combination with **ANY** of the following:
   a. Disopyramide
   b. Ranolazine
   c. Verapamil with a beta blocker
   d. Diltiazem with a beta blocker

9. Individual does not have **ANY** of the following:
   a. New York Heart Association (NYHA) Class IV
   b. Amyloidosis
   c. Fabry disease
   d. Noonan syndrome with left ventricular hypertrophy
   e. Severe hepatic impairment (Child-Pugh Class C)
   f. Severe (eGFR: 15 to 30 mL/min/1.73m$^2$) renal impairment and kidney failure (eGFR: less than 15 mL/min/1.73m$^2$; including individuals on dialysis)

**Initial approval duration**: 6 months

- **Criteria for continuation of coverage (renewal request):** Camzyos (mavacamten) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Cardiologist

2. Individual's condition has responded while on therapy with response defined as **THREE** of the following:
    a. A decrease in LVOT gradient of at least 30 mmHg with valsalva maneuvers
    b. Maintains LVEF of at least 50%
    c. Improvement in at least one NYHA class or no worsening in NYHA class
    d. Improvement of peak oxygen consumption (pVO2) by at least a 1.5 mL/kg/min plus improvement on NYHA class of one
    e. Improvement peak oxygen consumption (pVO2) by at least a 3 mL/kg/min plus no worsening in NYHA class

3. Individual has been adherent with the medication and is enrolled in the CAMZYOS REMS PROGRAM

4. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use as follows:
    a. Contraindications as listed in the criteria for initial therapy section
    b. Significant adverse effect such as:
        i. LVEF is less than 50%
        ii. Experiencing heart failure symptoms or worsening clinical status

6. Individual does not have **ANY** of the following:
    a. New York Heart Association (NYHA) Class IV
    b. Amyloidosis
    c. Fabry disease
    d. Noonan syndrome with left ventricular hypertrophy
    e. Severe hepatic impairment (Child-Pugh Class C)

7. Requested agent will not be used in combination with **ANY** of the following:
    a. Disopyramide
    b. Ranolazine
    c. Verapamil with a beta blocker
    d. Diltiazem with a beta blocker

8. Individual has not had two LVEF of less than 50% determinations while on a dose of 2.5 mg daily

**Renewal duration**: 12 months

- 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 a Non-Cancer Medication**

2. **Off-Label Use of a Cancer Medication**

**PHARMACY COVERAGE GUIDELINE**

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

**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.

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 provocable 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 ≥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.

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## 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 |
| 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.