mavacamten (Camzyos™)

Policy # 00812
Original Effective Date: 12/12/2022
Current Effective Date: 08/12/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider mavacamten (Camzyos™)‡ for the treatment of obstructive hypertrophic cardiomyopathy to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for mavacamten (Camzyos) will be considered when the following criteria are met:

Initial

- Patient is 18 years of age or older; AND
- Patient has a diagnosis of obstructive hypertrophic cardiomyopathy; AND
- Patient is a New York Heart Association (NYHA) Class II or III; AND
- Patient weighs 45 kg (99 lb) or more; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has maximal left ventricular wall thickness greater than or equal to 15 mm OR patient has familial hypertrophic cardiopathy and maximal left ventricular wall thickness greater than or equal to 13 mm; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has a peak left ventricular outflow tract gradient greater than or equal to 50 mmHg (at rest or after provocation [Valsalva maneuver or post exercise]); AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

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- Patient has a left ventricular ejection fraction greater than or equal to 55%; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has a resting oxygen saturation greater than or equal to 90%; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has tried and failed (e.g., intolerance or inadequate response) therapy with beta blockers (metoprolol, propranolol, atenolol) and/or calcium channel blockers (diltiazem, verapamil) unless there is clinical evidence or patient history that suggests the use of these agents will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient will not be using mavacamten (Camzyos) in combination with disopyramide or ranolazine; AND
- Patient will not be using a combination of BOTH a beta blocker (metoprolol, propranolol, atenolol) AND a non-dihydropyridine calcium channel blocker (diltiazem, verapamil) along with Camzyos.

Continuation

- Patient has an initial authorization; AND
- Patient has a left ventricular ejection fraction greater than or equal to 50%; AND
- Patient has experienced beneficial clinical response with Camzyos. (Beneficial clinical responses include improved peak oxygen consumption/mixed venous oxygen tension; decreases in left ventricular outflow tract gradient; reductions in N-terminal pro-B-type natriuretic peptide levels; decreased high-sensitivity cardiac troponin I levels; reduced ventricular mass index; a reduction in maximum left atrial volume index; improvement in symptoms associated with obstructive hypertrophic cardiomyopathy).
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

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When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of mavacamten (Camzyos) when the patient does not weigh 45 kg or more to be **not medically necessary.****

Based on review of available data, the Company considers the use of mavacamten (Camzyos) when the patient does not have maximal left ventricular wall thickness greater than or equal to 15 mm OR patient does not have familial hypertrophic cardiopathy and maximal left ventricular wall thickness greater than or equal to 13 mm to be **not medically necessary.****

Based on review of available data, the Company considers the use of mavacamten (Camzyos) when the patient does not have a peak left ventricular outflow tract gradient greater than or equal to 50 mmHg to be **not medically necessary.****

Based on review of available data, the Company considers the use of mavacamten (Camzyos) when the patient does not have a left ventricular ejection fraction greater than or equal to 55% to be **not medically necessary.****

Based on review of available data, the Company considers the use of mavacamten (Camzyos) when the patient does not have resting oxygen saturation greater than or equal to 90% to be **not medically necessary.****

Based on review of available data, the Company considers the use of mavacamten (Camzyos) when the patient has not tried and failed (e.g., intolerance or inadequate response) therapy with beta blockers (metoprolol, propranolol, atenolol) and/or calcium channel blockers (diltiazem, verapamil) to be **not medically necessary.****

For continuation requests: Based on review of available data, the Company considers the use of mavacamten (Camzyos) when the patient has not experienced a beneficial clinical response to be **not medically necessary.****

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When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of mavacamten (Camzyos) for any non-FDA approved indication to be **investigational.***

Based on review of available data, the Company considers the use of mavacamten (Camzyos) when the patient selection criteria are not met (EXCEPT those denoted as **not medically necessary****) to be **investigational.***

Background/Overview

Camzyos is a cardiac myosin inhibitor indicated for the treatment of adults with symptomatic NYHA class II-III obstructive hypertrophic cardiomyopathy (HCM) to improve functional capacity and symptoms. It is available as 2.5 mg, 5 mg, 10 mg, and 15 mg capsules. Dosing of Camzyos is individualized and based on clinical status and echocardiographic assessment of patient response. Treatment with Camzyos should only be initiated if the patient's LVEF is greater than or equal to 55%. Algorithms for initiation and maintenance therapy with Camzyos, as well as monitoring, can be found in the package insert. Treatment with Camzyos should be interrupted if the patient's LVEF goes below 50% and should be permanently discontinued if the patient's LVEF is less than 50% on two occasions while taking a dose of 2.5 mg daily.

Hypertrophic cardiomyopathy is a complex myocardial disorder in which the walls of the heart muscle thicken. In this condition, the left ventricle becomes stiff, which makes it more difficult for the heart to normally expand and fill with blood, and the amount of blood that the left ventricle can hold and pump is reduced. The heart muscle can also pump with too much force in this condition. In patients with hypertrophic cardiomyopathy, the path for blood flow out of the heart can narrow which restricts the amount available to the rest of the body. Many patients with hypertrophic cardiomyopathy have obstructive disease in which the path for blood flow out of the heart can narrow and the output to the rest of the body may be restricted which is referred to as left ventricular outflow tract obstruction. This can force the heart to pump harder to overcome the obstructive forces. Treatment for this condition consists of therapies such as beta blockers, non-dihydropyridine

calcium channel blockers, and disopyramide, which help to ease the symptoms and prevent complications associated with this condition. While Camzyos is the first medication approved for obstructive HCM, treatment guidelines currently recommend the therapies mentioned above as studies are still ongoing and long-term benefit with Camzyos has not been established at the time this policy was written.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Camzyos was approved in April 2022 and is indicated for the treatment of adults with symptomatic NYHA class II-III obstructive hypertrophic cardiomyopathy (HCM) to improve functional capacity and symptoms.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Explorer-HCM

The efficacy of Camzyos was evaluated in a Phase 3, double-blind, randomized, placebo-controlled, multicenter, international, parallel-group trial in 251 adults with symptomatic NYHA class II and III obstructive HCM, LVEF ≥55%, and Valsalva left ventricular outflow tract (LVOT) peak gradient ≥50 mmHg at rest or with provocation.

Patients were randomized in a 1:1 ratio to receive either a starting dose of 5 mg of Camzyos or placebo once daily for 30 weeks. Treatment assignment was stratified by baseline NYHA functional class, baseline use of beta blockers, and type of ergometer (treadmill or exercise bicycle).

The primary composite functional endpoint, assessed at 30 weeks, was defined as the proportion of patients who achieved either improvement of mixed venous oxygen tension (pVO2) by ≥1.5 mL/kg/min plus improvement in NYHA class by at least 1 or improvement of pVO2 by ≥3.0

mL/kg/min plus no worsening in NYHA class. A greater proportion of patients met the primary endpoint at week 30 in the Camzyos group compared to the placebo group (37% vs. 17%, respectively, p=0.0005).

The treatment effects of Camzyos on LVOT obstruction, functional capacity, and health status were assessed by change from baseline through week 30 in post-exercise LVOT peak gradient, change in pVO2, proportion of patients with improvement in NYHA class, Kansas City Cardiomyopathy Questionnaire-23 (KCCQ-23) Clinical Summary Score (CSS), and Hypertrophic Cardiomyopathy Symptom Questionnaire (HCMSQ) Shortness of Breath (SoB) domain score. At week 30, patients receiving Camzyos had greater improvement compared to the placebo group across all secondary endpoints. The post-exercise LVOT gradient decreased by a mean of -47 mmHg (baseline of 86 mmHg) vs. -10 mmHg (baseline of 84 mmHg) for Camzyos vs. placebo, respectively ($P < 0.0001$). The pVO2 increased by 1.4 mL/kg/min for Camzyos vs. a decrease of -0.1 mL/kg/min for placebo ($P < 0.0006$). NYHA class improved by at least one in 65% of patients given Camzyos vs. 31% given placebo ($P < 0.0001$).

Valor-HCM
The efficacy of Camzyos was evaluated in a Phase 3, double-blind, randomized, 16-week placebo-controlled trial in 112 patients (mean age of 60 years; 51% men; 93% ≥ NYHA class III) randomized 1:1 to receive treatment with Camzyos or placebo. At baseline, all patients had symptomatic obstructive HCM and were SRT eligible. Patients with severely symptomatic drug-refractory obstructive HCM (including 33% on any combination of beta-blocker, calcium channel blocker and/or disopyramide; 20% were on disopyramide alone or in combination with other treatment), and NYHA class III/IV or class II with exertional syncope or near syncope, were included in the study. Patients were required to have LVOT peak gradient ≥50 mmHg at rest or with provocation, and LVEF ≥60%. Patients must have been referred or under active consideration within the past 12 months for SRT and actively considering scheduling the procedure. Patients received Camzyos (2.5 mg, 5 mg, 10 mg, or 15 mg) or a placebo capsule once daily for 16 weeks. Dose adjustment was based on clinical echocardiogram parameters.

Camzyos was shown to be superior to placebo in reducing the proportion of patients who met the primary endpoint (the composite of patient decision to proceed with SRT prior to or at week 16 or

met SRT eligibility (LVOT gradient of ≥ 50 mmHg and NYHA class III-IV, or class II with exertional syncope or near syncope) at week 16 (18% vs. 77%, respectively, p<0.0001).

The treatment effects of Camzyos on LVOT obstruction, functional capacity, and health status were assessed by change from baseline through week 16 in post-exercise LVOT gradient, proportion of patients with improvement in NYHA class, and KCCQ-23 CSS. At week 16, patients receiving Camzyos had greater improvement compared to the placebo group across secondary endpoints. The post-exercise LVOT gradient decreased by a mean of -39 mmHg vs. -2 mmHg for Camzyos vs. placebo, respectively (P < 0.0001). NYHA class improved by at least one in 63% of patients given Camzyos vs. 21% given placebo (P < 0.0001).

References

1. Camzyos [package insert]. MyoKardia, Inc. Brisbane, California. Updated April 2024.
2. Camzyos Drug Evaluation. Express Scripts. May 2022.

Policy History

Original Effective Date: 12/12/2022
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11/03/2022	Medical Policy Committee review
11/09/2022	Medical Policy Implementation Committee approval. New policy.
11/02/2023	Medical Policy Committee review
11/08/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged
07/02/2024	Medical Policy Committee review
07/10/2024	Medical Policy Implementation Committee approval. Provided clarification in eligibility criteria that Camzyos should not be used in combination with both a beta blocker and non-dihydropyridine calcium channel blocker. Updated study information to include trial data from Valor-HCM trial. Removed Not Medically Necessary statements regarding the use of Camzyos in combination with ranolazine, disopyramide, or a non-dihydropyridine calcium channel blocker with a beta blocker as this should be denied as Investigational if not met.

Next Scheduled Review Date: 07/2025

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*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.