Drug Coverage Policy

Effective Date.....9/1/2025
Coverage Policy Number.....IP0480
Policy Title..... Camzyos

Cardiology – Camzyos

- Camzyos® (mavacamten capsules - MyoKardia/Bristol Myers Squibb)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

OVERVIEW

Camzyos, a cardiac myosin inhibitor, is indicated for the treatment of symptomatic New York Heart Association Class (NYHA) II to III **obstructive hypertrophic cardiomyopathy** in adults to improve functional capacity and symptoms.

Disease Overview

Hypertrophic cardiomyopathy (HCM) is a complex myocardial disorder in which the walls of the heart muscle, more specifically the left ventricle, are thickened or hypertrophied.[2-5] The condition is inherited in an autosomal dominant pattern. The estimated prevalence is one in 200 to 500 adults. Patients of any age can be impacted. However, many patients may be undiagnosed or asymptomatic. Diagnoses is usually by echocardiographic or magnetic resonance imaging which

reveals a hypertrophied, nondilated left ventricle without another identifiable cardiac, systemic, metabolic or syndromic disease. The left ventricle becomes stiff, which makes it more difficult for the heart to normally expand and fill with blood. The amount of blood that the left ventricle can hold and pump throughout the body is reduced; the hypertrophied heart muscle may also pump with too much force. Many patients with HCM 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 forces the heart to pump harder to overcome the obstructive forces. Symptoms that are commonly present with HCM include shortness of breath, palpitations, lightheadedness, chest pain, fatigue, and exercise intolerance. Many patients have heart failure, as well as atrial fibrillation or other ventricular arrhythmias. Sudden death may also result. HCM is due to enhanced interactions between two cardiac proteins, actin and myosin. Camzyos works by reducing the number of intersections formed between actin and myosin which leads to more optimized heart relaxation and filling; lessened heart muscle workload during contractions; and improved efficiency in energy utilized for each heartbeat. Before the approval of Camzyos, treatment for obstructive HCM focused on symptomatic relief with medications such as beta blockers, non-dihydropyridine calcium channel blockers (CCBs), and disopyramide. Septal reduction therapy is an option.

Clinical Efficacy

EXPLORER-HCM was a randomized, double-blind, placebo-controlled, parallel-group trial that evaluated Camzyos in over 250 patients with symptomatic NYHA Class II or III obstructive HCM[1,2] Patients had a left ventricular ejection fraction ≥ 55% and a left ventricular outflow tract peak gradient ≥ 50 mmHg (at rest or with provocation [Valsalva maneuver or post exercise]). Unexplained left ventricular hypertrophy was present with maximal left ventricular wall thickness of ≥ 15 mm or ≥ 13 mm if the patient had familial HCM.[2] Approximately 75% of patients were receiving beta blockers and 17% of patients were on CCBs for symptoms. The primary composite functional endpoint, evaluated at 30 weeks, was defined as the proportion of patients who achieved either improvement of mixed venous oxygen tension/peak oxygen consumption (pVO_2) by ≥ 1.5 mL/kg/min plus improvement in NYHA class by at least one or improvement of pVO_2 by ≥ 3.0 mL/kg/min plus no worsening in NYHA class. A greater proportion of patients receiving Camzyos met this composite endpoint compared with patients given placebo (37% vs. 17%, respectively; P = 0.0005). Regarding secondary endpoints, Camzyos led to greater improvements compared with placebo in measures assessing left ventricular outflow tract (LVOT) obstruction, functional capacity, and health status. These parameters were assessed by change from baseline through Week 30 in post-exercise LVOT peak gradient, change in pVO_2, proportion of patients with improvement in NYHA class, Kansas City Cardiomyopathy Questionnaire-23 (KCCQ-23) Clinical Summary Score (CSS), and Hypertrophic Cardiomyopathy Symptoms Questionnaire (HCMSQ) Shortness of Breath domain score.[1,2] At Week 30, there were also reductions in N-terminal pro B-type natriuretic peptide and high-sensitivity cardiac troponin I levels from baseline.[2] Other data are also available.[6]

Guidelines

The American Heart Association and American College of Cardiology, alongside other organizations, published updated guidelines for the diagnosis and treatment of patients with HCM in 2024.[7] For symptomatic patients with obstructive hypertrophic cardiomyopathy attributable to LVOT obstruction, non-vasodilating beta blockers are recommended to be titrated to effectiveness or maximally tolerated doses. In patients for whom beta blockers are not effective or not tolerated, substitution with nondihydropyridine CCBs (e.g., verapamil, diltiazem) is recommended. If patients continue to have severe symptoms despite beta blockers and nondihydropyridine CCBs, adding a myosin inhibitor (i.e., Camzyos) or disopyramide (in combination with an atrioventricular nodal blocking agent), or septal reduction performed at experienced centers is recommended. The guidelines note that Camzyos is only for adult patients. Camzyos is also contraindicated in pregnant patients due to potential teratogenic effects.

Safety
Camzyos has a Boxed Warning regarding the risk of heart failure.[1] The agent may cause heart failure due to systolic dysfunction. Echocardiogram assessment of left ventricular ejection fraction is required before and during Camzyos use. Initiation in patients with a left ventricular ejection fraction < 55% is not recommended. Therapy should be interrupted if left ventricular ejection fraction is less than 50% or if worsening clinical status occurs. Certain cytochrome P450 inhibitors and inducers are contraindicated in patients receiving Camzyos due to an increased risk of heart failure. Camzyos is available only through a restricted program called the Camzyos Risk Evaluation and Mitigation Strategy (REMS) program. Notable requirements include the following:

- Prescribers must be certified by enrolling in the Camzyos REMS program.
- Patients must enroll in the Camzyos REMS program and comply with ongoing monitoring requirements.
- Pharmacies must be certified by enrolling in the Camzyos REMS program and must only dispense to patients who are authorized to receive Camzyos.
- Wholesalers and distributors must only distribute the medication to certified pharmacies.

Coverage Policy

Policy Statement
Prior Authorization is recommended for prescription benefit coverage of Camzyos. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Camzyos as well as the monitoring required for adverse events and long-term efficacy, approval requires Camzyos to be prescribed by a physician who has consulted with or who specializes in the condition.

Camzyos is considered medically necessary when the following criteria are met:

FDA-Approved Indication

1. **Obstructive Hypertrophic Cardiomyopathy.** Approve for the duration noted below if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 8 months if the patient meets ALL of the following (i, ii, iii, iv, v, and vi):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient meets BOTH of the following (a and b):
       - **a)** Patient has at least one symptom associated with obstructive hypertrophic cardiomyopathy; AND
         Note: Examples of symptoms include shortness of breath, chest pain, lightheadedness, fainting, fatigue, and reduced ability to perform physical exercise.
       - **b)** Patient has New York Heart Association Class II or III symptoms of heart failure; AND
         Note: Class II signifies mild symptoms with moderate physical activity and some exercise limitations whereas Class III denotes noticeable symptoms with minimal physical activity and patients are only comfortable at rest.
     - **iii.** Patient with left ventricular hypertrophy meets ONE of the following (a or b):
       - **a)** Patient has maximal left ventricular wall thickness ≥ 15 mm; OR
       - **b)** Patient has familial hypertrophic cardiomyopathy with a maximal left ventricular wall thickness ≥ 13 mm; AND
     - **iv.** Patient has a peak left ventricular outflow tract gradient ≥ 50 mmHg (at rest or after provocation [Valsalva maneuver or post exercise]); AND
     - **v.** Patient has a left ventricular ejection fraction of ≥ 55%; AND

vi. The medication is prescribed by a cardiologist; OR

B) Patient Currently Receiving Camzyos. Approve for 1 year if the patient meets ALL of the following (i, ii, iii, iv, v and vi):

i. Patient has been established on therapy for at least 8 months; AND
Note: A patient who has received < 8 months of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).

ii. Patient is ≥ 18 years of age; AND

iii. Patient meets BOTH of the following (a and b):

a) Currently or prior to starting therapy, patient has or has experienced at least one symptom associated with obstructive hypertrophic cardiomyopathy; AND
Note: Examples of symptoms include shortness of breath, chest pain, lightheadedness, fainting, fatigue, and reduced ability to perform physical exercise.

b) Currently or prior to starting therapy, patient is in or was in New York Heart Association Class II or III heart failure; AND
Note: Class II signifies mild symptoms with moderate physical activity and some exercise limitations whereas Class III denotes noticeable symptoms with minimal physical activity and patients are only comfortable at rest.

iv. Patient has a current left ventricular ejection fraction of ≥ 50%; AND

v. Patient meets ONE of the following (a or b):

a) Patient experienced a beneficial clinical response when assessed by at least one objective measure; OR
Note: Examples 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; and/or a reduction in maximum left atrial volume index.

b) Patient experienced stabilization or improvement in at least one symptom related to obstructive hypertrophic cardiomyopathy; AND
Note: Examples of symptoms include shortness of breath, chest pain, lightheadedness, fainting, fatigue, ability to perform physical exercise, and/or favorable changes in the Kansas City Cardiomyopathy Questionnaire-23 (KCCQ-23) Clinical Summary Score (CSS) or Hypertrophic Cardiomyopathy Symptom Questionnaire (HCMSQ) Shortness of Breath domain scores.

vi. The medication is prescribed by a cardiologist.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Camzyos for any other use is considered not medically necessary. Criteria will be updated as newly published data are available.

References

1. Camzyos® capsules [prescribing information]. Princeton, NJ: MyoKardia/Bristol Myers Squibb; April 2025.

2. Olivotto I, Oreziak A, Barriales-Villa R, et al, for the EXPLORER-HCM study investigators. Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy (EXPLORER-HCM): a randomized, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2020;396(10253):759-769.
3. Maron BJ. Clinical course and management of hypertrophic cardiomyopathy. *N Engl J Med*. 2018;379(7):655-668.
4. Ommen SR, Semsarian C. Hypertrophic cardiomyopathy: a practical approach to guideline directed management. *Lancet*. 2021;398(10316):2102-2108.
5. Burstein Waldman CY, Owens A. A plain language summary of the EXPLORER-HCM study: mavacamten for obstructive hypertrophic cardiomyopathy. *Future Cardiol*. 2021;17(7):1269-1275.
6. Keam SJ. Mavacamten: first approval. *Drugs*. 2022;82:1127-1135.
7. 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. *Circulation*. 2024;149(23): e1239-1311.
8. Mital S, Burke MA, et al. 2020 AHA/ACC guideline for the diagnosis and treatment of patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol*. 2020;76(25):e159-240.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Policy Name Change: Updated** Policy Name from "Mavacamten" to "Cardiology – Camzyos." **Obstructive Hypertrophic Cardiomyopathy. Patient Currently Receiving Camzyos: Added** a requirement that patients should be established on therapy for at least 8 months and added a note stating that a patient who has received < 8 months of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).	09/01/2024
Annual Revision	No criteria changes.	9/1/2025

The policy effective date is in force until updated or retired.