PRIOR AUTHORIZATION POLICY

POLICY: Cardiology – Camzyos Prior Authorization Policy
- Camzyos® (mavacamten capsules – MyoKardia/Bristol Myers Squibb)

REVIEW DATE: 06/05/2024

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 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 be 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 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 forces the heart to pump harder to overcome the obstructive forces. Symptoms that are commonly present with hypertrophic cardiomyopathy include shortness of breath, palpitations, light headedness, 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. Hypertrophic cardiomyopathy 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 approval of Camzyos, treatment for obstructive hypertrophic cardiomyopathy 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 hypertrophic cardiomyopathy.[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 hypertrophic cardiomyopathy.[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

Guidelines have not incorporated Camzyos.

- **Hypertrophic Cardiomyopathy:** In 2020, the American Heart Association and the American College of Cardiology published guidelines for the diagnosis and treatment of patients with hypertrophic cardiomyopathy.[7] For symptomatic patients with obstructive hypertrophic cardiomyopathy attributable to LVOT obstruction, nonvasodilating 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 the patient 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. Also, septal reduction therapy, performed at experienced centers, is an option for selected patients. One of the other key steps in managing symptomatic, obstructive hypertrophic cardiomyopathy is to eliminate medication that may promote outflow tract obstruction like pure vasodilators (e.g., dihydropyridine CCBs, angiotensin converting enzyme inhibitors, angiotensin receptor blockers) and high-dose diuretics. Low-dose diuretics, when added to other first-line medications, may be useful for patients with persistent dyspnea or congestive symptoms.

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.

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 specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Camzyos is recommended in those who meet the following criteria:

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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Camzyos is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Camzyos® capsules [prescribing information]. Princeton, NJ: MyoKardia/Bristol Myers Squibb; April 2024.
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, 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.