Camzyos (mavacamten) Prior Authorization with Quantity Limit Program Summary

POLICY REVIEW CYCLE

Effective Date 10-01-2024

Date of Origin

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Camzyos® (mavacamten) Capsule	Treatment of adults with symptomatic New York Heart Association (NYHA) class II-III obstructive hypertrophic cardiomyopathy (HCM) to improve functional capacity and symptoms		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

HCM	Hypertrophic cardiomyopathy (HCM) is a common genetic heart disease reported in populations globally. Inherited in an autosomal dominant pattern, the distribution is equal by sex, although women are diagnosed less commonly than men. The prevalence of unexplained asymptomatic hypertrophy in young adults in the United States has been reported to range from 1:200 to 1:500. Symptomatic hypertrophy based on medical claims data has been estimated at <1:3000 adults in the United States; however, the true burden is much higher when unrecognized disease in the general population is considered. Clinical evaluation for HCM may be triggered by occurrence of symptoms, a cardiac event, detection of a heart murmur, an abnormal 12-lead electrocardiogram (ECG) identified on routine examinations, or through cardiac imaging during family screening studies.(2)
Efficacy	Mavacamten is a 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. In HCM patients, myosin inhibition with mavacamten reduces dynamic left ventricular outflow tract (LVOT) obstruction and improves cardiac filling pressures.(1) The efficacy of Camzyos was evaluated in EXPLORER-HCM, 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 greater than or equal to 55%, and Valsalva LVOT peak gradient greater than or equal to 50 mmHg at rest or with provocation. Patients on dual therapy with beta blocker and calcium channel blocker treatment or monotherapy with disopyramide or ranolazine were excluded. Patients with a known infiltrative or storage disorder causing cardiac hypertrophy that mimicked obstructive HCM, such as Fabry disease, amyloidosis, or Noonan syndrome with left ventricular hypertrophy, were also excluded. 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 disease severity NYHA functional class, baseline use of beta blockers, and type of ergometer (treadmill or exercise bicycle). Groups were well matched with respect to

	age (mean 59 years), BMI (mean 30 kg/m), heart rate (mean 62 bpm), blood pressure (mean 128/76 mmHg), and race (90% Caucasian). Males comprised 54% of the Camzyos group and 65% of the placebo group. At baseline, approximately 73% of the randomized patients were NYHA class II and 27% were NYHA class III. The mean LVEF was 74%, and the mean Valsalva LVOT gradient was 73 mmHg. About 10% had prior septal reduction therapy, 75% were on beta 2 blockers, 17% were on calcium channel blockers, and 14% had a history of atrial fibrillation. All patients were initiated on Camzyos 5 mg (or matching placebo) once daily, and the dose was periodically adjusted to optimize patient response (decrease in LVOT gradient with Valsalva maneuver) and maintain LVEF greater to or equal to 50%. The primary composite functional endpoint, assessed at 30 weeks, was defined as the proportion of patients who achieved either improvement of mixed peak oxygen consumption (pVO2) by greater than or equal to 1.5 mL/kg/min plus improvement in NYHA class by at least 1 or improvement of pVO2 by greater than or equal to 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).(1)
Safety	Camzyos has a boxed warning for the risk of heart failure. Camzyos reduces left ventricular ejection fraction (LVEF) and can cause heart failure due to systolic dysfunction.(1) Echocardiogram assessments of LVEF are required prior to and during treatment with Camzyos. Initiation of Camzyos in patients with LVEF <55% is not recommended. Interrupt Camzyos if LVEF is <50% at any visit or if the patient experiences heart failure symptoms or worsening clinical status.(1) Concomitant use of Camzyos with certain cytochrome P450 inhibitors or discontinuation of certain cytochrome P450 inducers may increase the risk of heart failure due to systolic dysfunction; therefore, the use of Camzyos is contraindicated with the following:(1) • Moderate to strong CYP2C19 inhibitors or strong CYP3A4 inhibitors • Moderate to strong CYP2C19 inducers or moderate to strong CYP3A4 inducers Because of the risk of heart failure due to systolic dysfunction, Camzyos is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called Camzyos REMS Program.(1)

REFERENCES

Number	Reference
1	Camzyos prescribing information. Bristol Meyers Squibb. June 2023.
2	Ommen SR, Mital S, Burke MA, et al. 2020 AHA/ACC Guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy. *Circulation (New York, NY)*. 2020;142(25). doi:10.1161/cir.0000000000000937

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Camzyos	mavacamten cap	10 MG ; 15 MG ; 2.5 MG ; 5 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Camzyos	Mavacamten Cap	2.5 MG	30	Capsules	30	DAYS			
Camzyos	Mavacamten Cap	5 MG	30	Capsules	30	DAYS			
Camzyos	Mavacamten Cap	10 MG	30	Capsules	30	DAYS			
Camzyos	Mavacamten Cap	15 MG	30	Capsules	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Camzyos	mavacamten cap	10 MG ; 15 MG ; 2.5 MG ; 5 MG	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Camzyos	Mavacamten Cap	10 MG	Commercial ; HIM ; ResultsRx
Camzyos	Mavacamten Cap	15 MG	Commercial ; HIM ; ResultsRx
Camzyos	Mavacamten Cap	2.5 MG	Commercial ; HIM ; ResultsRx
Camzyos	Mavacamten Cap	5 MG	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
PA	**Initial Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. The patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days **OR** B. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed **OR** C. The patient has a diagnosis of symptomatic New York Heart Association (NYHA) class II-III obstructive hypertrophic cardiomyopathy (HCM) AND ALL of the following: 1. The patient has a left ventricular ejection fraction (LVEF) of greater than or equal to 55% **AND** 2. The patient has a left ventricular outflow tract (LVOT) peak gradient greater than or equal to 50 mmHg at rest or with provocation (Valsalva or post-exercise) **AND** 3. The patient does not have a known infiltrative or storage disorder causing cardiac hypertrophy that mimics obstructive HCM (e.g., Fabry

Module	Clinical Criteria for Approval
	disease, amyloidosis, Noonan syndrome with left ventricular hypertrophy) **AND** 4. ONE of the following: A. The patient has tried and had an inadequate response to a beta blocker **OR** B. The patient has an intolerance or hypersensitivity to therapy with beta blockers **OR** C. The patient has an FDA labeled contraindication to ALL beta blockers **AND** 5. ONE of the following A. The patient has tried and had an inadequate response to a calcium channel blocker **OR** B. The patient has an intolerance or hypersensitivity to therapy with calcium channel blockers **OR** C. The patient has an FDA labeled contraindication to ALL calcium channel blockers **OR** D. The patient has another FDA labeled indication for the requested agent and route of administration **AND** 2. ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., cardiologist), or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. Patient has a left ventricular ejection fraction (LVEF) of greater than or equal to 50% **AND** 4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., cardiologist), or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Universal QL	**Quantity limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. The requested quantity (dose) exceeds the program quantity limit AND ONE of the following: A. BOTH of the following:

Module	Clinical Criteria for Approval
	1. The requested agent does NOT have a maximum FDA labeled dose for the requested indication **AND** 2. There is support for therapy with a higher dose for the requested indication **OR** B. BOTH of the following: 1. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** 2. There is support for why the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **OR** C. BOTH of the following: 1. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** 2. There is support for therapy with a higher dose for the requested indication **Length of Approval:** up to 12 months