mavacamten (Camzyos™)

EOCCO POLICY

Policy Type:PA/SP Pharmacy Coverage Policy: EOCCO253

Description

Mavacamten (Camzyos) is an orally administered selective allosteric inhibitor of cardiac myosin ATPase.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
mavacamten (Camzyos)	2.5 mg capsule	Symptomatic NYHA Class II-III obstructive hypertrophic cardiomyopathy (oHCM)	30 capsules/30 days
	5 mg capsule		
	10 mg capsule		
	15 mg capsule		

Initial Evaluation

I. **Mavacamten (Camzyos)** may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, a cardiologist who practices at or consults with a Center of Excellence for hypertrophic cardiomyopathy; **AND**
   C. A diagnosis of **symptomatic NYHA Class II-III obstructive hypertrophic cardiomyopathy (oHCM)** when the following are met:
      1. Provider attestation the member has undergone a comprehensive cardiac workup to diagnose hypertrophic cardiomyopathy (e.g., physical exam, ECG, ECHO, CMR, etc.); **AND**
      2. Provider attestation that baseline obstruction by left ventricular outflow tract (LVOT) gradient is 50 mm Hg or greater; **AND**
      3. Provider attestation that member has NYHA Class II-III symptoms of heart failure, including but not limited to, fatigue, dyspnea, chest pain, palpitations, and syncope; **AND**
   D. Treatment with one of the following regimens has been ineffective, contraindicated, or not tolerated:

1. Beta-blocker (e.g., metoprolol, carvedilol, bisoprolol, etc.) in combination with non-dihydropyridine calcium channel blocker (e.g., verapamil, diltiazem); **OR**
2. Disopyramide in combination with beta-blocker and/or non-dihydropyridine calcium channel blocker.

II. Mavacamten (Camzyos) is considered investigational when used for all other conditions, including but not limited to:
   A. Asymptomatic oHCM
   B. Non-obstructive hypertrophic cardiomyopathy
   C. Dilated, arrhythmogenic or restrictive cardiomyopathy
   D. Cardiac amyloidosis or amyloid cardiomyopathy
   E. Fabry disease

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited improvement or stability of disease [e.g., improved fatigue, dyspnea, chest pain, palpitations, and/or syncope, improved exercise capacity, reduction in LVOT gradient, etc.].

Supporting Evidence

I. Length of authorization for initial approval is six months as clinical benefits of mavacamten were realized in clinical trials as early as 18 weeks and were evaluated at 30 weeks of therapy. Treatment response is expected to be realized at six months duration.
II. Hypertrophic cardiomyopathy (HCM) is a genetic disease of the sarcomeres in cardiac muscle that causes structural and hemodynamic abnormalities of the heart. The disease typically manifests as left ventricular hypertrophy which can lead to LVOT obstruction, diastolic or systolic dysfunction, myocardial ischemia, and mitral regurgitation. Diagnosis of HCM is made by a cardiologist through a comprehensive cardiac workup, including, but not limited to, an electrocardiogram (ECG) and echocardiograph (ECHO) or cardiac magnetic resonance imaging (CMR). The LVOT gradient, an indicator of obstruction, is measured by ECHO, CMR, or invasive

assessment through cardiac catheterization; a value of 30 mm Hg or greater indicates obstruction, while resting or provoked gradients at or greater than 50 mm Hg represent a threshold for septal reduction therapy in patients who have drug-refractory symptoms. Symptoms of HCM include fatigue, dyspnea, chest pain, palpitations, and syncope. Several disease-related complications may also occur, including atrial fibrillation, ventricular arrhythmia, progressive heart failure, and embolic stroke. Given the specialized monitoring this condition entails, a specialist prescriber who practices at or consults with a Center of Excellence designed to care for HCM patients is required.

III. Current guidelines (2014 European Society of Cardiology, 2020 American Heart Association/American College of Cardiology) provide treatment recommendations for HCM based on presence of heart failure symptoms, obstruction, and disease-related comorbidities. Treatment is not recommended for asymptomatic patients. In patients with symptoms of heart failure and obstruction (oHCM), BB (metoprolol, carvedilol, bisoprolol) or non-dihydropyridine calcium CCB (verapamil, diltiazem), monotherapy is recommended. Second-line therapies include combination BB plus CCB, or addition of antiarrhythmic disopyramide to BB and/or CCB. If symptoms persist despite maximal pharmacologic therapy, septal reduction therapy (SRT) is indicated in the form of surgical myectomy or alcohol ablation; SRT may also be considered as an alternative to escalation of pharmacologic therapy if symptoms are severe. In patients with symptomatic HCM without obstruction, treatment includes BB, CCB, ACE-inhibitors and angiotensin-receptor blockers (ARB), and diuretics. Treatment of comorbid atrial fibrillation, ventricular arrhythmia, and thromboembolic risk includes rate and rhythm control strategies and anticoagulants; cardioversion, ICD placement, catheter ablation, and heart transplant may also be used if symptoms are severe or drug-refractory.

- Treatment Summary: In patients refractory to single-agent BB or CCB, escalation to combination BB plus CCB or addition of disopyramide to one or both of these therapies are viable treatment options. Given the known efficacy, established safety profile, and cost effectiveness of these medications, at least one dual therapy regimen is required prior to mavacamten.

IV. The FDA-approval of mavacamten (Camzyos) for oHCM was based on the results of one 30-week international, randomized, double-blind, placebo-controlled Phase 3 study: EXPLORER-HCM. A total of 251 adults with symptomatic oHCM were enrolled, as defined by unexplained left ventricular hypertrophy and at least one peak LVOT gradient 50 mm Hg or greater at rest, after Valsalva, or post-exercise, NYHA class II or III symptoms, left ventricular ejection fraction (LVEF) 55% or greater, and LVOT at screening of 30 mm Hg or greater. Population characteristics were as follows: 73% NYHA class II, 75% on BB, 16.5% on CCB, 14% with atrial fibrillation, 7.5% previous septal reduction procedure, average LVEF 74%. Mavacamten doses were titrated as guided by ECHO to achieve a target left ventricular outflow tract (LVOT) gradient of less than 30 mm Hg and drug plasma concentration of 350-700 ng/mL. The primary endpoint was the number of patients who achieved a clinical response composite at week 30, as defined by a ≥ 1.5 mL/kg/min increase in peak oxygen consumption (pVO^2) and ≥ 1 NYHA class improvement or ≥ 3

mL/kg/min increase in pVO2 and no worsening of NYHA class; this was met in 37% of the mavacamten group compared to 17% of the placebo group, with a clinically meaningful and statistically significant difference relative to placebo. Key secondary endpoints included change from baseline to week 30 in post-exercise left ventricular outflow tract (LVOT) gradient, pVO2, patient reported outcome measure of symptom reduction and physical function (Kansas City Cardiomyopathy Questionnaire-Clinical Summary Score, KCCQ-CSS) and number of patients with at least one NYHA class improvement; all secondary endpoints were met with a clinically meaningful difference relative to placebo. The most common adverse events were nasopharyngitis, dizziness, headache, and dyspnea.

V. Consistent with the mechanism of action, mavacamten (Camzyos) reduces LVEF and can cause systolic dysfunction, which can also be exacerbated when taken with certain cytochrome P450 inhibitors/inducers. As a result, mavacamten carries a warning for heart failure and is only available through a restricted REMS program called Camzyos REMS. ECHO assessments are required before and during treatment with mavacamten (Camzyos).

Investigational or Not Medically Necessary Uses

I. Mavacamten (Camzyos) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Asymptomatic oHCM
   B. Non-obstructive hypertrophic cardiomyopathy
   C. Dilated, arrhythmogenic or restrictive cardiomyopathy
   D. Cardiac amyloidosis or amyloid cardiomyopathy
   E. Fabry disease

References

1. Olivotto I, Oreziak A, Barriales-Villa R, et al. Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy (EXPLORER-HCM): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2020;396(10253):759-769.
2. Ho CY, Olivotto I, Jacoby D, et al. Study design and rationale of EXPLORER-HCM: evaluation of mavacamten in adults with symptomatic obstructive hypertrophic cardiomyopathy. *Circ: Heart Failure*. 2020;13(6).
3. Rader F, Choudhury L, Saberi S, et al. Long-term safety of Mavacamten in patients with obstructive hypertrophic cardiomyopathy: interim results of the MAVA-long term extension (LTE) study. *J AM Coll Cardiol*. 2021;77(18):532.
4. Institute for Clinical and Economic Review. Mavacamten for Hypertrophic Cardiomyopathy: Effectiveness and Value. October 7, 2021. Accessed November 9, 2021. https://icer.org/wp-content/uploads/2021/04/ICER_HCM_Revised_Report_100721.pdf
5. Ommen SR, Mital S, Burke MA, et al. 2020 AHA/ACC guideline for the diagnosis and treatment of patients with hypertrophic cardiomyopathy: executive summary: a report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. *J Am Coll Cardiol*. 2020;76(25):3022-3055.
6. 2014 ESC guidelines on diagnosis and management of hypertrophic cardiomyopathy: the task force for the diagnosis and management of hypertrophic cardiomyopathy of the European Society of Cardiology (ESC). *Eur Heart J*. 2014;35(39):2733-2779.

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created.	02/2022