New Drug Overview

Myqorzo (aficamten)

PDL Category: Cardiovascular Agents

Introduction

Disease Background:

- Hypertrophic cardiomyopathy (HCM) is a cardiovascular disease that is inherited and described by hypertrophy of the left ventricle and having an extensive clinical spectrum that may include sudden death while in the absence of any other cardiac or systemic disease such as hypertension (*Silver et al 2026*). A majority of cases (60-70%) are caused by mutations in one of the sarcomere genes, which encodes parts of the contractile apparatus of the heart (*Maron 2025*).
  - There are two types of HCM governed by the presence or absence of left ventricular outflow tract obstruction, which determines management (*Silver et al 2026*).
    - Approximately 66% of patients have the obstructive form of HCM, while the nonobstructive form transpires in approximately 33% of patients.
      - In patients with obstructive HCM, 50% have basal obstruction, which is described as obstruction at rest with ≥30mmHg gradient, and 50% have a labile obstruction, which is described as obstruction with provocation and <30mmHg gradient at rest but ≥30mmHg gradient with physiologic provocation.
- It is estimated from echocardiographic studies from various ethnic groups globally, that the prevalence of HCM in the general population is 0.2 percent or 1 out of every 500 adults (*Maron 2025*).
- While some patients with HCM are frequently asymptomatic, symptoms of patients with HCM may include chest pain (generally with exertional dyspnea), lightheadedness, and palpitations (*Silver et al 2026*).
- If symptoms due to left ventricular outflow tract obstruction are present, it is recommended to take a non-vasodilating beta-blocker or a non-dihydropyridine calcium channel blocker if patients are intolerant to beta-blockers or they are not effective (*Silver et al 2026*).
- Myqorzo was FDA approved in 2025.

Pharmacology/Usage

- Myqorzo (aficamten) is a cardiac myosin inhibitor. It is an allosteric and reversible inhibitor of cardiac myosin motor activity. Aficamten reduces the force generated by myosin at the cardiac sarcomere, which contributes to the pathophysiology of hypertrophic cardiomyopathy (HCM). In patients with HCM, myosin inhibition with aficamten reduces cardiac contractility and left ventricular outflow tract (LVOT) obstruction.

Indications

Table 1. Food and Drug Administration Approved Indications

Indication	Myqorzo (aficamten)
• For the treatment of adults with symptomatic obstructive hypertrophic cardiomyopathy (oHCM) to improve functional capacity and symptoms.	✔

(Prescribing information: Myqorzo 2026)

- Information on indications, mechanism of action, pharmacokinetics, dosing, safety, and clinical efficacy summary has been obtained from the prescribing information for the individual products, except where noted otherwise.

Dosing and administration

Table 2. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Myqorzo (aficamten)	Tablets: 5mg, 10mg, 15mg, and 20mg. -Swallow tablets whole.	PO	5mg QD. Increase the dose every 2 to 8 weeks by 5mg until a maintenance dose or the maximum recommended dose of 20mg QD is achieved. -The maintenance dose is individualized based on the patient's LVEF and LVOT-G. Recommendations for dosing based on LVEF and LVOT-G are provided in the PI.	• Initiation or up-titration of Myqorzo in patients with LVEF <55% is not recommended. • Patients may develop heart failure while taking Myqorzo. Regular LVEF and Valsalva left ventricular outflow tract gradient (LVOT-G) assessment is needed for titration to achieve an appropriate target Valsalva LVOT-G, while maintaining LVEF ≥50% and avoiding heart failure symptoms. • Perform an echocardiographic assessment 2 to 8 weeks after initiation of treatment or any dose adjustment. After a treatment interruption due to low LVEF, resume treatment, no earlier than 7 days, when LVEF ≥55% and re-initiate dose titration at the starting dose of 5mg. • After maintenance dose established, assess LVEF and Valsalva LVOT-G Q6M, or Q3M in patients with LVEF <55% to ≥50%. Consider monitoring LVEF and adjust dose per PI as needed, in patients with an intercurrent

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
				illness, new arrhythmia, or any other conditions that may impair systolic function.

See the current prescribing information for full details.

Clinical Efficacy Summary

- The efficacy of Myqorzo was assessed in a phase 3, multicenter, randomized, double-blind, placebo-controlled study (SEQUOIA-HCM) that included adults (N=282) with symptomatic New York Heart Association (NYHA) class II and III oHCM, LVEF ≥60%, and resting and post-Valsalva peak LVOT-G ≥30 and ≥50mmHg at screening, respectively. Patients who completed this trial were eligible to participate in an ongoing, open-label, single-arm extension study (FOREST-HCM). Patients with a known infiltrative or storage disorder causing cardiac hypertrophy such as Noonan syndrome, Fabry disease or amyloidosis were excluded.
- Patients were randomized to receive Myqorzo or placebo for 24 weeks. Randomization was stratified by use of beta-blockers (yes or no) and cardiopulmonary exercise testing (CPET) exercise modality (treadmill or bicycle).
  - Patients were started on Myqorzo at a dose of 5mg QD. Doses were individually titrated (or sham-titrated if on placebo) at week 2, 4, and 6 if Valsalva LVOT-G was ≥30mmHg and LVEF was ≥55% in 5mg dose increments up to a maximum dose of 20mg QD. At week 24, in the Myqorzo group, 46% of patients were on the 20mg dose, 35% were on the 15mg dose, 15% were on the 10mg dose, and 4% were on the 5mg dose.
- At baseline, 76% of the randomized patients were NYHA class II and 24% were NYHA class III. The mean peak oxygen uptake (pVO2) by CPET at baseline was 18.5ml/kg/min with 55% using treadmill and 45% using bicycle, respectively. At baseline, the median LVEF was 76%, the mean resting LVOT-G was 55mmHg, the mean Valsalva LVOTG was 83mmHg, and the mean Kansas City Cardiomyopathy Questionnaire-Clinical Summary Score (KCCQ-CSS) was 74. At baseline, 61% of patients were on beta-blockers, 29% were on non-dihydropyridine calcium channel blockers, 13% were on disopyramide, and 15% were not taking any background medication for oHCM.
  - Groups were balanced with respect to age (mean 59 years; range 18 to 84 years), sex (59% male), race (79% White), body mass index (mean 28kg/m^2), heart rate (mean 66 beats per minute [bpm]), and blood pressure (mean 124/74 mmHg).
- In SEQUOIA-HCM, the primary endpoint of change from baseline in pVO2 to week 24 was greater with Myqorzo compared to placebo.
  - Results are presented in the table below, which was adapted from the prescribing information.

Table 3. Efficacy results

pVO2	Myqorzo (N=142)	Placebo (N=140)
Baseline (ml/min/kg), mean	18.4	18.6
Change from baseline to week 24		
Least Squares (LS) mean	1.7	0.0
LS mean difference vs placebo	1.7	
p-value	<0.0001	

- The treatment effects of Myqorzo on health status, functional capacity, and LVOT obstruction were assessed by change in the KCCQ-CSS, proportion of patients with ≥1 class improvement in NYHA functional class, change from baseline in Valsalva LVOT-G, proportion of patients with Valsalva LVOT-G ≤30mmHg, duration of eligibility for septal reduction therapy (SRT), and change in total workload during CPET.
  - Results suggested that at week 24, patients receiving Myqorzo had greater improvement compared to the placebo group across all secondary endpoints.
  - Results are presented in the table below, which was adapted from the prescribing information.

Table 4. Efficacy results

Endpoints	Myqorzo (N=142)	Placebo (N=140)	LS mean difference	p-value
Mean Change from baseline in KCCQ-CSS				
Week 12	11.1	4.0	7.0	<0.0001
Week 24	11.6	4.3	7.3	<0.0001
Mean Change from baseline in Valsalva LVOT-G (mmHg)				
Week 12	-45.0	2.7	-47.7	<0.0001
Week 24	-46.7	2.2	-48.8	<0.0001
Mean Duration of SRT Eligibility				
Days spent SRT-eligible during 24 weeks of treatment	35	113	-78	<0.0001
Mean Change from baseline in Total Workload (Watts) during CPET				
Week 24	13.1	0.9	12.2	<0.0001
Endpoints	**Myqorzo (N=142)**	**Placebo (N=140)**	**Odds Ratio**	**p-value**
Proportion of patients with ≥1 NYHA Class Improvement				
Week 12	69	25	OR 4.6	<0.0001
Week 24	83	34	OR 4.4	<0.0001
Proportion of patients with Valsalva LVOT-G <30 (mmHg)				
Week 12	73	8	OR 16.9	<0.0001
Week 24	70	5	OR 22.9	<0.0001

- A 2025 head-to-head, phase 3, double-blind, double-dummy, randomized trial that compared aficamten plus placebo (in place of metoprolol) with metoprolol plus placebo (in place of aficamten) in adult patients with symptomatic obstructive HCM concludes that aficamten was superior to metoprolol for improving peak oxygen uptake and hemodynamics, while decreasing symptoms (*Garcia-Pavia et al 2025*).

Clinical guidelines

- **2024 American Heart Association (AHA)/American College of Cardiology (ACC)/American Medical Society for Sports Medicine (AMSSM)/Heart Rhythm Society (HRS)/Pediatric & Congenital Electrophysiology Society (PACES)/Society for Cardiovascular Magnetic Resonance (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** (*Ommen et al 2024*).
  - Recommendations for pharmacologic management of symptomatic patients with oHCM:
    - With oHCM and symptoms that are attributable to left ventricular outflow tract obstruction (LVOTO), non-vasodilating beta blockers titrated to efficacy or maximally tolerated doses, are recommended.
    - With oHCM and symptoms attributable to LVOTO where beta blockers are not effective or not tolerated, substitution with non-dihydropyridine calcium channel blockers (eg, verapamil, diltiazem) is recommended.
    - For patients with oHCM with persistent symptoms attributable to LVOTO despite beta-blockers or non-dihydropyridine calcium channel blockers, adding a myosin inhibitor (adult patients only) or disopyramide (in combination with an atrioventricular nodal blocking agent), or septal reduction therapy (SRT) performed at experienced centers is recommended.
    - With oHCM and acute hypotension who do not respond to fluid administration, IV phenylephrine (or other vasoconstrictor with no inotropic activity), alone or in combination with beta-blockers, is recommended.
    - With oHCM and persistent dyspnea with clinical evidence of volume overload and high left-sided filling pressures even with HCM guideline-directed management and therapy (GDMT), careful use of low-dose oral diuretics may be considered.
    - With oHCM, discontinuation of vasodilators (eg, ACE inhibitors, ARBs, dihydropyridine calcium channel blockers) or digoxin may be sensible as these treatments can worsen symptoms caused by dynamic outflow tract obstruction.

Safety summary

- **Contraindications:**
  - With concomitant use of rifampin.

- **Box Warning:**
  - Myqorzo has a box warning regarding risk of heart failure.
    - Myqorzo reduces left ventricular ejection fraction (LVEF) and can cause heart failure due to systolic dysfunction.
    - Echocardiogram assessments are required prior to and during Myqorzo treatment to monitor for systolic dysfunction. Initiation of Myqorzo in patients with LVEF <55% is not recommended. Decrease the dose of Myqorzo if LVEF is <50% and ≥40%. Interrupt the dose of Myqorzo if LVEF <40% or if the patient experiences heart failure symptoms or worsening clinical status due to systolic dysfunction.
    - Because of the risk of heart failure due to systolic dysfunction, Myqorzo is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Myqorzo REMS program.

- **Warnings and precautions:**
  - Myqorzo reduces cardiac contractility, which can reduce LVEF and cause heart failure.
    - Patients who experience a serious intercurrent illness or arrhythmia may be at greater risk of developing systolic dysfunction and heart failure. Asymptomatic LVEF reduction, intercurrent illness, and arrhythmias require additional monitoring considerations.
    - Assess the patient's clinical status and LVEF prior to and regularly during treatment and adjust the Myqorzo dose accordingly. New or worsening arrhythmia, dyspnea, chest pain, fatigue, leg edema, or elevations in N-terminal

pro-B-type natriuretic peptide (NT-proBNP) may be signs and symptoms of heart failure and should prompt an evaluation of cardiac function.
    - Initiation of Myqorzo in patients with LVEF <55% is not recommended.
  - Myqorzo is available only through a restricted program called the Myqorzo REMS Program, because of the risk of heart failure due to systolic dysfunction.
    - Notable requirements of the Myqorzo REMS Program include the following:
      - Prescribers must be certified by enrolling in the Myqorzo REMS Program.
      - Patients must enroll in the Myqorzo REMS Program and comply with ongoing monitoring requirements.
      - Pharmacies must be certified by enrolling in the Myqorzo REMS Program and must only dispense to patients who are authorized to receive Myqorzo.
      - Wholesalers and distributors must only distribute to certified pharmacies.
      - Further information is available at www.MYQORZOREMS.com or by calling 1-844-285-7367.
  - Myqorzo is metabolized primarily by CYP2C9, and to a lesser extent by CYP3A, CYP2D6, and CYP2C19 enzymes.
    - Advise patients of the potential for drug interactions. Advise patients to inform their healthcare provider of all concomitant medications prior to and during Myqorzo treatment.

- **Common adverse drug reactions**:
  - Listed % incidence for adverse drug reactions= reported % incidence for drug (Myqorzo) minus reported % incidence for placebo occurring in >5% of patients. Please note that an incidence of 0% means the incidence was the same as or less than placebo.
    - The most frequently reported adverse events included hypertension (6%).

- **Drug interactions:**
  - Myqorzo is primarily metabolized by CYP2C9, and to a lesser extent by CYP3A, CYP2D6, and CYP2C19.
    - Fluvoxamine is a strong CYP2C19 inhibitor, weak to moderate CYP3A inhibitor, weak CYP2C9 inhibitor, and weak CYP2D6 inhibitor.
      - Start Myqorzo at 5mg in patients on stable fluvoxamine therapy. In patients who are on Myqorzo treatment and intend to start fluvoxamine: reduce the Myqorzo dose (ie, 20mg to 10mg, 15mg to 5mg or 10mg to 5mg) or continue 5mg.
    - Fluconazole is a moderate CYP2C9 inhibitor, moderate CYP3A inhibitor and strong CYP2C19 inhibitor, while voriconazole is a strong CYP3A inhibitor, moderate CYP2C19 inhibitor, and weak CYP2C9 inhibitor.
      - Start Myqorzo at 5mg in patients on stable therapy with fluconazole or voriconazole. In patients currently receiving Myqorzo who intend to start fluconazole (if used more than 3 days) or voriconazole: reduce the Myqorzo dose to 5mg if currently receiving Myqorzo 15mg or 20mg. Avoid concomitant use if currently receiving Myqorzo 5mg or 10mg.
  - Coadministration with a strong CYP2C9 inhibitor is predicted to increase the exposure of Myqorzo.
    - Start Myqorzo at 5mg in patients who are on stable therapy with a strong CYP2C9 inhibitor. In patients who are on Myqorzo treatment and intend to start a strong CYP2C9 inhibitor: reduce the Myqorzo dose (ie, 20mg to 10mg, 15mg to 5mg, or 10mg to 5mg) or continue on 5mg.
  - Rifampin is a strong CYP3A inducer, strong CYP2C19 inducer, and moderate CYP2C9 inducer.
    - Concomitant use with rifampin is contraindicated.
  - Concomitant use with a moderate to strong CYP3A inducer decreases aficamten exposure, which may reduce Myqorzo effectiveness.
    - In patients who intend to discontinue a moderate to strong CYP3A inducer: reduce the dose of Myqorzo (20mg to 10mg, 15mg to 5mg, or 10mg to 5mg) or continue 5mg.

- **Special populations:**
  - There is no pregnancy category for this medication; however, the risk summary indicates that there are no available data on use in pregnant women to assess for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes.
    - There is a pregnancy safety study for Myqorzo. If Myqorzo is administered during pregnancy, or if a patient becomes pregnant while receiving Myqorzo or within 3 weeks after the last dose of Myqorzo, healthcare providers should report Myqorzo exposure by contacting Cytokinetics, Inc. at 1-833-633-2986.
    - Clinical considerations include that obstructive HCM in pregnancy has been associated with increased risk for preterm birth.
  - The safety and efficacy of use in the pediatric population have not been established.

Conclusion

- Hypertrophic cardiomyopathy (HCM) is a cardiovascular disease that is inherited and described by hypertrophy of the left ventricle and having an extensive clinical spectrum that may include sudden death while in the absence of any other cardiac or systemic disease such as hypertension (*Silver et al 2026*).
- Myqorzo is a cardiac myosin inhibitor indicated for the treatment of adults with symptomatic obstructive hypertrophic cardiomyopathy (oHCM) to improve functional capacity and symptoms.
- Myqorzo has a box warning regarding risk of heart failure.
  - Because of the risk of heart failure due to systolic dysfunction, Myqorzo is available only through a restricted program under a REMS called the Myqorzo REMS Program.
  - Initiation or up-titration of Myqorzo in patients with LVEF <55% is not recommended.
- Advise patients of the potential for drug interactions and to inform their healthcare provider of all concomitant medications prior to and during Myqorzo treatment.
- The efficacy of Myqorzo was assessed in a phase 3, multicenter, randomized, double-blind, placebo-controlled study that included adults with symptomatic NYHA class II and III oHCM, LVEF ≥60%, and resting and post-Valsalva peak LVOT-G ≥30 and ≥50 mmHg at screening, respectively.
  - The primary endpoint of change from baseline in pVO2 to week 24 was significantly greater with Myqorzo compared to placebo.
- While the guidelines included in this review were published prior to Myqorzo being FDA approved, the use of a myosin inhibitor was included in the guidelines for symptomatic patients with oHCM. A comparator with Myqorzo includes mavacamten capsules (under the brand name of Camzyos).

- It is recommended that Myqorzo should be non-preferred in order to confirm the appropriate diagnosis and clinical parameters for use.

- **PDL Placement:**
  - ☐ Preferred
  - ☒ Non-Preferred

References

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