MYQORZO™ (aficamten) 5·10·15·20 mg tablets

MYQORZO™ REMS

Education Program for Healthcare Providers and Pharmacies

Cytokinetics

Welcome to the MYQORZO REMS **Education Program for Healthcare Providers and Pharmacies**

MYQORZO™ (aficamten) 5·10·15·20 mg tablets

To prescribe MYQORZO (aficamten), healthcare providers must become certified in the MYQORZO Risk Evaluation and Mitigation Strategy (REMS), which includes reviewing this **Education Program for Healthcare Providers and Pharmacies.**

- Only certified healthcare providers are eligible to prescribe MYQORZO.
- MYQORZO can only be dispensed by certified pharmacies.
- Patients must be enrolled in the MYQORZO REMS to receive MYQORZO.

MYQORZO Indication and Mechanism of Action

MYQORZO™ (aficamten) 5·10·15·20 mg tablets

Indication:

MYQORZO is a cardiac myosin inhibitor indicated for the treatment of adults with symptomatic obstructive hypertrophic cardiomyopathy (oHCM) to improve functional capacity and symptoms.

Mechanism of Action:

Aficamten 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 HCM. In HCM patients, myosin inhibition with aficamten reduces cardiac contractility and left ventricular outflow tract (LVOT) obstruction.

See full Prescribing Information.

Healthcare providers must report adverse events of heart failure due to systolic dysfunction associated with MYQORZO to Cytokinetics at 1-833-633-2986.

MYQORZO™ (aficamten) 5·10·15·20mg tablets

MYQORZO REMS Risk Information

MYQORZO Boxed Warning

MYQORZO™ (aficamten) 5·10·15·20 mg tablets

WARNING: 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 treatment with MYQORZO 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 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.

Risk of Heart Failure Due to Systolic Dysfunction

Assess the patient's cardiovascular status and appropriateness of initiating or continuing treatment and adjust the MYQORZO dose accordingly

- Patients who experience a serious intercurrent illness (e.g., serious infection) or arrhythmia (e.g., new or uncontrolled atrial fibrillation) may be at greater risk of developing systolic dysfunction and heart failure.
- Asymptomatic LVEF reduction, intercurrent illnesses, and arrhythmias require additional monitoring considerations.
- 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.

Recommended Dosage and Administration

MYQORZO™ (aficamten) 5·10·15·20 mg tablets

Initiation or up-titration of MYQORZO in patients with LVEF <55% is not recommended.

- The recommended starting dose of MYQORZO is 5 mg orally once daily
- Increase the dose every 2 to 8 weeks by 5 mg increments until a maintenance dose or the maximum recommended dose of 20 mg once daily is achieved
    - The maintenance dose of MYQORZO is individualized based on the patient's LVEF and left ventricular outflow tract (LVOT) gradient
- Recommendations for dosing based on LVEF and LVOT gradient criteria are in Table 1 (right)

Table 1: Dose Adjustment of MYQORZO

LVEF	Valsalva LVOT Gradient	Dose Adjustment
≥55%	≥30 mm Hg	Increase dose by 5 mg (up to the maximum dose of 20 mg once daily)
≥55%	<30 mm Hg	Maintain Dose
<55% and ≥50%	Any	Maintain Dose
<50% and ≥40%	Any	Decrease dose by 5 mg* If already on 5 mg, interrupt treatment for at least 7 days
<40%	Any	Interrupt treatment for at least 7 days

*Decrease as follows: 20 mg to 15 mg; 15 mg to 10 mg; 10 mg to 5 mg.

Recommended Dosage and Administration

MYQORZO™ (aficamten) 5·10·15·20 mg tablets

The Use of Echocardiography in MYQORZO Dosing and Administration

Regular LVEF and Valsalva LVOT gradient assessment is required for titration to achieve an appropriate target Valsalva LVOT gradient, while maintaining LVEF ≥50%.

- An echocardiographic assessment should be **performed between 2 to 8 weeks**
  - after initiation of treatment,
  - after any dose adjustment, or
  - after treatment interruption
- After a treatment interruption, resume treatment at the starting dose of 5 mg when LVEF ≥55% and re-initiate dose titration
- After the maintenance dose has been established:
  - assess LVEF and Valsalva LVOT gradient every 6 months, or
  - every 3 months in patients with LVEF <55% to ≥50%
- Consider monitoring LVEF and adjust dose per Table 1 of the Prescribing Information, as needed, in patients during intercurrent illness (e.g., severe infection), new arrhythmia (e.g., new or uncontrolled atrial fibrillation or other uncontrolled tachyarrhythmia), or any other conditions that may impair systolic function
  - Do not increase dose until intercurrent illness or new arrhythmia has resolved or stabilized

MYQORZO™ (aficamten) 5·10·15·20mg tablets

MYQORZO REMS Overview

MYQORZO REMS Overview

A REMS is a drug safety program that the U.S. Food and Drug Administration (FDA) can require for certain medicines to ensure that the benefits of a drug outweigh its risks.

Because of the risk of heart failure due to systolic dysfunction, MYQORZO is only available through a restricted program called the MYQORZO REMS.

The objective of the MYQORZO REMS is:

- Healthcare providers monitor left ventricular ejection fraction (LVEF) by echocardiogram during treatment according to the frequency described in the Prescribing Information to detect heart failure due to systolic dysfunction.

MYQORZO™ (aficamten) 5·10·15·20mg tablets

Healthcare Provider Requirements

Healthcare Provider Requirements

MYQORZO can only be prescribed by certified healthcare providers.

How Does a Healthcare Provider Become Certified in the MYQORZO REMS?

To become certified in the MYQORZO REMS, healthcare providers must:

1. **Review** the MYQORZO Prescribing Information, **REMS Overview**, and **Education Program for Healthcare Providers and Pharmacies** (this presentation)
2. **Successfully complete** the **Healthcare Provider Knowledge Assessment** and submit it to the REMS.
3. **Enroll** by completing and submitting the **Healthcare Provider Enrollment Form** to the REMS.

   Complete certification:
   - Online at www.MYQORZOREMS.com, or
   - By faxing the completed forms to 1-844-285-7399

Upon completion of these steps, healthcare providers will be notified within 2 business days when they are certified in the MYQORZO REMS.

The healthcare provider certification confirmation will also include instructions for the healthcare provider to gain access to the REMS portal where they can enter patient monitoring information and add REMS support staff.

Healthcare Provider Requirements

MYQORZO™ (aficamten) 5·10·15·20 mg tablets

What Are the Healthcare Provider Requirements of the MYQORZO REMS?

To prescribe MYQORZO, certified healthcare providers must:

Before treatment initiation (first dose):

- Counsel the patient on the risk of heart failure due to systolic dysfunction using the **Patient Guide** and provide a copy to the patient.
- Assess the patient's cardiovascular status and the appropriateness of initiating treatment based on an echocardiogram.
  - Document and submit confirmation of an echocardiogram and authorization for treatment to the REMS using the **Patient Enrollment Form**.
  - Enroll the patient by completing and submitting the **Patient Enrollment Form** to the REMS.

During treatment, between 2 to 8 weeks after treatment initiation and each dose change, then every 3 or 6 months thereafter (depending on echocardiogram results):

- Counsel the patient on the risk of heart failure due to systolic dysfunction using the **Patient Guide**.
- Assess the patient's cardiovascular status and the appropriateness of continuing treatment by obtaining an echocardiogram.
- Document and submit confirmation of review of the patient's echocardiogram results and authorization for treatment to the REMS using the **Patient Monitoring Form**.

At all times:

- Report adverse events of heart failure due to systolic dysfunction to Cytokinetics, Inc.

Healthcare Provider Requirements

MYQORZO™ (aficamten) 5·10·15·20mg tablets

Patient Enrollment Form Submission

The **Patient Enrollment Form** is used to document and confirm the following:

- Patient has been counselled on the risk of heart failure due to systolic dysfunction
- Healthcare provider has reviewed the patient's echocardiogram results and has authorized treatment including the starting dose

Treatment Initiation & Dispense Limits

Treatment with MYQORZO **must** begin within **3 months** of submitting the **Patient Enrollment Form**.

- Note: If treatment is not initiated within 3 months, the patient will be moved to a deactivated status, and a new **Patient Enrollment Form** must be submitted to proceed.

Single dispense limits are **capped** at a **30-day supply** during initiation and titration phases.

- Note: The REMS system will deny any dispense request that exceeds the applicable supply limit.

Healthcare Provider Requirements

MYQORZO™ (aficamten) 5·10·15·20 mg tablets

Patient Monitoring Form Completion

The **Patient Monitoring Form** is used to document and confirm the following:

- Certified healthcare provider has reviewed the patient's echocardiogram results in accordance with the Prescribing Information
- The patient's most recent LVEF
- If the patient has experienced a clinical heart failure event requiring clinical intervention or hospitalization since the last submitted form
- Action that will be taken to the patient's dose based on the clinical visit
- If the patient is authorized to continue treatment

Patient Monitoring Form Submission Timing

Treatment Initiation

- Within 60 days of initiating the first dose

Titration/Dose Changes

- Within 60 days following any dose change

Maintenance Dose

- For patients with LVEF ≥55% every 6 months from the most recent **Patient Monitoring Form**
- For patients with LVEF <55% and ≥50% every 3 months from the most recent **Patient Monitoring Form**

Maintenance Phase Dispense Limits

Single dispense limits are **capped** at a **90-day supply**.

Important: Submit the **Patient Monitoring Form** as soon as possible after completing the echocardiogram. Failure to submit the **Patient Monitoring Form** according to the required schedule may result in dispensing holds and potentially treatment interruptions.

Healthcare Provider Requirements

MYQORZO™ (aficamten) 5·10·15·20 mg tablets

Patient Monitoring Form Completion for Patients With Documented LVEF <40%

Treatment should be interrupted for at least 7 days per the Prescribing Information.

The REMS enforces the following additional **Patient Monitoring Form** submission requirement and dispensing limitations:

- **Recovery Confirmation:** Before treatment can be reinitiated, a new **Patient Monitoring Form** documenting LVEF ≥55% must be submitted to the REMS
- **Dispensing Limitation:** No REMS Dispense Authorization (RDA) will be issued until recovery to LVEF ≥55% is confirmed via **Patient Monitoring Form**
- **Restart Protocol:** Treatment must be reinitiated at the starting dose of 5 mg once daily, with an echocardiogram required within 2 to 8 weeks

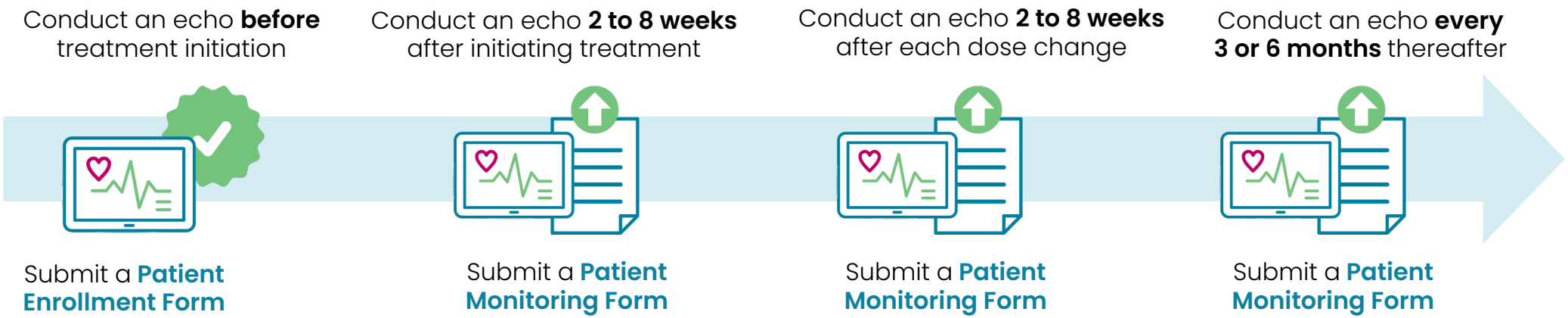
Healthcare Provider Requirements

MYQORZO™ (aficamten) 5·10·15·20 mg tablets

Echocardiogram & Patient Form Submission Timing Illustration

When prescribing MYQORZO, echocardiograms are required prior to initiation of treatment, after treatment initiation, after a dose change, and for routine monitoring. As depicted in the illustration below,

- An echocardiogram and **Patient Enrollment Form** are required prior to the patient initiating treatment.
- An echocardiogram is required 2 to 8 weeks after treatment initiation and any dose change, then every 3 or 6 months thereafter. A **Patient Monitoring Form** is required after each echocardiogram to confirm the patient's cardiovascular status has been assessed and the appropriateness of continuing treatment.



Healthcare Provider Requirements

MYQORZO™ (aficamten) 5·10·15·20 mg tablets

REMS Support Staff

To allow for flexibility in documentation management common within the healthcare delivery system and normal medical practice, the REMS allows for certified healthcare providers to designate up to four (4) REMS support staff per affiliated healthcare setting to complete certain REMS required documentation.

The certified healthcare provider of record is responsible for compliance with the REMS requirements, including monitoring, evaluation, and management of each patient under their care.

- REMS support staff can be added by the certified healthcare provider:
  - When completing and submitting the **Healthcare Provider Enrollment Form**
  - On the online portal accessible from www.MYQORZOREMS.com
  - By calling the REMS Call Center at 1-844-285-7367
- REMS support staff can be removed by the certified healthcare provider:
  - On the online portal accessible from www.MYQORZOREMS.com
  - By calling the REMS Call Center at 1-844-285-7367

Healthcare Provider Requirements

MYQORZO™ (aficamten) 5·10·15·20 mg tablets

REMS Healthcare Provider Delegate

To allow for flexibility in patient management common within the healthcare delivery system and normal medical practice, the REMS allows for certified healthcare providers to designate other certified healthcare providers as healthcare provider delegates to complete REMS-required documentation on their behalf.

Delegates must be enrolled and certified in REMS and attest to the requirements of the REMS.

- REMS healthcare provider delegates can be added or removed by the certified healthcare provider:
  - On the online portal accessible from www.MYQORZOREMS.com
  - By calling the REMS Call Center at 1-844-285-7367

Healthcare Provider Requirements

MYQORZO™ (aficamten) 5·10·15·20 mg tablets

REMS Responsibilities

Once appointed by a certified healthcare provider, REMS support staff and delegates can complete certain activities on behalf of the certified healthcare provider of record online or by hard copy as shown in the table below.

REMS Responsibilities	Certified Healthcare Provider	Healthcare Provider Delegate	Support Staff
Become REMS-certified	Yes	Yes	No
Counsel the patient on the risk of heart failure due to systolic dysfunction using the **Patient Guide**	Yes	Yes	No
Assess the patient's cardiovascular status and the appropriateness of initiating or continuing treatment by obtaining an echocardiogram	Yes	Yes	No
Enter patient data on a **Patient Enrollment Form** and **Patient Monitoring Form** up to, but not including, signature	Yes	Yes	Yes
Sign the **Patient Enrollment Form** and **Patient Monitoring Form**	Yes	Yes	No

The certified healthcare provider of record or their delegate is responsible for reviewing, signing, and submitting REMS forms, as well as ensuring compliance with the REMS requirements; this includes overseeing the monitoring, evaluation, and management of each patient under their care.

Healthcare Provider Requirements

MYQORZO™ (aficamten) 5·10·15·20 mg tablets

Managing Healthcare Provider Changes for REMS-Enrolled Patients

When enrolled patients need to transition to a new healthcare provider, whether they are no longer under their original provider's care or are planning a switch, the transition can be facilitated through the REMS website or the REMS Call Center. The new healthcare provider must be certified in the REMS program before patient care can be transferred, ensuring continuity of care and compliance with REMS requirements.

- Patient reassignments can be initiated by current or new certified healthcare providers:
  - On the online portal accessible from www.MYQORZOREMS.com
  - By calling the REMS Call Center at 1-844-285-7367

Upon successful reassignment, the REMS will send a notification to both healthcare providers, confirming that the patient is now associated with the new healthcare provider.

MYQORZO™ (aficamten) 5·10·15·20 mg tablets

Pharmacy Requirements

MYQORZO will be dispensed by a limited number of specialty pharmacies.
All pharmacies that dispense MYQORZO must be certified in the REMS.

Pharmacy Requirements

MYQORZO™ (aficamten) 5·10·15·20 mg tablets

How Does a Pharmacy Become Certified in the MYQORZO REMS?

To become certified to dispense, pharmacies must:

1. Designate an Authorized Representative to carry out the certification process and oversee implementation and compliance with the REMS on behalf of the pharmacy.
2. Have the Authorized Representative review the Prescribing Information, **REMS Overview**, and **Education Program for Healthcare Providers and Pharmacies** (this document).
3. Have the Authorized Representative enroll by completing and submitting the **Pharmacy Enrollment Form** to the REMS.
4. Train all relevant staff involved in dispensing MYQORZO using the **REMS Overview** and **Education Program for Healthcare Providers and Pharmacies**.

Pharmacy Requirements

MYQORZO™ (aficamten) 5·10·15·20 mg tablets

Eligible specialty pharmacies can complete certification:

- Online at www.MYQORZOREMS.com, or
- By faxing the completed form to 1-844-285-7399

Each pharmacy can designate up to 2 Authorized Representatives.

Pharmacies will be notified within two business days if they are certified to dispense MYQORZO.

The pharmacy certification confirmation will also include instructions for the Authorized Representative to gain access to the REMS portal where they can verify REMS requirements, obtain authorization to dispense MYQORZO, and add pharmacy staff.

Each certified Authorized Representative will have the ability to add staff on the online portal accessible from www.MYQORZOREMS.com, granting them access to the REMS portal. Any certified pharmacy staff member responsible for dispensing MYQORZO will receive unique login credentials.

Pharmacy Requirements

MYQORZO™ (aficamten) 5·10·15·20 mg tablets

What Are the Requirements of the MYQORZO REMS for Certified Pharmacies?

Before dispensing, all pharmacy staff must:

- Obtain authorization to dispense each prescription from the MYQORZO REMS online or by phone to verify that:
  - The healthcare provider is certified,
  - The patient is enrolled,
  - The healthcare provider has authorized the patient to receive MYQORZO, and
  - The requested dose is an allowable dose.
- Dispense no more than a 30 days' supply for patients initiating treatment, undergoing a dose adjustment, or re-initiating dose titration.
- Dispense no more than a 90 days' supply for patients on a maintenance dose.
- Each certified pharmacy will have the ability to obtain a REMS Dispense Authorization (RDA) for each prescription by:
  - Accessing a secure REMS verification portal through the REMS website, or
  - Contacting the REMS Call Center via phone at 1-844-285-7367

Pharmacy Requirements

MYQORZO™ (aficamten) 5·10·15·20 mg tablets

At all times, the pharmacy must:

- Report adverse events of heart failure due to systolic dysfunction to Cytokinetics, Inc.
- Not distribute, transfer, loan, or sell MYQORZO, except to a certified pharmacy.
- Maintain records of dispensing information and provide such data during audits conducted by Cytokinetics, Inc. or a third party acting on behalf of Cytokinetics, Inc.
- Maintain records of completion of the REMS training by relevant staff.
- Maintain records that all processes and procedures are in place and are being followed.
- Comply with audits carried out by Cytokinetics, Inc. or a third party acting on behalf of Cytokinetics, Inc. to ensure that all processes and procedures are in place and are being followed.

To maintain certification to dispense, any new Authorized Representative must:

- Enroll by completing and submitting the **Pharmacy Enrollment Form** to the REMS.

If the pharmacy opts to have a second Authorized Representative enroll, that Authorized Representative must complete and submit the **Pharmacy Enrollment Form** to the REMS.

MYQORZO™ (aficamten) 5·10·15·20 mg tablets

This concludes the MYQORZO REMS Education Program for Healthcare Providers and Pharmacies.

For more information or to obtain any REMS materials, visit www.MYQORZOREMS.com or call 1-844-285-7367. For MYQORZO REMS Call Center hours, visit www.MYQORZOREMS.com.

Report all adverse events, including those of heart failure due to systolic dysfunction, that occur in patients receiving MYQORZO to Cytokinetics, Inc. at 1-833-633-2986.

Phone: 1-844-285-7367 Fax: 1-844-285-7399 www.MYQORZOREMS.com

Cytokinetics