Aqvesme™
(mitapivat) tablets 100mg

Prescribe With Confidence:
AQVESME™ REMS Enrollment Overview

REMS=Risk Evaluation and Mitigation Strategy.

INDICATION

AQVESME is indicated for the treatment of anemia in adults with alpha- or beta-thalassemia.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: HEPATOCELLULAR INJURY

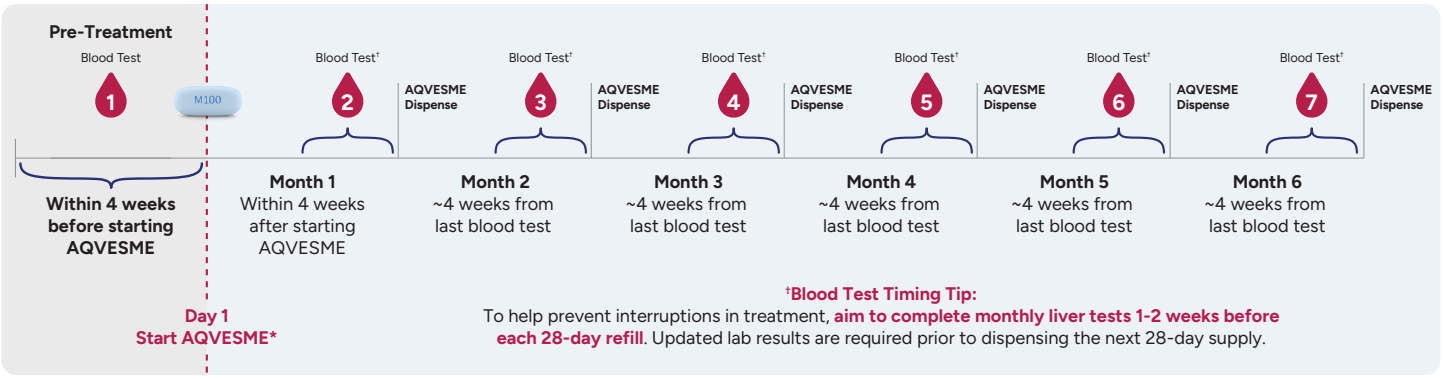
AQVESME can cause serious hepatocellular injury. Measure liver laboratory tests (ALT, AST, alkaline phosphatase and total bilirubin with fractionation) at baseline and every 4 weeks for 24 weeks and then as clinically indicated. Avoid use of AQVESME in patients with cirrhosis. Discontinue AQVESME if hepatic injury is suspected.
Because of the risk of hepatocellular injury, AQVESME is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the AQVESME REMS.

Please see additional Important Safety Information and full Prescribing Information for AQVESME, including Boxed Warning.

What is the purpose of AQVESME™ REMS?

- AQVESME has a REMS because of the potential risk of hepatocellular injury. The goal of AQVESME REMS is to help mitigate this risk by monitoring liver function (ALT, AST, alkaline phosphatase, and total bilirubin with fractionation) in patients receiving AQVESME
- Patient monitoring requirements include a pre-treatment liver test completed within 4 weeks of initiating therapy and monitoring liver function every 4 weeks during the first 24 weeks of treatment and as clinically indicated thereafter
- Prescribers monitor liver function tests to determine the appropriateness of continuing therapy

Liver function monitoring schedule for the first 24 weeks of treatment



*AQVESME is one pill taken twice daily, supplied as a 28-day pack.

- Under AQVESME REMS, only certified healthcare providers and pharmacies can prescribe and dispense AQVESME. Patients must be enrolled in AQVESME REMS and comply with all program requirements to receive AQVESME

How does an HCP become a certified provider for AQVESME REMS?

This **one-time certification** requires healthcare providers to become familiar with AQVESME REMS and enroll in it.

Review required materials

- AQVESME Prescribing Information
- Prescriber Guide

All materials can be found online at **AQVESMEREMS.com**.

Complete and submit forms

- Prescriber Knowledge Assessment
- Prescriber Enrollment Form

Complete and submit forms online via the portal at **AQVESMEREMS.com** or via fax at **1-800-905-8522**.

ALT=alanine aminotransferase; AST=aspartate aminotransferase; REMS=Risk Evaluation and Mitigation Strategy.

Please see Important Safety Information and full Prescribing Information for AQVESME, including Boxed Warning.

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What key REMS requirements must HCPs complete before patients can begin treatment with AQVESME™?

Counsel your patient

- Provide the **Patient Guide** and counsel your patients on:
  - The potential risk and signs and symptoms of hepatocellular injury associated with AQVESME
  - The need to contact the prescriber if they experience any signs or symptoms of hepatocellular injury
  - Liver function monitoring requirements, including the need to complete a pre-treatment liver test within 4 weeks of initiating therapy, every 4 weeks for the first 24 weeks, and as clinically indicated thereafter

Ensure your patient's pre-treatment liver test is completed

- Pre-treatment liver test **MUST** be completed **within 4 weeks of the first prescription being filled**
- Since prior authorization may take time to process, it is recommended that prior authorization be approved before you perform the pre-treatment liver test
- Once the prior authorization is approved, the myAgios® Patient Support Services team will follow up with you and your patient to remind your office to schedule the patient's pre-treatment liver test

Enroll your patient in AQVESME REMS

- To complete patient enrollment in AQVESME REMS, you and your patient must review, sign, and date the AQVESME REMS Patient Enrollment Form. Your patient can sign the form in person or electronically through the online portal
- You must also include in the form the date of the pre-treatment liver test and confirmation that the patient is appropriate for AQVESME

AQVESME REMS enrollment forms and guides

Submit all REMS forms online via the portal at **AQVESMEREMS.com** or by fax to **1-800-905-8522**

Prescriber guide and forms:	Patient guide and forms:
☑ REMS Prescriber Guide	☑ REMS Patient Guide
☑ REMS Prescriber Knowledge Assessment	☑ REMS Patient Enrollment Form
☑ REMS Prescriber Enrollment Form	

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Start AQVESME™ with 3 key actions

Once you and your patient have reviewed AQVESME clinical and REMS information and decided AQVESME is right for them, here's how to start treatment promptly:

1 HCP and patient complete and sign the AQVESME Start Form, and the HCP completes one-time HCP AQVESME REMS certification

- The AQVESME Start Form enrolls your patient in myAgios® Patient Support Services. The myAgios team can assist you and your patient in determining insurance coverage and exploring financial assistance options
- For the patient's convenience, your patient may get started with enrollment in AQVESME REMS by reviewing, signing, and dating the AQVESME REMS Patient Enrollment Form at the same time as the AQVESME Start Form either in person or electronically through the online portal at **AQVESMEREMS.com**

2 Pre-treatment liver test **MUST** be completed **within 4 weeks of the first prescription being filled**

- Since prior authorization may take time to process, it is recommended that prior authorization be approved before you perform the pre-treatment liver test
- Once the prior authorization is approved, the myAgios team will follow up with you and your patient to remind your office to schedule the patient's pre-treatment liver test

3 HCP completes enrollment of patient in AQVESME REMS

- To complete patient enrollment in AQVESME REMS, you must sign and submit the AQVESME REMS Patient Enrollment Form, including the date of the pre-treatment liver test and confirmation that your patient is appropriate for AQVESME
- If your patient has not yet signed the AQVESME REMS Patient Enrollment Form, it must be signed to ensure your patient is enrolled in AQVESME REMS. Refer to step 1 for options to sign the form in person or electronically through the online portal

The myAgios team will ensure that AQVESME is delivered directly to your patient's home through an exclusive REMS-certified Specialty Pharmacy.

We're here to support you

Submit REMS forms online at **AQVESMEREMS.com** or by fax to **1-800-905-8522**

Call **1-800-625-9951**, **Mon-Fri, 8 AM–8 PM ET** for more information

Submit the AQVESME Start Form **online** or by fax to **1-800-905-8522**

For more help, call myAgios at **1-877-77-AGIOS (1-877-772-4467), Mon-Fri, 8 AM–8 PM ET**

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Important Safety Information (cont.)

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WARNINGS AND PRECAUTIONS

Hepatocellular Injury

AQVESME can cause hepatocellular injury. Avoid use of AQVESME in patients with cirrhosis. In patients with thalassemia treated with AQVESME, liver injury with and without jaundice has been observed within the first 6 months of exposure. Obtain liver tests (including ALT, AST, alkaline phosphatase, total bilirubin with fractionation) prior to the initiation of AQVESME, then every 4 weeks for the first 24 weeks, and as clinically indicated thereafter. Interrupt AQVESME if clinically significant increases in liver tests are observed or alanine aminotransferase is >5 times the upper limit of normal (ULN). Complete a comprehensive evaluation to rule out other causes of liver injury when drug-induced liver injury is suspected. Discontinue AQVESME if hepatocellular injury due to AQVESME is suspected.

Symptoms and signs of early liver injury may mimic those of thalassemia. Advise patients to report new or worsening symptoms of loss of appetite, nausea, right-upper-quadrant abdominal pain, vomiting, scleral icterus, jaundice, or dark urine while on AQVESME treatment.

During the double-blind period, 2 of 301 patients (0.66%) with thalassemia treated with AQVESME experienced adverse reactions suggestive of hepatocellular injury. Three additional patients experienced adverse reactions suggestive of hepatocellular injury during the open-label extension periods after switching from placebo to AQVESME. Of these 5 patients, 2 had serious liver injury requiring hospitalization, including 1 patient who developed jaundice (peak bilirubin 32 mg/dL). Another patient developed jaundice (peak bilirubin 4 mg/dL) without requiring hospitalization. These reactions were characterized by a time to onset within the first 6 months of treatment with peak elevations of alanine aminotransferase of >5×ULN with or without jaundice. All patients discontinued treatment with AQVESME, and these reactions improved upon treatment discontinuation.

AQVESME REMS

AQVESME is available only through a restricted program under a REMS called the AQVESME REMS because of the risk of hepatocellular injury.

ADVERSE REACTIONS

The most common adverse reactions among patients taking AQVESME were headache and insomnia.

DRUG INTERACTIONS

- Strong CYP3A Inhibitors and Inducers: Avoid concomitant use.
- Moderate CYP3A Inhibitors: Avoid concomitant use.
- Moderate CYP3A Inducers: Consider alternatives that are not moderate inducers. If there are no alternatives, see full Prescribing Information for recommended dosage for drug interactions with moderate CYP3A inducers.
- Sensitive CYP3A Substrates, including hormonal contraceptives: Avoid concomitant use with substrates that have narrow therapeutic index.
- CYP2B6, CYP2C, and UGT1A1 Substrates: Monitor patients for efficacy of the substrates with narrow therapeutic index.
- P-gp Substrates: Monitor patients for adverse reactions of the substrates with narrow therapeutic index.

Hepatic Impairment

Avoid use of AQVESME in patients with cirrhosis (Child-Pugh Class A, B, or C).

Please see full Prescribing Information for AQVESME, including Boxed Warning.

Reference: AQVESME. Prescribing Information. Agios Pharmaceuticals, Inc.; 2025.

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