Guide to Managing Prior Authorizations for AQVESME™ (mitapivat)

Navigating Coverage Policies for Initial Authorization and Reauthorization

This resource serves as a detailed guide for HCPs and office staff on navigating the PA process and understanding coverage policies that may be required by health plans for use of AQVESME in your patients with alpha- or beta-thalassemia. Use this resource to ensure your office submits timely and accurate requests so patients can get started on therapy without unnecessary delays.

HCP=healthcare provider; PA=prior authorization.

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.

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.

Overview of the PA Process for Specialty Medications

Initial Authorization

- Initial authorization typically requires submission of a PA request
- Initial authorization allows the health plan to determine if use of a specific medication to treat the patient meets the appropriate criteria and is supported by clinical judgment of the HCP
- The health plan's coverage policy will state the duration of the initial authorization period, which generally ranges from 6 to 12 months

Reauthorization

- After the initial authorization period ends, the health plan typically requires reauthorization for the patient to continue receiving treatment
- Reauthorization is necessary to confirm that the medication continues to be medically necessary and that the patient is appropriately responding to treatment

PA Submission Checklist

PA submissions may require completion of a PA form, supporting clinical documentation, and sometimes a Letter of Medical Necessity.

The process can be streamlined by following the **checklist below,** but always confirm you provided all information requested on the PA form before submitting the request. PA forms required by various plans may be organized differently, but the type of information requested is similar.

- ◯ Complete the health plan's specific PA form, if available
- ◯ Provide relevant clinical documentation that supports medical necessity for the treatment decision, such as:
  - ○ Peer-reviewed literature, treatment guidelines, laboratory results, or relevant medical records

Pages 3 to 5 of this resource provide specific clinical information typically required to be documented in order to support medical necessity for AQVESME.

- ◯ Attach a Letter of Medical Necessity, if required

myAgios® can support your office as you navigate each step of the PA submission process (including appeals, if there is a denial of coverage) and can provide sample letter templates, if needed.

If a medication is not covered by the health plan on formulary, you can proactively submit an exception request form (or sometimes, the same PA form) provided by the plan. myAgios can support your office as you submit an exception request.

HCP=healthcare provider; PA=prior authorization.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Hepatocellular Injury (cont'd)

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.

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

Coverage Considerations for AQVESME™ (mitapivat)

This section provides potential coverage criteria for AQVESME that may be required by health plans to get your patients started on therapy and ensure those who are benefiting from therapy can continue treatment.
The criteria in this resource are examples that are provided for informational purposes only.

Potential PA criteria for AQVESME in the treatment of anemia in alpha- or beta-thalassemia

If a coverage policy is not yet established by the health plan, the following criteria may be helpful in facilitating the plan's review of your PA request.

Initial authorization

- ◯ Patient is 18 years of age or older
- ◯ Documented diagnosis of thalassemia (β-thalassemia with or without α-globin gene mutations, HbE/β-thalassemia, or α-thalassemia/HbH disease)
- ◯ Prescribed by or in consultation with a specialist (eg, hematologist)

Patient with non–transfusion-dependent thalassemia (NTDT):

- ◯ Documentation of baseline Hb level
- ◯ History of any RBC transfusions, units, and dates for the last year

Patient with transfusion-dependent thalassemia (TDT):

- ◯ History of RBC transfusions, units, and dates for the last year

Pages 4 and 5 provide key laboratory values to document in your patient's medical record.

Reauthorization

- ◯ Prescribed by or in consultation with a specialist (eg, hematologist)
- ◯ Patient has experienced a positive clinical response to treatment with AQVESME,* which may be defined as one of the following:
  - ◯ **NTDT:** Hb response
  - ◯ **TDT:** Transfusion reduction response

Some health plans may use clinical markers other than laboratory values to measure response to treatment with AQVESME, such as reduction in fatigue or improvement in shortness of breath.

*Discontinue AQVESME if no benefit in hemolytic anemia has been observed, based on the totality of laboratory results and clinical status of the patient, unless there is another explanation for response failure (eg, bleeding, surgery, other concomitant illnesses).

Please refer to the Full Prescribing Information for AQVESME for more detailed information on the inclusion and exclusion criteria and endpoints used in the ENERGIZE and ENERGIZE-T clinical trials.

Hb=hemoglobin; HbE=hemoglobin E; HbH=hemoglobin H; PA=prior authorization; RBC=red blood cell.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

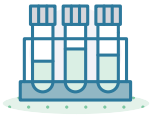
Hepatocellular Injury (cont'd)

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).

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

Coverage Considerations for AQVESME™ (mitapivat)

Clinical documentation recommended for AQVESME initial authorization



Baseline laboratory values prior to treatment initiation

For patients with non–transfusion-dependent (NTD) thalassemia, capture the following baseline laboratory values:

CBC panel including reticulocyte count and serum ferritin	Hb (g/dL)	Reticulocyte count (%)	Serum ferritin (ng/mL)
Standard hemolysis workup	Lactate dehydrogenase (U/L)	Haptoglobin (mg/dL)	Unconjugated bilirubin (mg/dL)

For patients with transfusion-dependent (TD) thalassemia, capture baseline Hb and transfusion units:

Hb (g/dL) (pre-transfusion)	
Number of transfusions (within the last 24 or 52 weeks)	
Total number of units per transfusion	

For patients with NTD and those with TD thalassemia, capture the following baseline laboratory values:

Hepatic function panel	ALT (U/L)	AST (U/L)	ALP (U/L)	Bilirubin, fractionated (mg/dL)		
				Total	Direct	Indirect

Some health plans may use clinical markers other than laboratory values to assess eligibility for treatment with AQVESME, such as fatigue or shortness of breath scores at baseline.

myAgios can help your office investigate all plan-specific criteria for initiation of therapy before you submit a PA request.

ALP=alkaline phosphatase; ALT=alanine aminotransferase; AST=aspartate aminotransferase; CBC=complete blood count; Hb=hemoglobin; PA=prior authorization.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Hepatocellular Injury (cont'd)

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 (≥5%) among patients taking AQVESME were headache and insomnia.

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

Coverage Considerations for AQVESME™ (mitapivat)

Clinical documentation recommended for AQVESME reauthorization

Ongoing laboratory values after treatment initiation

Documentation of the patient's response to treatment is important to meet coverage criteria for continuation of therapy. Use the table below to ensure the patient's ongoing laboratory values are captured in the **6 to 12 months** following initiation of treatment.

For patients with non–transfusion-dependent thalassemia who are not regularly transfused:

CBC panel including reticulocyte count	Hb (g/dL) ↑	Reticulocyte count (%) ↓
Standard hemolysis workup	Lactate dehydrogenase (U/L) ↓	Unconjugated bilirubin (mg/dL) ↓

Ideal improvement direction from baseline is represented by an arrow for each laboratory value.

For patients with transfusion-dependent thalassemia who are regularly transfused:

Number of transfusions (within the last 24 or 52 weeks)	
Total number of units per transfusion	

Measure and record the impact of thalassemia on the patient's quality of life:

Some health plans may use clinical markers other than laboratory values to measure response to treatment with AQVESME, such as reduction in fatigue or improvement in shortness of breath.

myAgios can help your office investigate all plan-specific criteria for continuation of therapy before you submit a reauthorization request.

CBC=complete blood count; Hb=hemoglobin.

IMPORTANT SAFETY INFORMATION (cont'd)

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 additional Important Safety Information throughout and Full Prescribing Information for AQVESME, including Boxed Warning.

myAgios® Patient Support Services

Single point of engagement for prescription and access support

Centralized enrollment for eligible patients, including prescription fulfillment, financial assistance, access, and adherence support

Access and benefits investigation services

- Support with insurance coverage
- Administration of patient assistance programs

Prescription fulfillment through exclusive specialty pharmacy

- Commercial product dispensing
- Guidance with dosing questions and coordination of refills

Dedicated team of Agios Clinical Educators (ACEs) and Patient Support Managers (PSMs)

- ACEs are there from the start to offer personalized guidance to patients living with thalassemia
- PSMs help patients prescribed AQVESME get access to and stay on therapy, and help your office navigate the acquisition and reimbursement process

There are 2 ways to enroll your patients in myAgios

Enroll online

- Complete the prescription for AQVESME online and it will be automatically directed to a myAgios PSM
- myAgios will reach out to your patient to obtain their authorization and complete their enrollment

Download and fax the AQVESME Start Form

- Download and fill out the AQVESME Start Form to request prescription fulfillment for eligible patients and connect them to a dedicated myAgios PSM, then fax to 1-800-951-7814

For more information on how myAgios can help support your office, please visit **myAgios.com/AQVESME/hcp** or call a **Patient Support Manager (PSM)** to learn more at **1-877-77-AGIOS (1-877-772-4467),** Mon-Fri, 8 AM to 8 PM ET.