MEDICAL MUTUAL®

Drug Policy

Policy:	Aqvesme™ (mitapivat tablets – Agios)	Annual Review Date: 08/20/2026 Last Revised Date: 08/20/2026

OVERVIEW

Aqvesme, a pyruvate kinase activator, is indicated for the **treatment of anemia in adults with alpha-thalassemia or beta-thalassemia**.[1]

POLICY STATEMENT

This policy involves the use of Aqvesme. Prior authorization is recommended for pharmacy benefit coverage of Aqvesme. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Aqvesme as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Aqvesme be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Aqvesme is recommended in those who meet the following criteria:

1. **Alpha-Thalassemia.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient meets ONE of the following* (a or b):
       - **a)** Patient has a baseline hemoglobin level of ≤ 10.0 g/dL; OR
         Note: Baseline is prior to treatment with therapies or before red blood cell transfusions.
       - **b)** According to the prescriber, the patient requires regular red blood cell transfusions as defined by meeting BOTH of the following [(1) and (2)]:
         - **(1)** Patient has received at least 6 red blood cell units within the preceding 24 weeks; AND
         - **(2)** Patient has not had any transfusion-free period > 35 days within the preceding 24 weeks; AND
     - **iii.** The medication is prescribed by or in consultation with a hematologist; OR

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B) Patient is Currently Receiving Aqvesme. Approve for 1 year if, according to the prescriber, the patient has experienced clinically meaningful benefit from Aqvesme*.
Note: Examples include improvement in hemolytic anemia, increases in hemoglobin levels, a reduction in transfusion burden, improvement in laboratory results (e.g., indirect bilirubin, lactate dehydrogenase), and/or symptomatic improvement (e.g., fatigue).

2. Beta-Thalassemia. Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, and v):
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Patient meets ONE of the following* (a or b):
  - **a)** Patient has a baseline hemoglobin level of ≤ 10.0 g/dL; OR
    Note: Baseline is prior to treatment with therapies or before red blood cell transfusions.
  - **b)** According to the prescriber, the patient requires regular red blood cell transfusions as defined by meeting BOTH of the following [(1) and (2)];
    - **(1)** Patient has received at least 6 red blood cell units within the preceding 24 weeks; AND
    - **(2)** Patient has not had any transfusion-free period > 35 days within the preceding 24 weeks; AND
- **iii.** Patient is not currently receiving Reblozyl (luspatercept-aamt subcutaneous injection); AND
- **iv.** Patient has not received a gene therapy for transfusion-dependent beta-thalassemia in the past; AND
  Note: Examples include Zynteglo (betibeglogene autotemcel intravenous infusion) and Casgevy (exagamglogene autotemcel intravenous infusion).
- **v.** The medication is prescribed by or in consultation with a hematologist; OR

B) Patient is Currently Receiving Aqvesme. Approve for 1 year if the patient meets ALL of the following (i, ii, and ii):
- **i.** According to the prescriber, the patient has experienced clinically meaningful benefit from Aqvesme*; AND
  Note: Examples include improvement in hemolytic anemia, increases in hemoglobin levels, a reduction in transfusion burden, improvement in laboratory results (e.g., indirect bilirubin, lactate dehydrogenase), and symptomatic improvement (e.g., fatigue).
- **ii.** Patient is not currently receiving Reblozyl (luspatercept-aamt subcutaneous injection); AND
- **iii.** Patient has not received a gene therapy for transfusion-dependent beta-thalassemia in the past.
  Note: Examples include Zynteglo (betibeglogene autotemcel intravenous infusion) and Casgevy (exagamglogene autotemcel intravenous infusion).

Initial Approval/ Extended Approval.
A) *Initial Approval: 6 months*
B) *Extended Approval: 1 year*

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Aqvesme has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

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1. **Pyruvate Kinase Deficiency.** Pyrukynd® (mitapivat tablets) is another mitapivat product that is indicated for the treatment of hemolytic anemia in adults with pyruvate kinase deficiency.[5] The recommended dosing differs from Aqvesme.[1,5] Unlike Aqvesme, Pyrukynd does not have a Risk Evaluation and Mitigation Strategy program.[5]

2. **Patient is Currently Receiving Pyrukynd.** Pyrukynd is another mitapivat product that is indicated for the treatment of hemolytic anemia in adults with pyruvate kinase deficiency.[5] Concomitant use is not recommended.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

***Documentation Requirements:**
The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational, or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Aqvesme™ tablets [prescribing information]. Cambridge, MA: Agios; December 2025.
2. Taher AT, Farmakis D, Porter JB, Cappellini MD, Musallam KM, editors. Guidelines for the Management of Transfusion-Dependent β-Thalassaemia (TDT) [Internet]. 5th ed. Nicosia, Cyprus: Thalassaemia International Federation; 2025. PMID: 40367250.
3. Taher AT, Musallam KM, Cappellini MD. Guidelines for the Management of Non-Transfusion-Dependent β-Thalassaemia [Internet]. 3rd ed. Nicosia (Cyprus): Thalassaemia International Federation; 2023. PMID: 38446917.
4. Amid A, Lal A, Coates TD, Fucharoen S, editors. Guidelines for the Management of α-Thalassaemia [Internet]. Nicosia (Cyprus): Thalassaemia International Federation; 2023. PMID: 38556968.
5. Pyrukynd® tablets [prescribing information]. Cambridge, MA: Agios; December 2025.

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