VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Hematology – Aqvesme Prior Authorization Policy
- Aqvesme™ (mitapivat tablets – Agios)

REVIEW DATE: 01/07/2026; selected revision 02/11/2026

OVERVIEW

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

Clinical Efficacy

There were two multinational, randomized, double-blind, placebo-controlled, Phase III pivotal trials that evaluated Aqvesme in patients with alpha-thalassemia or beta-thalassemia.[1] ENERGIZE-T involved 258 adults with transfusion-dependent alpha-thalassemia or beta-thalassemia and ENERGIZE included 194 adults with non-transfusion-dependent alpha-thalassemia or beta-thalassemia. Randomization in both trials was in a 2:1 ratio to Aqvesme or placebo. In ENERGIZE-T, transfusion dependence was defined as having 6 to 20 red blood cell (RBC) units transfused and no longer than a 6-week transfusion-free period during the 24 weeks prior to randomization. In ENERGIZE, non-transfusion dependence was defined as having had no more than five RBC units transfused during the 24-week period prior to randomization and no RBC transfusions within 8 weeks. A baseline hemoglobin level ≤ 10 g/dL was required. In ENERGIZE-T, a transfusion reduction response, defined as ≥ 50% reduction from baseline in RBC units transfused with a reduction of at least 2 units of RBCs transfused in any consecutive 12-week period through Week 48 compared with baseline, occurred in 30.4% of patients given Aqvesme vs. 12.6% of patients who received placebo (P = 0.0003). In ENERGIZE, hemoglobin response, defined as a ≥ 1 g/dL increase in the average hemoglobin level from Week 12 through Week 24 compared with baseline, was 42.3% for Aqvesme vs. 1.6% with placebo (P < 0.0001).

Guidelines

The Thalassaemia International Federation (TIF) has extensive guidelines for the management of transfusion-dependent beta-thalassemia (2025),[2] non-transfusion-dependent beta-thalassemia (2023),[3] and alpha-thalassemia (2023).[4] Aqvesme is not specifically addressed post-approval, but the TIF guidelines recognized that data are promising with this agent.[2-4]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Aqvesme. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. 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, approval requires Aqvesme to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Aqvesme is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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
   - **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).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Aqvesme is not recommended in the following situations:

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.

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.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	01/07/2026
Selected Revision	**Conditions Not Recommended for Approval:** The condition of Pyruvate Kinase Deficiency was added. Also, an exclusion was added regarding a patient who is currently receiving Pyrukynd.	02/11/2026