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5.85.046

Section:	Prescription Drugs	**Effective Date:**	July 1, 2026
Subsection:	Hematological Agents	**Original Policy Date:**	March 11, 2022
Subject:	Aqvesme Pyrukynd	**Page:**	1 of 6

Last Review Date: June 11, 2026

Aqvesme Pyrukynd

Description

Pyrukynd (mitapivat)
Aqvesme (mitapivat)

Background
Pyrukynd and Aqvesme (mitapivat) are pyruvate kinase activators that act by allosterically binding to the pyruvate kinase tetramer and increasing pyruvate kinase (PK) activity. In PK deficiency, the red blood cell (RBC) form of pyruvate kinase (PK-R) is mutated, which leads to reduced adenosine triphosphate (ATP), shortened RBC lifespan, and chronic hemolysis. In nonclinical models of beta-thalassemia, Aqvesme improved energy homeostasis, RBC longevity, ineffective erythropoiesis, and hemolysis by increasing PK activity (1-2).

Regulatory Status
FDA-approved indication: Pyrukynd is a pyruvate kinase activator indicated for the treatment of hemolytic anemia in adults with pyruvate kinase (PK) deficiency. Aqvesme is a pyruvate kinase activator indicated for the treatment of anemia in adults with alpha- or beta-thalassemia (1-2).

Pyrukynd dosing is driven by hemoglobin levels and transfusion requirements. If no benefit has been observed by 24 weeks, Pyrukynd should be discontinued (1).

Aqvesme carries a boxed warning regarding 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 in patients with cirrhosis (Child-Pugh Class A, B, or C) due to increased risk of severe outcomes if hepatocellular injury occurs.

Aqvesme is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Aqvesme REMS (2).

Acute hemolysis with subsequent anemia has been observed following abrupt interruption or discontinuation of Pyrukynd. Pyrukynd should not be discontinued abruptly. The dose should be gradually tapered to discontinue treatment if possible. When discontinuing treatment, patients should be monitored for signs of acute hemolysis and anemia including jaundice, scleral icterus, dark urine, dizziness, confusion, fatigue, or shortness of breath (1).

Patients were included in the Pyrukynd clinical trial if they had documented presence of at least 2 variant alleles in the pyruvate kinase liver and red blood cell (PKLR) gene, of which at least 1 was a missense variant, and hemoglobin (Hb) less than or equal to 10 g/dL. Patients who were homozygous for the c.1436G>A (p.R479H) variant or had 2 non-missense variants (without the presence of another missense variant) in the PKLR gene were excluded because these patients did not achieve Hb response (change from baseline in Hb ≥1.5 g/dL at >50% assessments) in the dose-ranging study (1).

The safety and effectiveness of Pyrukynd and Aqvesme in pediatric patients less than 18 years of age have not been established (1-2).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Pyrukynd and Aqvesme may be considered **medically necessary** if the conditions indicated below are met.

Pyrukynd and Aqvesme may be considered **investigational** for all other indications.

Prior-Approval Requirements

Pyrukynd only

Age 18 years of age and older

Diagnosis

Patient must have the following:

1. Hemolytic anemia with pyruvate kinase (PK) deficiency
    a. Confirmed by a PK deficiency test OR a mutation in the PKLR gene

AND ALL of the following:

1. Patient has **ONE** of the following:
    a. Hemoglobin ≤ 10 g/dL
    b. Six or more RBC transfusion episodes in the last 52 weeks (1 year)
2. **NO** moderate to severe hepatic impairment (Child-Pugh Class B or C)
3. Prescriber agrees to dose the patient based on hemoglobin levels and transfusion requirements
4. Prescriber agrees to discontinue treatment with Pyrukynd if no clinical benefit is observed by 24 weeks
5. Prescriber agrees to taper the Pyrukynd dose when discontinuing therapy to reduce the risk of acute hemolysis

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Aqvesme only

Age 18 years of age and older

Diagnosis

Patient must have the following:

1. Anemia with alpha- or beta-thalassemia

AND ALL of the following:

1. Patient has **ONE** of the following:
    a. Pretreatment or pretransfusion hemoglobin ≤ 10 g/dL
    b. Six or more RBC transfusion episodes in the last 24 weeks
2. **NO** liver cirrhosis (Child-Pugh Class A, B, or C)
3. Patient and prescriber are enrolled in the Aqvesme REMS program

Prior–Approval *Renewal* Requirements

Pyrukynd only

Age 18 years of age and older

Diagnosis

Patient must have the following:

1. Hemolytic anemia with pyruvate kinase (PK) deficiency

AND ALL of the following:

1. Patient has clinical benefit from therapy as defined by **ONE** of the following:
   a. Increase in hemoglobin level
   b. Reduction in need for RBC transfusion
2. **NO** moderate to severe hepatic impairment (Child-Pugh Class B or C)
3. Prescriber agrees to dose the patient based on hemoglobin levels and transfusion requirements
4. Prescriber agrees to taper the Pyrukynd dose when discontinuing therapy to reduce the risk of acute hemolysis

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Aqvesme only

Age 18 years of age and older

Diagnosis

Patient must have the following:

1. Anemia with alpha- or beta-thalassemia

AND ALL of the following:

a. Patient has clinical benefit from therapy as defined by **ONE** of the following:
    i. Increase in hemoglobin level
    ii. Reduction in need for RBC transfusion
2. **NO** liver cirrhosis (Child-Pugh Class A, B, or C)
3. Patient and prescriber are enrolled in the Aqvesme REMS program

Policy Guidelines

Pre–PA Allowance

None

Prior–Approval Limits

Quantity 168 tablets per 84 days

Duration 6 months

Prior–Approval *Renewal* Limits

Quantity 168 tablets per 84 days

Duration 12 months

Rationale

Summary

Pyrukynd (mitapivat) is indicated for the treatment of hemolytic anemia in adults with pyruvate kinase (PK) deficiency. Aqvesme is indicated for the treatment of anemia in adults with alpha- or beta-thalassemia. Pyrukynd dosing is driven by hemoglobin levels and transfusion requirements. If no benefit has been observed by 24 weeks, Pyrukynd should be discontinued. Abrupt interruption or discontinuation should be avoided to minimize the risk of acute hemolysis. The safety and effectiveness of Pyrukynd and Aqvesme in pediatric patients less than 18 years of age have not been established (1-2).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Pyrukynd and Aqvesme while maintaining optimal therapeutic outcomes.

References

1. Pyrukynd [package insert]. Cambridge, MA: Agios Pharmaceuticals, Inc.; December 2025.
2. Aqvesme [package insert]. Cambridge, MA: Agios Pharmaceuticals, Inc.; December 2025.

Policy History

Date	Action
March 2022	Addition to PA
June 2022	Annual review. Removed renewal requirement: “Confirmed by a PK deficiency test OR a mutation in the PKLR gene”
September 2023	Annual review. Changed policy number to 5.85.046
June 2024	Annual review
June 2025	Annual review and reference update
April 2026	Addition of Aqvesme to policy. Renamed policy Aqvesme Pyrukynd
June 2026	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 11, 2026 and is effective on July 1, 2026.