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5.85.046

Section:	Prescription Drugs	**Effective Date:**	July 1, 2024
Subsection:	Hematological Agents	**Original Policy Date:**	March 11, 2022
Subject:	Pyrukynd	**Page:**	1 of 4

Last Review Date: June 13, 2024

Pyrukynd

Description

Pyrukynd (mitapivat)

Background
Pyrukynd (mitapivat) is a pyruvate kinase activator that acts by allosterically binding to the pyruvate kinase tetramer and increasing pyruvate kinase (PK) activity. The red blood cell (RBC) form of pyruvate kinase (PK-R) is mutated in PK deficiency, which leads to reduced adenosine triphosphate (ATP), shortened RBC lifespan, and chronic hemolysis (1).

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 (1).

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

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 in pediatric patients less than 18 years of age have not been established (1).

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

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

Prior-Approval Requirements

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

Prior–Approval *Renewal* Requirements

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

Policy Guidelines

Pre–PA Allowance
None

Prior–Approval Limits

Quantity 168 tablets per 84 days

Duration 6 months

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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. 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 in pediatric patients less than 18 years of age have not been established (1).

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

References

1. Pyrukynd [package insert]. Cambridge, MA: Agios Pharmaceuticals, Inc.; February 2022.

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

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 13, 2024 and is effective on July 1, 2024.