COMMON GROUND
HEALTHCARE COOPERATIVE

PHARMACY POLICY STATEMENT
Common Ground Healthcare Cooperative (CGHC)

DRUG NAME	Pyrukynd (mitapivat)
BENEFIT TYPE	Pharmacy
STATUS	Prior Authorization Required

Pyrukynd, approved by the FDA in 2022, is a pyruvate kinase activator indicated for treatment of adults with hemolytic anemia caused by pyruvate kinase (PK) deficiency.
PK deficiency is caused by mutations in the *PKLR* gene that encodes for the PK enzyme. PK catalyzes the production of ATP which is essential for RBC function. Deficiency of PK activity results in inadequate ATP and premature RBC destruction (hemolytic anemia). Standard treatments include RBC transfusions and splenectomy. Pyrukynd increases PK activity, addressing the underlying cause of hemolysis.

Pyrukynd (mitapivat) will be considered for coverage when the following criteria are met:

Pyruvate Kinase (PK) deficiency

For **initial** authorization:
1. Member is at least 18 years of age; AND
2. Medication must be prescribed by or in consultation with a hematologist; AND
3. Member has a diagnosis of PK deficiency confirmed by genetic testing (two or more documented mutant *PKLR* alleles, at least one of which is a missense mutation); AND
4. Member's hemoglobin level is 10 g/dL or less OR member has had a minimum of 6 transfusions in the past 52 weeks; AND
5. Member is currently taking at least 0.8 mg oral folic acid; AND
6. Member does NOT have any of the following:
   a) Homozygous R479H mutation or have 2 non-missense mutations, without the presence of another missense mutation, in the *PKLR* gene
   b) Moderate to severe hepatic impairment
   c) Prior bone marrow or stem cell transplant.
7. **Dosage allowed/Quantity limits:**
   a) **Starting Dose**: 5 mg orally twice daily for the first 4 weeks
   b) **Maintenance Doses**: Titrate to 20 mg twice daily, and then to the maximum recommended dose of 50 mg twice daily, with these dose increases occurring every 4 weeks, based on assessments of Hb and transfusion requirements, as directed in prescribing information.
   c) **Quantity Limit:** 56 tablets/28 days.

If all the above requirements are met, the medication will be approved for 6 months.

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For **reauthorization**:

1. Chart notes must show hemoglobin increase of at least 1.5 g/dL OR clinically significant decrease in transfusion burden.

If all the above requirements are met, the medication will be approved for an additional 6 months.

CareSource considers Pyrukynd (mitapivat) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
04/16/2022	New policy for Pyrukynd created.
04/23/2024	Updated references. Removed geneticist as prescriber. Corrected QL from 58/28 to 56/28. Removed LFT's from reauth. Corrected hemoglobin from <10 to 10 or less. Removed anabolic steroid/testosterone restriction. Removed splenectomy restriction. Added regularly transfused as an alternate criterion to hemoglobin qualifier.

References:

1. Pyrukynd [package insert]. Cambridge, Massachusetts: Agios Pharmaceuticals, Inc.; 2022.
2. Al-Samkari H, van Beers EJ. Mitapivat, a novel pyruvate kinase activator, for the treatment of hereditary hemolytic anemias. *Ther Adv Hematol*. 2021;12:20406207211066070. Published 2021 Dec 21. doi:10.1177/20406207211066070
3. Grace RF, Mark Layton D, Barcellini W. How we manage patients with pyruvate kinase deficiency [published correction appears in Br J Haematol. 2019 May;185(4):807]. *Br J Haematol*. 2019;184(5):721-734. doi:10.1111/bjh.15758
4. Grace RF, Barcellini W. Management of pyruvate kinase deficiency in children and adults. *Blood*. 2020;136(11):1241-1249. doi:10.1182/blood.2019000945.
5. Al-Samkari H, Galactéros F, Glenthøj A, et al. Mitapivat versus Placebo for Pyruvate Kinase Deficiency. *N Engl J Med*. 2022;386(15):1432-1442. doi:10.1056/NEJMoa2116634
6. Al-Samkari H, Shehata N, Lang-Robertson K, et al. Diagnosis and management of pyruvate kinase deficiency: international expert guidelines. *Lancet Haematol*. 2024;11(3):e228-e239. doi:10.1016/S2352-3026(23)00377-0

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