# PRIOR AUTHORIZATION POLICY

**POLICY:** Hematology – Pyrukynd Prior Authorization Policy
- Pyrukynd® (mitapivat tablets – Agios)

**REVIEW DATE:** 02/28/2024

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## OVERVIEW

Pyrukynd, a pyruvate kinase activator, is indicated for the treatment of **hemolytic anemia due to pyruvate kinase deficiency** in adults.[1]

It is recommended to discontinue Pyrukynd if no benefit has been observed by 24 weeks as evaluated by hemoglobin and hemolysis laboratory results and transfusion requirements.

### Disease Overview

Pyruvate kinase deficiency is a rare (three to nine cases per one million people), autosomal recessive enzyme defect in red blood cells that is caused by mutations in the pyruvate kinase liver and red blood cell (*PKLR*) gene.[2,3] These alterations result in a deficit of pyruvate kinase activity in red blood cells which leads to hemolytic anemia of varying severity.[2] Other complications include iron overload (and its sequelae), bilirubin gallstones, pulmonary hypertension, thrombosis, and extramedullary hematopoiesis. Commonly present are compound heterozygous mutations in the gene encoding the L and R isozymes of *PKLR* with more than 300 mutations noted; most patients have at least on missense mutation. More notable management strategies involve blood transfusions, splenectomy, and chelation therapy.

## POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Pyrukynd. 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 Pyrukynd as well as the monitoring required for adverse events and long-term efficacy, approval requires Pyrukynd to be prescribed by or in consultation with a physician who specializes in the condition being treated.

**Documentation:** Documentation is required for use of Pyrukynd as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, and/or other information.

**Automation:** None.

## RECOMMENDED AUTHORIZATION CRITERIA

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

### FDA-Approved Indication

1. **Hemolytic Anemia Due to Pyruvate Kinase Deficiency.** Approve for the duration noted below if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets the following (i, ii, iii, and iv):
     - **i.** Patient is ≥ 18 years of age; AND

**ii.** Patient meets both of the following (a and b):
- **a)** Presence of at least two variant/mutant alleles in the pyruvate kinase liver and red blood cell (*PKLR*) gene **[documentation required]**; AND
- **b)** At least one of the variant/mutant alleles was a missense variant **[documentation required]**; AND

**iii.** Patient meets one of the following (a or b):
- **a)** Patient has a current hemoglobin level ≤ 10 g/dL; OR
- **b)** Patient is currently receiving red blood cell transfusions regularly, defined as at least six transfusions within the last year; AND

**iv.** The medication is prescribed by or in consultation with a hematologist.

**B)** Patient is Currently Receiving Pyrukynd. Approve for 1 year if the patient meets the following (i, ii, iii, and iv):

**i.** Patient is ≥ 18 years of age; AND

**ii.** Patient meets both of the following (a and b):
- **a)** Presence of at least two variant/mutant alleles in the pyruvate kinase liver and red blood cell (*PKLR*) gene **[documentation required]**; AND
- **b)** At least one of the variant/mutant alleles was a missense variant **[documentation required]**; AND

**iii.** According to the prescriber, the patient has experienced a benefit from therapy based one of the following (a, b, or c):
- **a)** Increase in or maintenance of hemoglobin levels; OR
- **b)** Improvement in or maintenance of hemolysis laboratory parameters; OR
  Note: Examples of laboratory parameters that are markers of hemolysis include indirect bilirubin, lactate dehydrogenase, and haptoglobin.
- **c)** Decrease in or maintenance of transfusion requirements; AND

**iv.** The medication is prescribed by or in consultation with a hematologist.

## CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Pyrukynd is not recommended in the following situations:

1. **Patient with Pyruvate Kinase Deficiency Homozygous for the c.1436G>A (p.R479H) Variant/Mutation in the Pyruvate Kinase Liver and Red Blood Cell (*PKLR*) Gene.** Such patients were excluded from the pivotal studies investigating Pyrukynd in patients with pyruvate kinase deficiency because they did not achieve a hemoglobin response in the dose-ranging study.[1]

2. **Patient with Pyruvate Kinase Deficiency with Two Non-Missense Variants/Mutations (without the presence of another missense variant/mutation) in the Pyruvate Kinase Liver and Red Blood Cell (*PKLR*) Gene.** Such patients were excluded from the pivotal studies investigating Pyrukynd because they did not achieve a hemoglobin response in the dose-ranging study.[1]

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. Pyrukynd® tablets [prescribing information]. Cambridge, MA: Agios; February 2022.
2. Grace RF, Barcellini W. Management of pyruvate kinase deficiency in children and adults. *Blood*. 2020;136(11):1241-1249.
3. Fattizzo B, Cavallaro F, Marcello APML, et al. Pyruvate kinase deficiency: current challenges and future prospects. *J Blood Med*. 2022;13:461-471.