MEDICAL MUTUAL®

Drug Policy

Policy:	Pyrukynd (mitapivat)	Annual Review Date:
SD		04/17/2025
		Last Revised Date:
		04/17/2025

OVERVIEW

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

POLICY STATEMENT

This policy involves the use of Pyrukynd. Prior authorization is recommended for pharmacy benefit coverage of Pyrukynd. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

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, initial approval requires Pyrukynd be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

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

1. **Hemolytic Anemia due to Pyruvate Kinase Deficiency, initial therapy**
   Criteria. *Patient must meet the following criteria*
   - **A.** The patient is ≥ 18 years of age; AND
   - **B.** The patient meets both of the following:
     - **a.** Presence of at least two variant/mutant alleles in the pyruvate kinase liver and red blood cell (*PKLR*) gene *; AND
     - **b.** At least one of the variant/mutant alleles was a missense variant *; AND
   - **C.** The patient meets one of the following:
     - **a.** The patient has a current hemoglobin level ≤ 10 g/dL; OR
     - **b.** The patient is currently receiving red blood cell transfusions regularly, defined as at least six transfusions within the last year; AND
   - **D.** The medication is prescribed by or in consultation with a hematologist.

2. **Hemolytic Anemia due to Pyruvate Kinase Deficiency, continuation of therapy**
Criteria. *Patient must meet the following criteria*

A. The patient is ≥ 18 years of age; AND
B. The patient meets both of the following:
  a. Presence of at least two variant/mutant alleles in the pyruvate kinase liver and red blood cell (*PKLR*) gene *; AND
  b. At least one of the variant/mutant alleles was a missense variant *; AND
C. According to the prescriber, the patient has experienced a benefit from therapy based on one of the following:
  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
D. The medication is prescribed by or in consultation with a hematologist.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 6 months
B) *Extended Approval:* 1 year

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Pyrukynd has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

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.

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.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

*** Documentation Requirements:**

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

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.
4. Mitapivat. In: DRUGDEX [online database]. Truven Health Analytics; Greenwood Village, CO. Last updated 24 January 2024. Accessed on 16 April 2024.