Pharmacy Policy Bulletin

Title:	Mitapivat (Pyrukynd®)
Policy #:	Rx.01.266

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for **Mitapivat (Pyrukynd®)** as provided under the member's prescription drug benefit.

Description:

Hemolytic anemia is a disease that results in the premature death (hemolysis) of red blood cells (RBC) at a faster rate than the body can produce. Hemolytic anemia can be categorized as intrinsic and extrinsic. Intrinsic hemolytic anemia is genetically inherited and results in abnormalities in the cell membrane and overall blood cell production. Extrinsic hemolytic anemia is acquired as a secondary effect resulting from certain immunologic diseases, infections and medications. The glycolytic pathway is a metabolic pathway that breaks down glucose into pyruvate via the Pyruvate kinase (PK) enzyme, which leads to the production of ATP and NADH. A deficiency in the pyruvate kinase enzyme in homozygous patients causes a defect in the glycolytic pathway that is known to cause hemolytic anemia. The exact mechanism of hemolysis is unknown.

Mitapivat is a Pyruvate Kinase activator that targets defective PK enzymes in RBC's.

Mitapivat (Pyrukynd®) is indicated for the treatment of low RBC's resulting from hemolytic anemia in adults with a PK enzyme deficiency.

Policy:

INITIAL CRITERIA: Mitapivat (Pyrukynd®) is approved when ALL of the following are met:

1. Diagnosis of hemolytic anemia confirmed by the presence of chronic hemolysis (e.g., increased indirect bilirubin, elevated lactated dehydrogenase [LDH], decreased haptoglobin, increased reticulocyte count); and
2. Diagnosis of pyruvate kinase deficiency confirmed by molecular testing of ALL of the following mutations on the PLKR gene:
    a. 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
    b. Member is not homozygous for the c.1436G>A (p.R479H) variant; and
    c. Member does not have 2 non-missense variants (without the presence of another missense variant) in the PKLR gene; and
3. Hemoglobin is less than or equal to 10g/dL; and
4. Member has symptomatic anemia or is transfusion dependent; and
5. Other causes of hemolytic anemias (e.g., infections, toxins, drugs) were ruled out; and
6. Member is 18 years of age and older; and
7. Prescribed by or in consultation with a hematologist

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Mitapivat (Pyrukynd®) re-approved when ALL of the following are met:

1. Documentation of positive clinical response to therapy (e.g., hemoglobin greater than or equal to 1.5g/dL from baseline sustained on 2 or more follow ups (weeks 16, 20 and 24) during the fixed dose period without transfusions; reduction in transfusions of greater than or equal to 33% in the number of red blood cell units transfused during the fixed dose period compared with the member's historical transfusion burden; improvement in markers of hemolysis from baseline (e.g., bilirubin, lactated dehydrogenase [LDH], haptoglobin, reticulocyte count)); and
2. Prescribed by or in consultation with a hematologist

Reauthorization duration: 12 months

Black Box Warning as shown in the drug Prescribing Information:

N/A

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Pyrukynd® (mitapivat) [prescribing information]. Agios Pharmaceuticals, Inc.; 2022. https://www.pyrukynd.com/hcp/. Accessed August 23, 2022.

Braunstein EM. Glycolytic Pathway Defects. Merck & Co., Inc., Rahway, NJ.; June 2022. https://www.merckmanuals.com/professional/hematology-and-oncology/anemias-caused-by-hemolysis/glycolytic-pathway-defects. Accessed August 23, 2022.

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Pyrukynd®	Mitapivat

Cross References:

Rx.01.33 Off Label Use

Policy Version Number:	1.00
P&T Approval Date:	June 09, 2022
Policy Effective Date:	October 01, 2022
Next Required Review Date:	June 09, 2023

to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.