Clinical Policy Title:	mitapivat
Policy Number:	RxA.755
Drug(s) Applied:	Pyrukynd®
Original Policy Date:	04/18/2022
Last Review Date:	04/18/2022
Line of Business Policy Applies to:	All lines of business

Background

Pyrukynd® is a pyruvate kinase activator indicated for the treatment of hemolytic anemia in adults with pyruvate kinase (PK) deficiency.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
mitapivat (Pyrukynd®)	Hemolytic anemia in adults with pyruvate kinase (PK) deficiency	5 mg orally twice daily	100 mg/day orally

Dosage Forms

- Tablets: 5 mg, 20 mg, and 50 mg.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Hemolytic anemia with pyruvate kinase (PK) deficiency (must meet all):

1. Diagnosis of hemolytic anemia with pyruvate kinase (PK) deficiency;
2. Member is ≥ 18 years of age;
3. Prescribed in consultation with a hematologist;
4. Member has diagnosis of PKD with at least two mutant alleles in the PKLR gene, of which at least one is a missense mutation;
5. Member is not homozygous for the R479H mutation or had two non-missense variants, without the presence of another missense variant, in the PKLR gene;
6. Documentation required for RBC transfusions for hemolytic anemia due to PKD within the previous year;
7. Member has a current hemoglobin level ≤ 10 mg/dL;
8. Dose does not exceed 100 mg/day orally.

Approval Duration

Commercial: 3 months
Medicaid: 3 months

II. Continued Therapy Approval

A. Hemolytic anemia in adults with pyruvate kinase (PK) deficiency (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to the therapy as documented by increase in Hb ≥ 1.5 mg/dL over baseline and/or reduction in transfusion burden;
3. If request is for a dose increase, new dose does not exceed 100 mg/day orally.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
PK: pyruvate kinase
PKLR: pyruvate Kinase L/R
PKD: pyruvate kinase deficiency
FDA: Food and Drug Administration
Hb: hemoglobin
CYP3A: Cytochrome P3A
RBC: red blood cell

APPENDIX B: Therapeutic Alternatives
Not applicable.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- Acute Hemolysis: Avoid abrupt interruption or abrupt discontinuation of Pyrukynd® to minimize the risk of acute hemolysis. A gradual reduction in dosing rather than abrupt cessation is recommended when possible.
- Strong CYP3A Inhibitors Avoid co-administration of strong CYP3A inhibitors with Pyrukynd®.
- Moderate CYP3A Inhibitors Monitor Hb and for increased risks of adverse reactions from Pyrukynd®. When used with a moderate CYP3A inhibitor, do not titrate Pyrukynd® beyond 20 mg twice daily.
- Strong CYP3A Inducers Avoid co-administration of strong CYP3A inducers with Pyrukynd® .
- Moderate CYP3A Inducers Consider alternative therapies that are not moderate CYP3A inducers during treatment with Pyrukynd®. If there are no alternative therapies, monitor Hb and titrate beyond the 50 mg twice daily dose, if necessary, but do not exceed a maximum recommended dose of 100 mg twice daily.

References

1. Pyrukynd® Prescribing Information. Cambridge, MA: Agios Pharmaceuticals, Inc.; February 2022. Available at:

https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=4ccee896-e313-4c6c-9674-b4746ada0a90&type=display. Accessed March 14, 2022.
2. IPD Analytics Rx Insights_New Drug Review_ Pyrukynd®_02.2022. Available at: https://secure.ipdanalytics.com/User/Pharma/RxStrategy/Search?q=Pyrukynd . Accessed March 14, 2022.
3. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2020. Available at: http://www.clinicalkey.com. Accessed March 14, 2022.
4. Micromedex® Healthcare Series [Internet database]. Greenwood Village, CO: Thomson Healthcare. Updated periodically. Available at: http://www.micromedexsolutions.com. Accessed March 14, 2022.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	03/14/2022	04/18/2022