Pyrukynd (mitapivat)

Override(s)	Approval Duration
Prior Authorization Quantity Limit	Initial: 6 months Maintenance therapy requests for clinical response to treatment: 6 months Tapering for therapy discontinuation: 1 month

Medications	Quantity Limit
Pyrukynd (mitapivat) 5mg, 20mg, 50mg tablets Pyrukynd (mitapivat) Taper Packs	May be subject to quantity limit

APPROVAL CRITERIA

Initial requests for Pyrukynd (mitapivat) may be approved if the following criteria are met:

I. Individual is 18 years of age or older; **AND**
II. Individual has a diagnosis of hemolytic anemia due to pyruvate kinase (PK) deficiency; **AND**
III. Documentation is provided that diagnosis of pyruvate kinase deficiency is confirmed by one (A or B) of the following:
    A. Low levels of red blood cells (RBC) PK enzymatic activity; **OR**
    B. At least two (2) mutations of the pyruvate kinase liver and red blood cell (PKLR) gene known or expected to impair PK activity, one (1) of which is a missense mutation;

AND

IV. Documentation is provided for one of the following (A or B):
    A. Hemoglobin (HGB) 10 g/dL or below (NCT03548220); **OR**
    B. Six (6) or more RBC transfusions for hemolytic anemia due to PKD in the last fifty-two (52) weeks prior to initiation of Pyrukynd (mitapivat) (NCT03559699).

Continuation requests for Pyrukynd (mitapivat) may be approved if the following criteria are met:

I. Documentation is provided that individual has a diagnosis of hemolytic anemia due to pyruvate kinase (PK) deficiency;
AND
II. Individual has a positive clinical response to treatment; **OR**
III. Individual has not had a positive clinical response to treatment and is tapering off of therapy.

Requests for Pyrukynd (mitapivat) may not be approved for the following:

I. Individual with moderate or severe hepatic impairment; **OR**
II. Individual is currently using strong CYP3A4 inhibitors or inducers.

Key References:

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2025. URL: http://www.clinicalpharmacology.com. Updated periodically.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Updated periodically.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2025; Updated periodically.
5. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). Identifier NCT03548220, A Study to Evaluate Efficacy and Safety of AG-348 in Not Regularly Transfused Adult Participants With Pyruvate Kinase Deficiency (PKD); 2018 June 7. Available from: https://clinicaltrials.gov/ct2/show/NCT03548220. Accessed March 7, 2022.
6. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). Identifier NCT03548220, A Study Evaluating the Efficacy and Safety of AG-348 in Regularly Transfused Adult Participants With Pyruvate Kinase Deficiency (PKD); 2018 June 18. Available from: https://clinicaltrials.gov/ct2/show/NCT03548220. Accessed March 7, 2022.
7. Al-Samkari, Hanny et al. “Mitapivat versus Placebo for Pyruvate Kinase Deficiency. Reply.” The New England journal of medicine vol. 386,26 (2022): 2539. doi:10.1056/NEJMc2206275
8. Glenthøj, Andreas et al. “Mitapivat in adult patients with pyruvate kinase deficiency receiving regular transfusions (ACTIVATE-T): a multicentre, open-label, single-arm, phase 3 trial.” The Lancet. Haematology vol. 9,10 (2022): e724-e732. doi:10.1016/S2352-3026(22)00214-9
9. van Dijk MJ, Rab MAE, van Oirschot BA, et al. One-year safety and efficacy of mitapivat in sickle cell disease: follow-up results of a phase 2, open-label study. *Blood Adv*. 2023;7(24):7539-7550. doi:10.1182/bloodadvances.2023011477

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.