Drug Quantity Management – Per Days
Hematology – Pyrukynd® (mitapivat tablets)

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Product Identifier(s)

Effective 1/1/23 to 4/11/23: 110199

Effective 4/12/23: 104082

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

National Formulary Medical Necessity

This Drug Quantity Management program has been developed to promote the safe, effective, and economic use of Pyrukynd. If the Drug Quantity Management rule is not met for the requested medication at the point of service, coverage will be determined by the Criteria below. All approvals are provided for the duration noted below.

Drug Quantity Limits

Product	Strength and Form	Maximum Quantity per 28 Days
Pyrukynd® (mitapivat tablets)	5 mg 28-Day Pack	56 tablets
	20 mg 28-Day Pack	56 tablets
	50 mg 28-Day Pack	56 tablets
	5 mg Taper Pack (7 x 5 mg tablets blister wallet)	7 tablets (1 x 5 mg wallet [1 taper pack])
	5 mg and 20 mg Taper Pack	14 tablets (1 x 5 mg wallet and 1 x 20 mg wallet [1 taper pack])
	20 mg and 50 mg Taper Pack	14 tablets (1 x 20 mg wallet and 1 x 50 mg wallet [1 taper pack])

Cigna covers quantities as medically necessary when the following criteria are met:

Pyrukynd 50 mg 28-Day Pack

1. If an individual is taking Pyrukynd concomitantly with a CYP3A4 inducer, approve up to 112 tablets per 28 days.

Conditions Not Covered

Any other exception is considered not medically necessary.

Background

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.

Dosing

Pyrukynd is administered orally with or without food and must be swallowed whole.[1] Tablets cannot be split, crushed, chewed, or dissolved. The recommended initial dose of Pyrukynd is 5 mg twice daily (BID). The dose should then be titrated from 5 mg BID to 20 mg BID and then to the maximum recommended dose of 50 mg BID, with dose increases every 4 weeks. The titration schedule is in Table 1. Prior to increasing to the next dose level, hemoglobin should be assessed. If no benefit has been observed by 24 weeks, based on hemoglobin and hemolysis laboratory results and transfusion requirements, discontinue Pyrukynd.

Table 1. Pyrukynd Dose Titration Schedule.[1]

Duration	Clinical Parameters	Dose Recommendations
Week 1 through Week 4	N/A	5 mg BID
Week 5 through Week 8	Hemoglobin is below normal range or patient has required a transfusion within the last 8 weeks	Increase to 20 mg BID and maintain for 4 weeks.
	Hemoglobin is within normal range and patient has not required a transfusion within the last 8 weeks.	Maintain 5 mg BID.
Week 9 through Week 12	Hemoglobin is below normal range or patient has required a transfusion within the last 8 weeks	Increase to 50 mg BID and maintain thereafter.
	Hemoglobin is within normal range and patient has not required a transfusion within the last 8 weeks.	Maintain the current dose (i.e., 5 mg BID or 20 mg BID)
Maintenance	If hemoglobin decreases.	Consider up-titration to the maximum dose of 50 mg BID.

N/A – Not applicable; BID – Twice daily.

Patients should avoid abrupt interruption or abrupt discontinuation of Pyrukynd to reduce the risk of acute hemolysis.[1] The recommended taper schedule is in Table 2.

Table 2. Pyrukynd Taper Schedule.[1]

Current Dose	Dose Taper Schedule		
	Day 1 – 7	Day 8 – 14	Day 15
5 mg BID	5 mg QD	Discontinue	N/A
20 mg BID	20 mg QD	5 mg QD	Discontinue
50 mg BID	50 mg QD	20 mg QD	Discontinue

BID – Twice daily; QD – Once daily; N/A – Not applicable.

The use of Pyrukynd along with strong cytochrome P450 (CYP)3A inhibitors or inducers should be avoided.[1] If co-administration with a moderate CYP3A inhibitor cannot be avoided, monitor hemoglobin and do not titrate

Pyrukynd beyond 20 mg BID. If co-administration with a moderate CYP3A inducer cannot be avoided, monitor hemoglobin and titrate beyond 50 mg BID, if necessary, but do not exceed a maximum recommended dose of 100 mg BID. If the patient requires a dose reduction due to tolerability, an adverse event, or elevated hemoglobin, the dose may be reduced to the next lower dose level. If Pyrukynd needs to be discontinued, the taper schedule in Table 2 should be used. However, there are some situations outlined in the prescribing information, when discontinuing Pyrukynd without a taper may be warranted.

Availability

Table 3. Pyrukynd Availability.[1]

Dosage Form	Strength/Quantity
5 mg 28-Day Pack	5 mg tablets x 56 tablets
20 mg 28-Day Pack	20 mg tablets x 56 tablets
50 mg 28-Day Pack	50 mg tablets x 56 tablets
5 mg Taper Pack	5 mg blister wallet (7 tablets)
5 mg and 20 mg Taper Pack	5 mg blister wallet (7 tablets) and 20 mg blister wallet (7 tablets)
20 mg and 50 mg Taper Pack	20 mg blister wallet (7 tablets) and 50 mg blister wallet (7 tablets)

References

1. Pyrukynd® tablets [prescribing information]. Cambridge, MA: Agios; February 2022.

Revision History

Type of Revision	Summary of Changes	Approval Date
New Policy	--	03/30/2022