DRUG QUANTITY MANAGEMENT POLICY – PER DAYS

POLICY: Hematology – Pyrukynd Drug Quantity Management Policy – Per Days
- Pyrukynd® (mitapivat tablets – Agios)

REVIEW DATE: 05/02/2025

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. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. 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.

CIGNA NATIONAL FORMULARY COVERAGE:

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	NA	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

NA – 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		
	Days 1 – 7	Days 8 – 14	Day 15
5 mg BID	5 mg QD	Discontinue	NA
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; NA – 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)

POLICY STATEMENT

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 1 year in duration.

Drug Quantity Limits

Product	Strength and Form	Retail Maximum Quantity per Days	Home Delivery Maximum Quantity per Days
Pyrukynd® (mitapivat tablets)	5 mg tablets (28-Day Pack)	56 tablets per 28 days	168 tablets per 84 days
	20 mg tablets (28-Day Pack)	56 tablets per 28 days	168 tablets per 84 days
	50 mg tablets (28-Day Pack)	56 tablets per 28 days	168 tablets per 84 days
	5 mg tablets Taper Pack (7 x 5 mg tablets blister wallet)	7 tablets per 365 days	
	5 mg and 20 mg Taper Pack (1 x 5 mg wallet and 1 x 20 mg wallet)	14 tablets per 365 days	
	20 mg and 50 mg Taper Pack (1 x 20 mg wallet and 1 x 50 mg wallet)	14 tablets per 365 days	

EXCEPTIONS TO THE QUANTITY LIMITS LISTED ABOVE ARE COVERED AS MEDICALLY NECESSARY WHEN THE FOLLOWING CRITERIA ARE MET. ANY OTHER EXCEPTION IS CONSIDERED NOT MEDICALLY NECESSARY.

CRITERIA

Pyrukynd 50 mg 28-Day Pack

1. If a patient is taking Pyrukynd concomitantly with a cytochrome P450 (CYP)3A4 inducer, approve 112 tablets per 28 days at retail or 336 tablets per 84 days at home delivery.

REFERENCES

1. Pyrukynd® tablets [prescribing information]. Cambridge, MA: Agios; January 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	Policy was updated to reflect the existing quantity limits when a product is obtained via home delivery. No criteria changes.	05/04/2023
Annual Revision	No criteria changes.	05/15/2024
Annual Revision	No criteria changes.	05/02/2025