DRUG QUANTITY MANAGEMENT POLICY – PER RX

POLICY: Phenylketonuria – Palynziq Drug Quantity Management Policy – Per Rx
- Palynziq® (pegvaliase-pqpz subcutaneous injection – BioMarin)

REVIEW DATE: 03/11/2026

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

Palynziq is indicated to reduce blood phenylalanine concentrations in adult patients with **phenylketonuria** (PKU) who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on existing management.[1] Treatment with Palynziq should be managed by a healthcare provider experienced in the management of PKU. Baseline blood phenylalanine concentrations should be obtained before initiating treatment.

Dosing

Dosing of Palynzq is individualized. During titration and maintenance of Palynziq treatment, patients may experience blood phenylalanine concentrations below 30 micromol/L.[1] For blood phenylalanine concentrations below 30 micromol/L, the dosage of Palynziq may be reduced and/or dietary protein and phenylalanine intake may be modified to maintain blood phenylalanine concentrations within a clinically acceptable range and above 30 micromol/L. In the Phase III PRISM-2 open-label

extension study (n = 261), the maintenance dose of Palynziq could be adjusted between 5 mg/day and 60 mg/day based on investigator-determined efficacy and tolerability.[2]

Table 1. Palynziq Dose Titration.[1]

Treatment	Palynziq Dose	Duration*
Induction	2.5 mg once weekly	4 weeks
Titration	2.5 mg twice weekly	1 week
	10 mg once weekly	1 week
	10 mg twice weekly	1 week
	10 mg four times per week	1 week
	10 mg QD	1 week
Maintenance	20 mg QD	24 weeks
	40 mg QD	16 weeks
Maximum	60 mg QD	16 weeks

* Additional time may be required prior to each dosage escalation based on patient tolerability; QD – Once daily.

Availability

Palynziq is available in the following strengths: 2.5 mg/0.5 mL (1 syringe per carton), 10 mg/0.5 mL (1 syringe per carton), and 20 mg/1 mL syringes (1 syringe or 10 syringes per carton).[1] The product is provided in a 1 mL glass syringe with a 26 gauge, 0.5 inch needle.

POLICY STATEMENT

This Drug Quantity Management program has been developed to manage potential dose escalation of Palynziq and to provide a sufficient quantity for approvable indications. 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.

Drug Quantity Limits

Product	Strength and Form	Retail Maximum Quantity per Rx	Home Delivery Maximum Quantity per Rx
Palynziq® (pegvaliase-pqpz subcutaneous injection)	2.5 mg/0.5 mL syringe	8 syringes	
	10 mg/0.5 mL syringe	30 syringes	90 syringes
	20 mg/1 mL syringe	60 syringes	180 syringes

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

Palynziq 2.5 mg/0.5 mL syringe

1. If the patient requires a dose of 5 mg per day due to blood phenylalanine concentrations below 30 micromol/L while taking a dose > 5 mg per day,

approve 60 syringes per dispensing at retail or 180 syringes per dispensing at home delivery.

Palynziq 20 mg/1 mL syringe

1. If the patient requires a maintenance dose of 60 mg per day, approve 90 syringes per dispensing at retail or 270 syringes per dispensing at home delivery.

Palynziq 10 mg/0.5 mL syringe

No overrides recommended.

Note: For patients who are receiving ≥ 20 mg/day, refer the patient to the 20 mg/1 mL syringe.

REFERENCES

1. Palynziq subcutaneous injection [prescribing information]. Novato, CA: BioMarin; November 2025.
2. Thomas J, Levy H, Amato S, et al; PRISM investigators. Pegvaliase for the treatment of phenylketonuria: results of a long-term phase 3 clinical trial program (PRISM). *Mol Genet Metab*. 2018 May;124(1):27-38.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	03/27/2024
Annual Revision	No criteria changes.	03/03/2025
Annual Revision	No criteria changes.	03/11/2026