UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2026 P 2150-11
Program	Prior Authorization/Medical Necessity
Medication	Palynziq™ (pegvaliase-pqpz)
P&T Approval Date	9/2018, 7/2019, 7/2020, 6/2021, 7/2021, 7/2022, 7/2023, 7/2024, 7/2025, 11/2025, 6/2026
Effective Date	9/1/2026

1. Background:

Palynziq is a phenylalanine-metabolizing enzyme indicated to reduce blood phenylalanine concentrations in adult and pediatric patients 12 years of age and older with phenylketonuria (PKU) who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on existing management.

2. Coverage Criteria[a]:

A. Initial Authorization

1. **Palynziq** will be approved based on **all** of the following criteria:

   a. Diagnosis of phenylketonuria (PKU)

   -AND-

   b. Patient is actively on a phenylalanine-restricted diet

   -AND-

   c. **One** of the following:

      (1) Patient has a contraindication to sapropterin dihydrochloride (list reason)

      -OR-

      (2) History of failure or intolerance to sapropterin dihydrochloride (document date of trial and list reason for therapeutic failure or intolerance)

      -OR-

      (3) Patient is not an appropriate candidate for sapropterin dihydrochloride due to biallelic *PAH* pathogenic variants with no residual enzyme activity

   -AND-

   d. Physician attestation that the patient will not be receiving Palynziq in combination with sapropterin dihydrochloride (e.g., Javygtor, Kuvan, Zelvysia) or Sephience (sepiapterin)

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-AND-

e. Submission of medical records (e.g., chart notes, laboratory values) documenting that the patient has a blood phenylalanine concentration greater than 600 micromol/L

Authorization will be issued for 12 months.

B. Reauthorization

1. **Palynziq** will be approved based on **all** of the following criteria:

a. Patient is actively on a phenylalanine-restricted diet

-AND-

b. **One** of the following:

(1) Submission of medical records (e.g., chart notes, laboratory values) documenting that the patient has a blood phenylalanine concentration less than 600 micromol/L

-OR-

(2) Submission of medical records (e.g., chart notes, laboratory values) documenting that the patient has achieved a 20% reduction in blood phenylalanine concentration from pre-treatment baseline

-OR-

(3) Patient is in initial titration/maintenance phase of dosing regimen and dose is being titrated based on blood phenylalanine concentration response up to maximum labeled dosage of 60 mg once daily

-AND-

c. Submission of medical records (e.g., chart notes, laboratory values) documenting that the patient is not receiving Palynziq in combination with sapropterin dihydrochloride (e.g., Javygtor, Kuvan, Zelvysia) or Sephience (sepiapterin) [Prescription claim history that does not show any concomitant sapropterin dihydrochloride or Sephience (sepiapterin) claim within 60 days of reauthorization request may be used as documentation.]

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

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3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may also be in place.

4. References:

1. Palynziq [package insert], Novato, CA: BioMarin Pharmaceutical Inc.; February 2026.
2. Thomas J, Levy H, Amato S, et al. Pegvaliase for the treatment of phenylketonuria: Results of a long-term phase 3 clinical trial program (PRISM). Mol Genet Metab. 2018;124(1):27-38.
3. Smith WE, Berry SA, Bloom K, et al. Phenylalanine hydroxylase deficiency diagnosis and management: A 2023 evidence-based clinical guideline of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2025;27(1):101289.

Program	Prior Authorization/Medical Necessity - Palynziq (pegvaliase-pqpz)
Change Control	
9/2018	New program
7/2019	Annual review with no change to coverage criteria.
7/2020	Annual review with no change to coverage criteria.
6/2021	Added history of failure, contraindication, or intolerance to sapropterin dihydrochloride to criteria. Updated titration criteria in re-authorization. Updated reference.
7/2021	Updated contraindication, failure, intolerance criteria.
7/2022	Annual review with no change to coverage criteria.
7/2023	Annual review with no change to coverage criteria.
7/2024	Annual review. Updated authorization durations to 12 months. Updated references.
7/2025	Annual review with no change to coverage criteria. Updated references.
11/2025	Added Sephience to combination use criterion. Revised requirement for trial of sapropterin therapy to remove specified length of trial and to exclude patients with two null mutations in *trans*. Updated references.
6/2026	Annual review. Updated background with expanded indication in pediatric patients 12 years of age and older. Added examples of branded and branded generics of sapropterin to combination use criterion. Updated language in sapropterin step bypass due to biallelic *PAH* pathogenic variants with no residual enzyme activity with no change in clinical intent. Updated references.

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