

Clinical Policy: Pegvaliase-pqpz (Palynziq)

Reference Number: PA.CP.PHAR.140

Effective Date: 10/2018

Last Review Date: 04/2026

Description

Pegvaliase-pqpz (Palynziq[™]) is a PEGylated phenylalanine ammonia lyase (PAL) enzyme that converts phenylalanine to ammonia and trans-cinnamic acid. It substitutes for the deficient phenylalanine hydroxylase (PAH) enzyme activity in patients with phenylketonuria (PKU) and reduces blood phenylalanine concentrations.

FDA Approved Indication(s)

Palynziq is indicated to reduce blood phenylalanine concentrations in adult and pediatric patients ≥ 12 years of age with PKU who have uncontrolled blood phenylalanine concentrations > 600 $\mu\text{mol/L}$ on existing management.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness[®] that Palynziq is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Phenylketonuria (must meet all):

1. Diagnosis of PKU;
2. Prescribed by or in consultation with an endocrinologist, metabolic disease specialist, or genetic disease specialist;
3. Age ≥ 12 years;
4. Recent (within 90 days) phenylalanine (Phe) blood level is > 600 $\mu\text{mol/L}$;
5. Failure of generic sapropterin (Kuvan[®]) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Palynziq is not prescribed concurrently with sapropterin (Kuvan, Javygtor, Zelvysia) or Sephience[™];
7. Dose does not exceed 20 mg per day.

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

A. Phenylketonuria (must meet all):

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.PHARM.01) applies;

2. Palynziq is not prescribed concurrently with sapropterin (Kuvan, Javygtor, Zelvysia) or Sepience;
3. Member meets one of the following (a, b, or c):
 - a. Member has achieved blood Phe control (i.e., blood Phe level is ≤ 600 $\mu\text{mol/L}$);
 - b. Request is for 40 mg per day and member has previously used 20 mg per day continuously for at least 6 months without achieving blood Phe control;
 - c. Request is for 60 mg per day and member meets both of the following (i and ii):
 - i. Member has previously used 40 mg per day continuously for at least 16 weeks without achieving blood Phe control;
 - ii. Member has not used 60 mg per day continuously for more than 16 weeks without achieving blood Phe control;
4. If request is for a dose increase, new dose does not exceed 60 mg per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PAPHARM.01) applies.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

PAH: phenylalanine hydroxylase

PAL: phenylalanine ammonia lyase

Phe: phenylalanine

PKU: phenylketonuria

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
sapropterin (Kuvan, Javygtor, Zelvysia)	Age 1 month to ≤ 6 years (starting dose): 10 mg/kg PO QD Age ≥ 7 years (starting dose): 10 to 20 mg/kg PO QD	20 mg/kg/day

Therapeutic alternatives are listed as Brand name[®] (generic) when the drug is available by brand name only and generic (Brand name[®]) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s): risk of anaphylaxis

Appendix D: General Information

- Palynziq has a black box warning for the potential to cause anaphylaxis and enrollment in a REMS program is required, along with supervision of the initial dose by a healthcare professional and the need to carry auto-injectable epinephrine at all times while using Palynziq. Use of premedication with H₁ blockers, H₂ blockers, and/or antipyretics can also be considered.
- Per the Palynziq PI, discontinuation of Palynziq is recommended if a patient has not achieved an adequate response (blood Phe concentration ≤ 600 $\mu\text{mol/L}$) after 16 weeks of continuous treatment with the maximum dosage of 60 mg QD.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PKU	Initiate dosing with 2.5 mg SC once weekly for 4 weeks. Administer the initial dose under the supervision of a healthcare provider. Titrate the Palynziq dosage in a step-wise manner, based on tolerability, over ≥ 5 weeks, to achieve a dosage of 20 mg SC QD. Maintain the Palynziq dosage at 20 mg SC QD for ≥ 24 weeks. Consider increasing the Palynziq dosage to 40 mg SC QD in patients who have been maintained continuously on 20 mg QD for ≥ 24 weeks and who have not achieved a blood Phe concentration ≤ 600 $\mu\text{mol/L}$. Consider increasing the dosage to a maximum of 60 mg SC QD in patients who have been on 40 mg QD continuously for ≥ 16 weeks and who have not achieved a blood Phe concentration ≤ 600 $\mu\text{mol/L}$. Discontinue Palynziq in patients who have not achieved a response (blood Phe concentration ≤ 600 $\mu\text{mol/L}$) after 16 weeks of continuous treatment with the maximum dosage of 60 mg QD.	60 mg/day

VI. Product Availability

Injection, single-dose prefilled syringe: 2.5 mg/0.5 mL, 10 mg/0.5 mL, 20 mg/mL

VII. References

1. Palynziq Prescribing Information. Novato, CA: BioMarin Pharmaceutical Inc.; February 2026. Available at: <http://www.palynziq.com>. Accessed March 5, 2026.
2. Vockley J, Andersson HC, et al. Phenylalanine hydroxylase deficiency: diagnosis and management guideline. Genet Med. Feb 2014;16(2):188-200.
3. Thomas J, Levy H, et al. Pegvaliase for the treatment of phenylketonuria: results of a long-term phase 3 clinical trial program (PRISM). Molecular Genetics and Metabolism. 2018;124:27-38.
4. Harding CO, Amato RS, et al. Pegvaliase for the treatment of phenylketonuria: a pivotal, double-blind randomized discontinuation phase 3 clinical trial. Molecular Genetics and Metabolism. 2018;124:20-26.
5. 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). Genetics in Medicine. 2025;27:101289. doi: <https://doi.org/10.1016/j.gim.2024.101289>.
6. Van Wegberg AMJ, MacDonald A, Ahring K, et al. European guidelines on diagnosis and treatment of phenylketonuria: first revision. Molecular Genetics and Metabolism. June 2025;145(2):109125. <https://doi.org/10.1016/j.ymgme.2025.109125>.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPSC Codes	Description
J3590, C9399	Unclassified biologics

Reviews, Revisions, and Approvals	Date
Policy created	10/2018
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019
4Q 2020 annual review: added age limit; added requirement for current and continued use of Phe-restricted diet; added requirement for a prior trial of Kuvan; referenced reviewed and updated.	10/2020
4Q 2021 annual review: RT4: revised continuation criteria to reflect updated dosing recommendations in the package labeling; references reviewed and updated.	10/2021
4Q 2022 annual review: no significant changes; references reviewed and updated.	10/2022
4Q 2023 annual review: no significant changes; references reviewed and updated.	10/2023
4Q 2024 annual review: no significant changes; added exclusion against concomitant use with sapropterin (Kuvan) for Continued Therapy to mirror Initial Approval Criteria; references reviewed and updated.	10/2024

Reviews, Revisions, and Approvals	Date
4Q 2025 annual review: added Sephience (newly FDA-approved for PKU) as an agent that should not be used concomitantly with Palynziq; references reviewed and updated.	10/2025
2Q 2026 annual review: bringing forward to align with the annual review cycle for Kuvan; removed adherence to Phe-restricted diet; references reviewed and updated. RT4: updated criteria to reflect the newly FDA-approved pediatric use for patients ≥ 12 years of age.	04/2026