Clinical Policy: Pegvaliase-pqpz (Palynziq)

Reference Number: ERX.SPA.292
Effective Date: 12.01.18
Last Review Date: 11.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 patients with PKU who have uncontrolled blood phenylalanine concentrations > 600 µmol/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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 ≥ 18 years;
4. Recent (within 90 days) phenylalanine (Phe) blood level is > 600 µmols/L;
5. Member is currently on a Phe-restricted diet and will continue this diet during treatment with Palynziq;
6. Failure of Kuvan® at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
7. Palynziq is not prescribed concurrently with Kuvan;
8. Dose does not exceed 20 mg per day.

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Phenylketonuria (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is currently on a phenylalanine-restricted diet and will continue this diet during treatment with Palynziq;

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 µmol/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 a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 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
Kuvan (sapropterin)	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 H_1 blockers, H_2 blockers, and/or antipyretics can also be considered.
- Per the Palynziq prescribing information, discontinuation of Palynziq is recommended if a patient has not achieved an adequate response (blood Phe concentration ≤ 600 µmol/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 either a blood Phe concentration ≤ 600 µmol/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 µmol/L. Discontinue Palynziq in patients who have not achieved a response (blood Phe concentration ≤ 600 µmol/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 syringes: 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.; November 2020. Available at: www.palynziq.com. Accessed August 25, 2022.
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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	07.31.18	11.18
4Q 2019 annual review: no significant changes; references reviewed and updated.	09.10.19	11.19
4Q 2020 annual review: added requirement for current and continued use of Phe-restricted diet; added requirement for a prior trial of Kuvan; revised continuation criteria to reflect updated dosing recommendations in the package labeling; references reviewed and updated.	11.03.20	11.20
4Q 2021 annual review: no significant changes; references reviewed and updated.	08.17.21	11.21
4Q 2022 annual review: no significant changes; references reviewed and updated.	08.25.22	11.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.