Clinical Policy: Pegvaliase-pqpz (Palynziq)

Reference Number: PA.CP.PHAR.140
Effective Date: 10.17.18
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Revision Log

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.

It is the policy of health plans affiliated with 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. Recent (within 90 days) phenylalanine (Phe) blood level is > 600 µmols/L;
4. Palynziq is not prescribed concurrently with Kuvan;
5. 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 Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
2. Member meets one of the following (a, b, or c):
   a. Blood Phe level has decreased by ≥ 20% from pre-treatment baseline;
   b. Blood Phe level is ≤ 600 µmol/L;

c. Member has been using 20 mg per day for at least 6 months, but a dose titration to 40 mg per day is being requested after failure to meet therapeutic targets (a or b above) [only the 40 mg per day dose will be approved];

3. If request is for a dose increase, new dose does not exceed 40 mg per day.

Approval duration: 12 months

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.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

Not applicable

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 PI, discontinuation of Palynziq is recommended if a patient has not achieved a response (≥ 20% reduction in blood Phe concentration from pre-treatment baseline or a blood Phe concentration ≤ 600 µmol/L) after 16 weeks of continuous treatment with the maximum dosage of 40 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 20% reduction in blood Phe concentration from pre-treatment baseline or a blood Phe concentration ≤ 600 µmol/L. Discontinue Palynziq in patients who have not achieved a response (≥ 20% reduction in blood Phe concentration from pre-treatment baseline or a blood Phe concentration ≤ 600 µmol/L) after 16 weeks of continuous treatment with the maximum dosage of 40 mg QD.	40 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.; May 2018. Available at: http://www.palynziq.com. Accessed July 3, 2018.
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	10/18	
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/30/19	