RXADVANCE
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Clinical Policy Title:	pegvalise-pqpz
Policy Number:	RxA.247
Drug(s) Applied:	Palynziq™
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of business

Background

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.

It is indicated to reduce blood phenylalanine concentrations in adult patients with PKU who have uncontrolled blood phenylalanine concentrations > 600 µmol/L on existing management

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Pegvaliase-pqpz (Palynziq™)	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, (after 4-week induction): 2.5 mg twice weekly for 1 week, then 10 mg once weekly for 1 week, then 10 mg twice weekly for 1 week, then 10 mg 4 times/week for 1 week, then 10 mg once daily for 1 week. Additional time may be required prior to each dosage escalation based on patient tolerability. 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	40mg/day

		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.	

Dosage Forms

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

Clinical Policy

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

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. Palynziq is not prescribed concurrently with Kuvan;
6. Dose does not exceed 20 mg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. Phenylketonuria (must meet all):

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
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
Commercial: 12 months

Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
Phe: phenylalanine
PAH: phenylalanine hydroxylase
PAL: phenylalanine ammonia lyase
PKU: phenylketonuria

APPENDIX B: Therapeutic Alternatives

Not Applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported

- Boxed Warning(s):
  - None reported

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

References

1. Palynziq Prescribing Information. Novato, CA: BioMarin Pharmaceutical Inc.; May 2018. Available at: http://www.palynziq.com. Accessed June 28, 2020.
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 longterm 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.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed 1. Clinical policy table was updated. 2. Continued Therapy criteria II.A.1 was	06/28/2020	09/14/2020

rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 3. Dosing information: Titration dose updated on a weekly basis. 4. Reference reviewed and updated.		