Clinical Policy Title:	pegvalise-pqpz
Policy Number:	RxA.247
Drug(s) Applied:	Palynziq®
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2021
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	Initial dosage is 2.5 mg subcutaneously once weekly for 4 weeks. Titrate the dosage in a step-wise manner over at least 5 weeks based on tolerability to achieve a dosage of 20 mg once daily. Consider increasing the dosage to 40 mg once daily in patients who have been on 20 mg once daily continuously for at least 24 weeks and who have not achieved blood Phe control (blood phenylalanine concentration less than or equal to 600 micromol/L). Consider increasing the dosage to a maximum of 60 mg once daily in patients who have been on 40 mg once daily continuously for at least 16 weeks and who have not achieved blood Phe control.	60mg/day

Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
		Discontinue Palynziq® in patients who have not achieved an adequate response after 16 weeks of continuous treatment with the maximum dosage of 60 mg once daily. Reduce the dosage and/or modify dietary protein and Phe intake, as needed, to maintain blood Phe concentrations within a clinically acceptable range and above 30 micromol/L.	

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. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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 40 mg per day.

Approval Duration

Commercial: 12 months

Medicaid: 12 months

II. Continued Therapy Approval

A. Phenylketonuria (must meet all):

1. Member is 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. The member has not responded to Palynziq® at a dose of 20 mg/day for 24 weeks followed by 40

mg/day for 16 weeks, but a dose titration to 60 mg per day is being requested after failure to meet therapeutic targets (a or b above) [only the 60 mg per day dose will be approved];

3. If request is for a dose increase, new dose does not exceed 60 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
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
sapropterin (Kuvan®)	10 to 20 mg/kg/dose orally once daily	20 mg/kg/day

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed Warning(s):
  - 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 60 mg once daily.

References

1. Palynziq® Prescribing Information. Novato, CA: BioMarin Pharmaceutical Inc.; November 2020. Available at: http://www.palynziq.com. Accessed July 12, 2021.
2. Vockley J, Andersson HC, et al. Phenylalanine hydroxylase deficiency: diagnosis and management guideline. Genet Med. Feb 2014;16(2):188-200. Available at: https://pubmed.ncbi.nlm.nih.gov/24385074/. Accessed July 12, 2021.

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. Available at: https://pubmed.ncbi.nlm.nih.gov/29653686/. Accessed July 12, 2021.
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5. Palynziq®, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed July 13, 2021.
6. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2021. Accessed with subscription at: http://www.clinicalkey.com. Updated June 18, 2021. Accessed July 13, 2021.

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 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.	06/28/2020	09/14/2020
Policy was reviewed. 1. Dosing Information dosing regimen was updated from “Initiate dosing with 2.5 mg SC once weekly for 4 weeks. Administer …” to “Consider increasing the dosage to a maximum of 60 mg once daily in patients who have been on 40 mg once daily continuously for at least 16 weeks and who have not achieved blood Phe control…”. 2. Dosing Information maximum dose was updated from “40 mg/day” to “60 mg/day”. 3. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 4. Initial Approval Criteria I.A.6 was updated from “20 mg per day” to “40 mg per day”. 5. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 6. Continued Therapy Criteria II.A.2.c was	07/13/2021	9/14/2021

updated from “Member has been using 20 mg per day for at least 6 months, but a dose titration to 40 mg per day is being…” to “The member has not responded to Palynziq® at a dose of 20 mg/day for 24 weeks followed by 40 mg/day for 16 weeks.”. 7. Therapeutic Alternatives verbiage was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..". 8. Appendix B: Therapeutic Alternatives was updated to include alternative drug "sapropterin (Kuvan®)"and its dosing regimen and maximum dose. 9. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 10. Appendix C was updated to include Boxed Warning “Anaphylaxis.”. 11. References were reviewed and updated.		