Medical Drug Clinical Criteria

Subject:	Palynziq (pegvaliase-pqpz)		
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Table of Contents

Overview

This document addresses the use of Palynziq (pegvaliase-pqpz) approved for use in adult patients with phenylketonuria (PKU) who have uncontrolled blood phenylalanine (PHE) levels on existing management.

PKU results in accumulation of PHE in the blood due to a deficiency in the hepatic enzyme phenylalanine hydroxylase (PAH). If left untreated, elevated blood PHE levels can result in intellectual disability. Treatment of PKU is lifelong with a goal of maintaining blood PHE levels in the range of 120 - 360 micromol/L. Dietary phenylalanine and protein restriction, often with the use of medical foods, is the mainstay of therapy for PKU. If dietary manipulation is insufficient to control blood PHE levels, pharmacotherapy may be utilized.

Palynziq (pegvaliase-pqpz) is a pegylated formulation of phenylalanine ammonia lyase (PAL) which is an enzyme that degrades PHE. Palynziq is approved for adults who have PHE levels greater than 600 micromol/L on existing management which includes dietary therapy with restriction of phenylalanine and/or treatment with Kuvan (sapropterin dihydrochloride). Due to the significant risk of anaphylaxis, Palynziq must be titrated slowly which may take 65 weeks or longer. Maintenance dosage should be individualized to achieve blood phenylalanine control and should be discontinued in non-responders after 16 weeks of treatment at a maximum dose of 60 mg per day. There is no data to support the safety and efficacy of combination use with Kuvan and Palynziq. Individuals in the clinical trial were required to discontinue Kuvan prior to Palynziq initiation.

Palynziq (pegvaliase-pqpz) has a black box warning for anaphylaxis which may occur at any time during treatment. The initial dose must be administered under the supervision of a healthcare provider equipped to manage anaphylaxis and closely observe individual for at least 60 minutes following injection. Concurrent auto-injectable epinephrine must be prescribed and individuals are instructed to carry epinephrine with them at all times during treatment. Due to the risk of anaphylaxis, Palynziq is only available through a restricted REMS program. Additional information and forms for individuals, prescribers, and pharmacists may be found on the Palynziq REMS program website: www.palynziqrems.com.

Treatment with Palynziq (pegvaliase-pqpz) should be directed by physicians knowledgeable in the management of PKU. The initiation of therapy does not eliminate the need for appropriate monitoring by trained professionals. Individuals being treated with Palynziq should have frequent blood PHE measurements and nutritional counseling with their physician and other individuals of the health care team to encourage maintenance of blood PHE levels in the desirable range.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Palynziq (pegvaliase-pqpz)

Initial requests for Palynziq (pegvaliase-pqpz) may be approved if the following criteria are met:

I. Individual is 18 years of age or older; **AND**
II. Individual has a prescription for an auto-injectable epinephrine agent; **AND**
III. Individual has a diagnosis of phenylketonuria (PKU); **AND**
IV. Documentation is provided that individual has uncontrolled blood phenylalanine (PHE) concentrations (> 600 micromol/L) on existing management, including but not limited to the following:
    A. Dietary therapy with restriction of dietary PHE;
    B. Sapropterin dihydrochloride (Kuvan, Javygtor).

Requests for continued use of Palynziq (pegvaliase-pqpz) may be approved if the following criteria are met:

I. Documentation is provided that there is positive response to therapy as evidenced by a reduction and maintenance of blood PHE levels below 600 micromol/L; **OR**
II. Individual is showing signs of continuing improvement but has not completed titration to maximum tolerated dose.

Palynziq (pegvaliase-pqpz) may not be approved for the following:

I. Individual is using in combination with sapropterin dihydrochloride (Kuvan, Javygtor); **OR**
II. When the above criteria are not met and for all other indications not included above.

Initial and continued approval duration: 1 year

Quantity Limits

Palynziq (pegvaliase-pqpz) Quantity Limits

Drug	Limit
Palynziq (pegvaliase-pqpz) 20 mg/mL prefilled syringe	1 syringes per day
Override	
Initial requests for up to two 20 mg syringes per day may be approved if the following criteria are met: I. Individual has been on treatment with 20 mg per day for at least 24 weeks; **AND** II. Individual has not achieved a blood PHE level below 600 micromol/L. Initial requests for up to three 20 mg syringes per day may be approved if the following criteria are met: I. Individual has been on treatment with 40 mg per day for at least 16 weeks; **AND** II. Individual has not achieved a blood PHE level below 600 micromol/L. Requests for continued use of 2 or 3 syringes per day may be approved if increased dosing resulted in reduction and maintenance of blood PHE levels below 600 micromol/L.	

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

C9399	Unclassified drugs or biologicals (Outpatient Hospital Use ONLY)
J3590	Unclassified biologics (when specified as [Palynziq] (pegvaliase-pqpz)

ICD-10 Diagnosis

E70.0	Classical phenylketonuria
E70.1	Other hyperphenylalaninemias
Z71.3	Dietary counseling and surveillance

Document History

Revised: 06/10/2024
Document History:

- 06/10/2024 – Annual Review: Wording and formatting updates. Coding Reviewed: No changes.
- 06/12/2023 – Annual Review: Add generic formation names for Kuvan. Wording and formatting updates. Coding Reviewed: No changes.
- 06/13/2022 – Annual Review: Wording and formatting updates. Coding Reviewed: No changes.
- 08/01/2021 – Administrative update to add documentation.

- 06/14/2021 – Annual Review: Update continuation of use requirement and quantity limit override to require PHE levels only per label; allow continuation of use for individuals titrating dose; add quantity limit override to allow up to three syringes per day for max dose. Coding Reviewed: No changes.
- 08/21/2020 – Annual Review: Add may not be approved section for combination use with Kuvan; update quantity limit to ensure appropriate use of max dosing. Administrative update to add drug specific quantity limit. Coding Reviewed: No changes
- 06/10/2019 – Annual Review: Clarify continuation of use requirements. Coding Reviewed: Added Z71.3
- 11/09/2018 – Added ICD-10 codes E70.1, E70.0
- 11/02/2018 – Added HCPCS codes:J9399 and J3590
- 08/17/2018 – Annual Review: Add new clinical guideline for Palynziq.

References

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2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2024; Updated periodically.
4. Longo N, Dimmock D, Levy H, et al. Evidence- and consensus-based recommendations for the use of pegvaliase in adults with phenylketonuria. *Genet Med* 2018; doi: 10.1038/s41436-018-0403-z. [Epub ahead of print]. Available at: https://www.nature.com/articles/s41436-018-0403-z
5. American College of Medical Genetics and Genomics Therapeutic Committee. Phenylalanine hydroxylase deficiency: diagnosis and management guideline. *Genet Med.* 2014; 16(2):188-200. doi:10.1038/gim.2013.157. Available from: http://www.nature.com/gim/journal/v16/n2/pdf/gim2013157a.pdf.