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Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Endocrine and Metabolic Drugs	**Original Policy Date:**	June 29, 2018
Subject:	Palynziq	**Page:**	1 of 5

Last Review Date: March 7, 2025

Palynziq

Description

Palynziq (pegvaliase-pqpz)

Background
Palynziq (pegvaliase-pqpz) is a phenylalanine-metabolizing enzyme indicated to reduce blood phenylalanine concentrations in adult patients with phenylketonuria (PKU) who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L. Prolonged high blood phenylalanine (Phe) levels are neurotoxic and lead to impairment of intelligence and other brain functions, such as attentiveness. Reduction of blood Phe levels through dietary control is an important determinant of long-term neurologic outcome in phenylketonuria (PKU) patients, and reduction of blood Phe levels in patients with PKU has been shown to decrease the long-term risk of neurologic injury. Palynziq substitutes for the deficient phenylalanine hydroxylase (PAH) enzyme activity in patients with PKU and reduces blood phenylalanine concentrations (1).

Regulatory Status
FDA-approved indication: Palynziq is a phenylalanine-metabolizing enzyme indicated to reduce blood phenylalanine concentrations in adult patients with phenylketonuria who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on existing management (1).

Palynziq has a boxed warning that anaphylaxis may occur at any time during Palynziq treatment (1).

Administration of the initiation dose of Palynziq must be under the supervision of a healthcare provider equipped to manage anaphylaxis, and patients must be closely observed for at least 60 minutes following injection. Prior to self-administration, confirm patient competency with self-administration, and patient's and observer's (if applicable) ability to recognize signs and symptoms of anaphylaxis and to administer auto-injectable epinephrine, if needed (1).

The prescriber should prescribe an auto-injectable epinephrine and provide instructions on its appropriate use. The patient should be advised to carry the epinephrine injector at all times while on Palynziq and if used, to seek follow up medical care (1).

Palynziq is available only through a restricted program called the Palynziq REMS Program (1).

The safety and effectiveness of Palynziq in pediatric patients have not been established (1).

Related policies
Kuvan

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Palynziq may be considered **medically necessary** if the conditions indicated below are met.

Palynziq may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age and older

Diagnosis

Patient must have the following:

Phenylketonuria (PKU)

AND ALL of the following:

1. Blood phenylalanine concentration > 600 micromol/L after a trial of sapropterin dihydrochloride (Kuvan)
2. Physician agrees to assess patient tolerability, blood phenylalanine concentration, and dietary protein and phenylalanine intake throughout treatment
3. Prescriber and patient must be enrolled with the Palynziq REMS Program
4. Auto-injectable epinephrine has been prescribed and the patient or caregiver has been instructed in its use
5. **NOT** to be used in combination with sapropterin dihydrochloride (Kuvan)

Prior–Approval *Renewal* Requirements

Age 18 years of age and older

Diagnosis

Patient must have the following:

Phenylketonuria (PKU)

1. **NOT** to be used in combination with sapropterin dihydrochloride (Kuvan)
2. Auto-injectable epinephrine has been prescribed and the patient or caregiver has been instructed in its use
3. Patient had adequate response to treatment

Policy Guidelines

Pre–PA Allowance

None

Prior–Approval Limits

Duration 6 months

Prior–Approval *Renewal* Limits

Duration 12 months

Rationale

Summary
Palynziq (pegvaliase-pqpz) is a phenylalanine-metabolizing enzyme indicated to reduce blood phenylalanine concentrations in adult patients with phenylketonuria (PKU) who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L. Palynziq substitutes for the deficient phenylalanine hydroxylase (PAH) enzyme activity in patients with PKU and reduces blood phenylalanine concentrations. The safety and effectiveness of Palynziq in pediatric patients have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Palynziq while maintaining optimal therapeutic outcomes.

References

1. Palynziq [package insert]. Novato, CA. BioMarin Pharmaceutical, Inc.; November 2020.

Policy History

Date	Action
June 2018	Addition to PA
September 2018	Annual review Addition of auto-injectable epinephrine requirements and trial of Kuvan per SME
December 2019	Annual review
October 2020	Removal of renewal requirement that patient needed to have at least 20% reduction in phenylalanine concentration from baseline or reduction in phenylalanine concentration to ≤ 600 micromol/L Addition of renewal requirement that patient must have adequate response to treatment
December 2020	Annual review
September 2021	Annual review and reference update
September 2022	Annual review
September 2023	Annual review
March 2024	Annual review

March 2025	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.