Pharmacy Policy Bulletin: J-0769 Palynziq (pegvaliase-pqpz) – Commercial and Healthcare Reform	
Number: J-0769	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1):** 1. Miscellaneous Specialty Drugs Injectable = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0769-010	**Original Date:** 08/01/2018
Effective Date: 10/08/2025	**Review Date:** 09/17/2025

Drugs Product(s):	• Palynziq (pegvaliase-pqpz)
FDA-Approved Indication(s):	• To reduce blood phenylalanine concentrations in adult patients with phenylketonuria (PKU) who have uncontrolled blood phenylalanine (Phe) concentrations greater than 600 micromol/L on existing management.

Background:	• Palynziq is a pegylated phenylalanine ammonia lyase enzyme that converts phenylalanine to ammonia and trans-cinnamic acid. Palynziq substitutes for the deficient phenylalanine hydroxylase (PAH) enzyme to reduce blood Phe concentrations in the body. • PKU, also known as PAH deficiency, is associated with elevated Phe concentrations in the body. PKU is a rare disorder, affecting 1 every 10,000 to 15,000 people in the United States. The normal Phe blood level in an unaffected individual is 60 micromol/L, while patients with PKU may have levels that exceed 1,200 micromol/L. These elevations may cause chronic intellectual, neurodevelopmental and psychiatric disabilities due to damage to the central nervous system. The target range for blood Phe levels of a treated patient is 120–360 micromol/L. • PKU is treated first with dietary restriction of Phe, an amino acid commonly found in proteins. Subsequent therapy involves Kuvan (sapropterin dihydrochloride); however, this therapy is only effective in patients with residual PAH activity. Palynziq has been studied in patients without an adequate response to either or both of these therapies. Existing management options included prior or current restriction of dietary phenylalanine and protein intake, and/or prior treatment with sapropterin dihydrochloride. • In clinical trials, patients previously treated with Kuvan (saproprterin dihydrochloride) were required to discontinue use prior to the first dose of Palynziq. Kuvan is available as generic sapropterin dihydrochloride. Javygtor is also a generic product for Kuvan. • Palynziq has a black box warning for anaphylaxis, and close observation is recommended for at least 60 minutes following the first injection. Patients are

	also instructed to carry auto-injectable epinephrine with them at all times during treatment with Palynziq. • Prescribing considerations: ○ Palynziq is only available through a restricted REMS program with the goal of mitigating the risk of anaphylaxis associated with treatment. The Palynziq REMS program requires the prescriber certified with the program to prescribe auto-injectable epinephrine with Palynziq. ○ Consider premedication with an H1-receptor antagonist, H2-receptor antagonist, and/or antipyretic prior to administration. ○ 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 subcutaneously once daily. ○ Patients who have been on 20 mg once daily for 24 weeks without achieving a blood phenylalanine concentration less than or equal to 600 micromol/L should be increased to 40 mg once daily. ○ Patients who have been on 40 mg once daily continuously for at least 16 weeks without achieving a blood phenylalanine concentration less than or equal to 600 micromol/L should be increased to 60 mg once daily. ○ Palynziq should be discontinued in patients who have not achieved a blood phenylalanine concentration less than or equal to 600 micromol/L after 16 weeks of continuous treatment with the maximum dosage of 60 mg once daily. ○ Obtain blood Phe concentrations every 4 weeks until a maintenance dosage is established, then periodically throughout treatment. ○ Monitor patients' dietary protein and Phe intake while on Palynziq.

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Palynziq may be approved when all of the following criteria are met **(A. through D.)**:

A. The member is 18 years of age or older.
B. The member has a diagnosis of PKU (ICD-10: E70.0).
C. The member's baseline Phe level is > 600 µM/L.
D. The member has experienced therapeutic failure, contraindication, or intolerance to both of the following **(1. and 2.)**:
  1. Dietary therapy with a Phe-restrictive diet
  2. sapropterin dihydrochloride

II. Reauthorization

When a benefit, reauthorization of Palynziq may be approved when one (1) the following criteria is met **(A. or B.)**:

A. The member's blood Phe concentration less than or equal to 600 micromol/L.
B. The prescriber attests that additional therapy with Palynziq is needed and meets one (1) of the following criteria **(1. or 2.)**:
  1. The member is not currently taking 60 mg/day of Palynziq.
  2. The member has not had an adequate trial of 60 mg/day of Palynziq for 16 weeks.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. The member is not using Palynziq in combination with Kuvan or Javygtor (sapropterin dihydrochloride).
II. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
III. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Palynziq [package insert]. Novato, CA: BioMarin Pharmaceutical Inc; November 2020.
2. Harding CO, Amato RS, Stuy M, et al. Pegvaliase for treatment of phenylketonuria: a pivotal, double-blind randomized discontinuation phase 3 clinical trial. *Mol Genet Metab*. 2018;124(1):20-26.
3. Palynziq REMS (Risk Evaluation and Mitigation Strategy) program. Available at: https://palynziqrems.com/. Accessed June 10, 2024.
4. Vockley J, Andersson HC, Antshel KM, et al. Phenylalanine hydroxylase deficiency: diagnosis and management guideline. *Genetics in Medicine*. 2014;16:188-200.