09-J3000-07

Original Effective Date: 09/15/18

Reviewed: 06/12/24

Revised: 07/15/24

Subject: Pegvaliase-pqpz (Palynziq™)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Phenylketonuria (PKU) is a rare genetic disease resulting in the inability to break down phenylalanine (Phe), an amino acid present in protein-containing foods and high-intensity sweeteners used in a variety of foods and beverages. PKU affects about 1 in 10,000 to 15,000 people in the United States. If untreated, PKU can cause chronic intellectual, neurodevelopmental and psychiatric disabilities. Lifelong restriction of phenylalanine intake through the diet is needed to prevent buildup of Phe in the body, which can cause long-term damage to the central nervous system.

Pegvaliase-pqpz (Palynziq) was approved by the U.S. Food and Drug Administration in May 2018 for the treatment of adult PKU patients who have uncontrolled blood Phe concentrations on current treatment.

The safety and efficacy of pegvaliase-pqpz were studied in an open-label clinical trial of adult patients with PKU (n=261) with blood phenylalanine concentrations greater than 600 µmol/L on existing management. Subjects were treated with pegvaliase-pqpz administered as a subcutaneous injection up to a target dose of either 20 mg or 40 mg once daily.

In the randomized PRISM-1 study (n=261), pegvaliase-pqpz reduced mean blood phenylalanine concentrations from 1232.7 micromol/L at baseline to 564.5 micromol/L at 12 months and 311.4 micromol/L at 24 months. A 20% or greater reduction was achieved by 71.8%. Reductions to 360 micromol/L or less were achieved by 44% at 12 months and 60.7% at 24 months. Reductions to 120 micromol/L or less were achieved by 51.2% at 24 months. Additionally, inattention and mood symptoms (measured with the inattention subscale of the ADHD Rating Scale IV and the Profile of Mood States scale) were improved with treatment; these improvements were maintained throughout the study. Acute systemic hypersensitivity reactions were reported in 12 patients; 6 patients discontinued therapy while the other 6 continued treatment.

The most serious adverse reaction was anaphylaxis, which occurred most frequently during upward titration of the dose within the first year of treatment. Because of this serious risk, the labeling includes

a Boxed Warning and the product is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Palynziq REMS Program.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of pegvaliase-pqpz (Palynziq) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with phenylketonuria (PKU) - documentation from the medical record must be provided
2. Member's baseline blood phenylalanine concentration exceeds 600 micromol/L - laboratory documentation must be provided
3. Member had an inadequate response, persistent intolerable adverse effects, or a contraindication to management with sapropterin (Kuvan)
4. Pegvaliase-pqpz is prescribed by or in consultation with a metabolic disease specialist or a provider specializing in the treatment of PKU
5. Pegvaliase-pqpz will not be used in combination with sapropterin (Kuvan)
6. Member is 18 years of age or older
7. Dosage does not exceed:
    a. Initial: 2.5 mg weekly x 4 weeks
    b. Maintenance: 20 mg daily

Approval duration: 6 months

Continuation of pegvaliase-pqpz (Palynziq) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years for treatment of PKU, **OR** the member has previously met all indication-specific criteria.
2. Member meets **ONE** of the following:
    a. 20% reduction in pre-treatment phenylalanine concentrations – documentation from the medical record must be provided
    b. Phenylalanine concentration is below 600 micromol/L – documentation from the medical record must be provided

c. Member currently demonstrates a beneficial response to treatment **AND** has been receiving pegvaliase-pqpz for a minimum of 6 months **AND** provider is requesting to increase dose to 40 mg daily or 60 mg daily

3. Pegvaliase-pqpz is not being used in combination with sapropterin (Kuvan)
4. Dose does not exceed 20 mg daily with the following exception:
    a. Member was uncontrolled at 20 mg daily and provider has requested to increase dose to 40 mg daily
    b. Member was uncontrolled at 40 mg daily and provider has requested to increase dose to 60 mg daily

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Obtain baseline blood phenylalanine concentration before initiating treatment.
- The recommended initial dosage is 2.5 mg subcutaneously once weekly for 4 weeks.
- Titrate the dosage in a stepwise manner over at least 5 weeks based on tolerability to achieve a dosage of 20 mg subcutaneously once daily. See full prescribing information for titration regimen.
- Assess patient tolerability, blood phenylalanine concentration, and dietary protein and phenylalanine intake throughout treatment.
- Consider increasing the dosage to a maximum of 40 mg subcutaneously once daily in patients who have been on 20 mg once daily continuously for at least 24 weeks and who have not achieved either a 20% reduction in blood phenylalanine concentration from pre-treatment baseline or a blood phenylalanine concentration less than or equal to 600 micromol/L.
- Discontinue Palynziq in patients who have not achieved at least a 20% reduction in blood phenylalanine concentration from pre-treatment baseline or a blood phenylalanine concentration less than or equal to 600 micromol/L after 16 weeks of continuous treatment with the maximum dosage of 40 mg once daily.
- Reduce the dosage and/or modify dietary protein and phenylalanine intake, as needed, to maintain blood phenylalanine concentrations within a clinically acceptable range and above 30 micromol/L.
- Rotate injection sites. If more than one injection is needed for a single dose, the injection sites should be at least 2 inches away from each other.

Dose Adjustments

- Obtain blood phenylalanine concentrations every 4 weeks until a maintenance dosage is established.
- After a maintenance dosage is established, periodically monitor blood phenylalanine concentrations.

- Counsel patients to monitor dietary protein and phenylalanine intake, and adjust as directed by their healthcare provider.

Drug Availability

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

PRECAUTIONS:

Boxed Warning

- Anaphylaxis has been reported after administration of Palynziq and may occur at any time during treatment.
- Administer the initial dose of Palynziq under the supervision of a healthcare provider equipped to manage anaphylaxis, and closely observe patients for at least 60 minutes following injection. Prior to self‑injection, 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.
- Prescribe auto‑injectable epinephrine. Prior to first dose, instruct the patient and observer (if applicable) on its appropriate use. Instruct the patient to seek immediate medical care upon its use. Instruct patients to carry auto-injectable epinephrine with them at all times during Palynziq treatment.
- Palynziq is available only through a restricted program called the Palynziq REMS

Contraindications

- None

Precautions/Warnings

- Hypersensitivity Reactions, Other than Anaphylaxis: Management should be based on the severity of the reaction, recurrence, and clinical judgement, and may include dosage adjustment, temporary drug interruption, or treatment with antihistamines, antipyretics, and/or corticosteroids

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J3590	Unclassified biologics

ICD-10 Diagnosis Codes That Support Medical Necessity

E70.0	Classical phenylketonuria

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. BioMarin. Palynziq (pegvaliase-pqpz) injection. 2021 [cited 6/2/23]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=6dba844a-db02-44f8-8593-ce497ed9406c/.
2. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2024 [cited 6/2/24]. Available from: http://www.clinicalpharmacology.com/.
3. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 6/2/24]. Available from: http://clinicaltrials.gov/.
4. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 6/2/24].
5. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2024 [cited 6/2/24]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 06/12/24.

GUIDELINE UPDATE INFORMATION:

09/15/18	New Medical Coverage Guideline.
10/15/18	Revision to guideline, consisting of updating position statement.

07/15/19	Review and revision to guideline; consisting of updating references and position statement.
07/15/20	Revision to guideline, consisting of updating references.
07/15/21	Review and revision to guideline; updated references.
07/15/22	Review and revision to guideline; updated references.
07/15/23	Review and revision to guideline; updated references.
07/15/24	Review and revision to guideline; updated references.