PRIOR AUTHORIZATION POLICY

POLICY: Phenylketonuria – Palynziq® (pegvaliase-pqpz injection for subcutaneous use – BioMarin Pharmaceuticals) Prior Authorization Policy

REVIEW DATE: 06/17/2020

OVERVIEW

Palynziq is indicated to reduce blood phenylalanine concentrations in adult patients with phenylketonuria (PKU) who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L (µmol/L) on existing management.[1] Treatment with Palynziq should be managed by a healthcare provider experienced in the management of PKU. Baseline blood phenylalanine concentrations should be obtained before initiating treatment.

Dose Titration

Palynziq is titrated up over a period of 9 weeks to the maintenance dose of 20 mg administered subcutaneously (SC) once daily (QD). Therapeutic response may not be achieved until the patient is titrated to an effective maintenance dosage. Palynziq 20 mg SC QD should be maintained for at least 24 weeks. The dose can be increased to a maximum dose of Palynziq 40 mg SC QD in patients who have been maintained continuously on the 20 mg QD dose for at least 24 weeks and who have not achieved either a 20% reduction in blood phenylalanine concentration from pre-treatment baseline levels or a blood phenylalanine concentration ≤ 600 µmol/L. Palynziq should be discontinued in patients who have not achieved a response after 16 weeks of continuous treatment with the maximum dosage of 40 mg QD. In patients who experience blood phenylalanine concentrations < 30 µmol/L during the titration and maintenance phase, the dosage of Palynziq may be reduced and/or dietary protein and phenylalanine intake may be modified to maintain phenylalanine levels within a clinically acceptable range and above 30 µmol/L. Because of the risk of anaphylaxis Palynziq is available only through a restricted Risk Evaluation and Mitigation Strategy (REMS) program. It was unclear from the Palynziq clinical trials if all patients had tried and were non-responders to Kuvan.

Guidelines/Recommendations

The American College of Medical Genetics and Genomics (ACMG) published practice guidelines (2014) for the diagnosis and management of phenylalanine hydroxylase (PAH) deficiency.[2] The guidelines recommend initiating treatment as early as possible, preferably within the first week of life. Dietary restriction of phenylalanine intake is the mainstay of therapy for PKU. Blood phenylalanine levels in all patients should be maintained in the range of 120 to 360 µmol/L. The guidelines state that approximately 25% to 50% of patients with PAH deficiency are responsive to Kuvan™ (sapropterin dihydrochloride tablets and powder for oral solution). A significant decline in blood phenylalanine level is expected in responders once treatment is initiated (with phenylalanine-restricted diet). An improvement in neuropsychiatric symptoms or increase in phenylalanine tolerance without a decrease in blood levels is sufficient reasoning to continue therapy. According to the guidelines, there is strong evidence to support life-long treatment and maintenance of metabolic control in patients with PAH deficiency.

According to the European guidelines for phenylketonuria (2017), there is consensus in the literature that patients with blood phenylalanine concentration > 600 µmol/L should be treated.[3] There is also consensus that patients with blood Phe concentration < 360 µmol/L can remain untreated, but should be monitored. Patients with blood Phe concentration between 360 to 600 µmol/L should be treated until 12 years of age. Treatment for life is recommended for any patient with PKU; however, it is also noted that patients ≥ 12 years of age with blood Phe concentration < 600 µmol/L do not require treatment. All adults with PKU

should have lifelong systematic follow-ups in specialized metabolic centers, due to specific risks which may occur during adulthood. With regards to target Phe levels, in treated PKU patients up to 12 years of age, the target Phe levels should be 120 to 360 µmol/L; in treated PKU patients ≥ 12 years of age, the target Phe levels should be 120 to 600 µmol/L.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Palynziq. Because of the specialized skills required for evaluation and diagnosis of patients treated with Palynziq as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Palynziq to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for 1 year in duration unless otherwise noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Palynziq is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Phenylketonuria.** Approve for the duration noted if the patient meets one of the following (A or B):
   - **A)** Initial Therapy: Approve for 1 year if the patient meets the following criteria (i, ii, and iii):
     - **i.** The patient is ≥ 18 years of age; AND
     - **ii.** The patient has uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on at least one existing treatment modality; AND
       Note: Examples of treatment modalities include restriction of dietary phenylalanine and protein intake and prior treatment with Kuvan (sapropterin dihydrochloride tablets and powder for oral solution).
     - **iii.** The medication is prescribed by or in consultation with a metabolic disease specialist (or specialist who focuses in the treatment of metabolic diseases).
   - **B)** Patients Continuing Therapy: Approve for 1 year if the patient meets the following criteria (i, ii, and iii):
     Note: Patients who have received < 1 year of therapy or those who are restarting therapy with Palynziq should be considered under criterion 1 (Phenylketonuria – Initial Therapy).
     - **i.** The patient is ≥ 18 years of age; AND
     - **ii.** The patient meets one of the following (a or b):
       - **a)** The patient's blood phenylalanine concentration is ≤ 600 micromol/L; OR
       - **b)** The patient has achieved a ≥ 20% reduction in blood phenylalanine concentration from pre-treatment baseline (i.e., blood phenylalanine concentration before starting Palynziq therapy); AND
     - **iii.** The patient is not receiving concomitant therapy with sapropterin dihydrochloride (Kuvan).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Palynziq has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Palynziq™ injection [prescribing information]. Novato, CA: BioMarin Pharmaceuticals; May 2018.
2. Vockley J, Andersson HC, Antshel KM, et al. Phenylalanine hydroxylase deficiency: diagnosis and management guideline. Available at: https://www.acmg.net/docs/Phenylalanine_Hydrosylase_Deficiency_Practice_Guideline_AOP_Jan_2013.pdf. Accessed on June 5, 2020.
3. van Wegberg AMJ, MacDonald A, Ahring A, et al. The complete European guidelines on phenylketonuria: diagnosis and treatment. *Orphanet J Rare Dis.* 2017;12:162.