Washington State Health Care Authority

Endocrine and Metabolic Agents: Metabolic Modifiers - Phenylketonuria (PKU) Agents - Pegvaliase-pqpz (Palynziq)

Medical policy no. 30.90.85.50-1 Effective Date: July 1, 2019

Note:

- *For non-preferred agents in this class/category, patients must have had an inadequate response or have had a documented intolerance due to severe adverse reaction or contraindication to at least TWO* preferred agents.*
  **If there is only one preferred agent in the class/category documentation of inadequate response to ONE preferred agent is needed*
- *If a new-to-market drug falls into an existing class/category, the drug will be considered non-preferred and subject to this class/category prior authorization (PA) criteria*

Background:

Phenylketonuria (PKU) is a rare genetic disorder that effects the metabolism of the amino acid phenylalanine (PHE). The enzyme phenylalanine hydroxylase (PAH) is responsible for breaking down ingested phenylalanine into tyrosine, which leads to the downstream production of necessary neurotransmitters.

Genetic mutations that cause reduced levels of PAH are the most common cause of PKU. Patients with a deficiency of PAH will build up phenylalanine when they eat foods with aspartame or protein. Elevated levels of phenylalanine can cause seizures, intellectual disabilities, brain damage, and other neurological problems. The estimated rate of PKU in the U.S. is about 1 in every 10,000-15,000 births.

The standard of care for PKU treatment is dietary restriction of phenylalanine. Typically, phenylalanine-free protein substitutes are used. If dietary restrictions are not adequate as monotherapy, many patients have success with the oral therapy sapropterin in addition to dietary changes. Pegvaliase-pgpz was approved by the FDA in May 2018 for patients with uncontrolled phenylalanine levels (> 600 µmol/L) on existing management.

Medical Necessity:

Drug	Medical Necessity
pegvaliase-pqpz (Palynziq)	Pegvaliase-pqpz may be considered medically necessary when it is used to reduce blood phenylalanine concentrations in adult patients with phenylketonuria who have uncontrolled blood phenylalanine concentrations greater than 600 µmol/L on existing management.

Clinical policy:

Drug	*Clinical Criteria (Initial Approval)*
pegvaliase-pqpz (Palynziq)	1. Patient has confirmed diagnosis phenylketonuria (PKU) established by a metabolic specialist; **AND** 2. Patient has uncontrolled blood phenylalanine (PHE) concentrations greater than 600 µmol/L over the last 6 months prior to starting pegvaliase (Palynziq); **AND**

	3. Treatment with sapropterin (Kuvan) has been ineffective, not tolerated, or is contraindicated a. Ineffectiveness is defined as a decrease in blood PHE levels of less than 30% from baseline after one month of treatment; **AND** 4. Patient is greater than or equal to 18 years of age; **AND** 5. Palynziq is not to be used in combination with Kuvan. If ALL criteria are met, the request will be approved 12 months
	Criteria (Reauthorization)
	1. The blood PHE level should have decreased at least 20% from baseline or is less than or equal to 600 µmol/L at the maximum dose of 40 mg/day. If ALL criteria are met, the request will be approved 12 months

Dosage and quantity limits:

Drug Name	Dose and Quantity Limits
pegvaliase-pqpz (Palynziq)	40mg/day

Definitions:

Term	Description
PHE	Phenylalanine
PKU	Phenylketonuria

Evidence review:

The key studies leading to the approval of Palynziq® (pegvaliase-pgpz) were two clinical trials conducted together, PRISM-1 and PRISM-2. PRISM-1 was an open-label, parallel-group, randomized controlled trial in adults with blood Phe > 600 µmol/L, and PRISM-2 is a 4 part clinical trial that includes an ongoing long-term open-label extension period. PRISM-1 patients were randomized to receive either 20 mg/day or 40 mg/day maintenance dose of pegvaliase-pgpz. Study participants were eligible to be included in PRISM-2 where they were randomized again to receive either the 20 mg/day dose, 40 mg/day dose, or placebo. Pegvaliase-pgpz exposure reached at least 12 months in 72.0% of patients and reached at least 24 months in 32.6% of patients. Mean blood Phe of the treatment group decreased from 1232.7 µmol/L at baseline to 564.5 µmol/L at 12 months and 311.4 µmol/L at 24 months.

References:

1) Vockley, Jerry, et al. "Phenylalanine hydroxylase deficiency: diagnosis and management guideline." Genetics in Medicine 16.2 (2014): 188.
2) Thomas J, Levy H, Amato S, et al. Pegvaliase for the treatment of phenylketonuria: Results of a long-term phase 3 clinical trial program (PRISM). Mol Genet Metab. 2018;124 (1):27-38.
3) U.S Food and Drug Administration (FDA). FDA approves a new treatment for PKU, a rare and serious genetic disease. FDA News Release. Silver Spring, MD: FDA; May 24, 2018.
4) Palynziq (pegvaliase-pqpz) prescribing information. BioMarin Pharmaceutical, Novato CA. May 2018.
5) Kuvan® (sapropterin dihydrochloride) prescribing information. BioMarin Pharmaceutical, Novato CA. July 2015.

6) https://rarediseases.info.nih.gov/diseases/7383/phenylketonuria
7) https://ghr.nlm.nih.gov/condition/phenylketonuria

History:

Date	Action and Summary of Changes
05.06.2019	New Policy
05.17.2019	Update to Policy – Separated Sapropterin (Kuvan) and Pegvaliase-pqpz (Palynziq) into individual policies