Washington State Health Care Authority

Endocrine and Metabolic Agents: Metabolic Modifiers - Phenylketonuria (PKU) Agents – sapropterin (Kuvan)

Medical policy no. 30.90.85.65-1 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
sapropterin (Kuvan)	Sapropterin may be considered medically necessary when it is used to reduce blood phenylalanine (Phe) levels in patients with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin- (BH4-) responsive phenylketonuria (PKU) in conjunction with a Phe-restricted diet

Clinical policy:

Drug	Clinical Criteria (Initial Approval)
sapropterin (Kuvan)	1. Patient has confirmed diagnosis phenylketonuria (PKU) established by a metabolic specialist; **AND** 2. Phenylalanine (PHE) levels cannot be maintained within the recommended maintenance range [120-360 µmol/dL (2 – 6 mg/dL)] with dietary intervention alone; **AND** 3. Documentation of an elevated average baseline blood PHE level ≥ 360 µmol/L, prior to initiating therapy with sapropterin (Kuvan); **AND**

	4. Documentation of the current body weight of the patient to verify appropriate dosing. If ALL criteria are met, the request will be approved 6 months
	Criteria (Reauthorization)
	1. The blood PHE level; **AND** 2. The patient continues with a phenylalanine-restricted diet; **AND** 3. The dose does not exceed 20 mg/kg/day, based on the patient's recent weight (within the last 90 days). If ALL criteria are met, the request will be approved 12 months

Dosage and quantity limits:

Drug Name	Dose and Quantity Limits
sapropterin (Kuvan)	20mg/kg/day

Definitions:

Term	Description
PHE	Phenylalanine
PKU	Phenylketonuria

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