I. Medication Description

Sapropterin is a synthetic form of tetrahydrobiopterin (BH4), which acts as a cofactor for phenylalanine hydroxylase (PAH). BH4 activates residual PAH to increase the breakdown of phenylalanine in patients with phenylketonuria (PKU). Because it requires PAH to work, Kuvan will not work in classic PKU, which is characterized by a complete lack of PAH.

II. Position Statement

Coverage is determined through a prior authorization process with supporting clinical documentation for every request.

III. Policy

Coverage for Kuvan® and sapropterin dihydrochloride is provided when the following criteria are met:

- Member has confirmed diagnosis of phenylketonuria (PKU) AND
- Medication is being requested for the treatment of hyperphenylalaninemia (HPA) due to tetrahydrobiopterin (BH4)-responsive PKU where the following apply AND
- Pre-treatment serum concentration of phenylalanine (Phe) is elevated AND
- Member is compliant with a Phe-restricted diet

IV. Quantity Limitations

Coverage is available to allow coverage for up to 20 mg/kg/day.

V. Coverage Duration

- Initial coverage is provided for 2 months.
- Subsequent coverage durations for responsive patients will be approved for 12 months.

VI. Coverage Renewal Criteria

Coverage is renewable in the following situations:

- Drug treatment is in conjunction with ongoing dietary management of Phe intake AND
- Blood Phe levels are being monitored regularly AND
- Absence of unacceptable toxicity from the drug AND
• Significant reduction in Phe levels after trial period, defined as:
  o A 30% or more decrease from baseline blood Phe levels **OR**
  o If less than a 30% reduction of phenylalanine levels is realized, but target phenylalanine levels are still achieved (120 – 130 uM/L in patients of all ages) **OR**
  o An improvement in neuropsychiatric symptoms or increase in Phe tolerance from additional Phe to the diet without a decrease in blood Phe

VII. **Billing/Coding Information**

Kuvan is available as:
• 100 mg and 500 mg powders for oral solution
• 100 mg tablets

Sapropterin dihydrochloride is available as:
• 100 mg and 500 mg powders for oral solution
• 100 mg tablets

VIII. **Summary of Policy Changes**

• 6/1/11: policy reformatted, modification of initial authorization period to 2 months.
• 6/15/12: no changes
• 6/15/13: condensed Contraindications/Warnings section
• 6/15/14: no policy changes
• 6/15/15: coverage renewal criteria updated to reflect 2014 ACMG guidelines for treatment of PKU
• 7/1/15: formulary distinctions made
• 6/15/16: no policy changes
• 4/5/17: no policy changes
• 5/1/18: no policy changes
• 3/28/19: no policy changes
• 5/1/20: no policy changes
• 2/26/21: added generic formulation to policy

IX. **References**


The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

The preceding policy applies only to members for whom the above named pharmacy benefit medications are included on their covered formulary. Members with closed formulary benefits are subject to trying all appropriate formulary alternatives before a coverage exception for a non-formulary medication will be considered.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.