I. Medication Description

Kuvan® is a synthetic form of BH4, the cofactor for the enzyme phenylalanine hydroxylase (PAH). PAH hydroxylates phenylalanine to form tyrosine. BH4 activates residual PAH enzyme, improving normal phenylalanine metabolism and decreasing phenylalanine levels in patients responsive to Kuvan® treatment. BH4 responsiveness is more prevalent in patients with residual enzyme activity, such as in mild hyperphenylalaninemia or mild PKU, and less prevalent in patients with classical phenylketonuria (complete enzyme deficiency). Kuvan® responsiveness can be determined through a trial of drug treatment.

II. Position Statement

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

III. Policy

Coverage for Kuvan® is initially provided for the treatment of hyperphenylalaninemia (HPA) due to tetrahydrobiopterin (BH4)-responsive phenylketonuria (PKU) where the following apply:

- Patient has confirmed diagnosis of PKU AND
- Pre-treatment serum concentration of phenylalanine (Phe) is elevated AND
- Patient is compliant with a Phe-restricted diet

IV. Quantity Limitations

100mg tablet, 50mg and 100mg powders for oral solution: covered to supply 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

Pertinent indication: Phenylketonuria (PKU) – E70.0

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

IX. References

1. UpToDate Online, retrieved February 2011.
3. Facts and Comparisons Online, retrieved February 2012.

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.

Drug therapy initiated with samples will not be considered as meeting medical necessity for coverage for non-preferred or prior authorized medications.

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 agent 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.