Kuvan (sapropterin)

Policy Number: 5.01.543
Origination: 6/2013
Last Review: 6/2017
Next Review: 6/2018

Policy

Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for Kuvan when it is determined to be medically necessary because the following criteria are met.

When Policy Topic is covered

The use of Kuvan may be considered medically necessary for the following:

Food and Drug Administration (FDA)-Approved Indications

1. Hyperphenylalaninemia (HPA) due to Phenylketonuria (PKU) [Initial Therapy]. Approve for 12 weeks if the patient meets the following criteria (A and B):
   A) Kuvan is prescribed in conjunction with a phenylalanine (Phe)-restricted diet; AND
   B) The medication is prescribed by or in consultation with a metabolic disease specialist (or specialist who focuses in the treatment of metabolic diseases).

Kuvan is indicated to reduce blood Phe levels in patients with HPA due to BH4-responsive PKU in conjunction with a Phe-restricted diet.¹

2. Hyperphenylalaninemia (HPA) due to Phenylketonuria (PKU) [Patients Continuing Therapy]. Approve if the patient meets the following criteria (A or B):
   A) Patient has had a clinical response (e.g., cognitive and/or behavioral improvements) as determined by the prescribing physician; OR
   B) Patient had a ≥ 20% reduction in blood Phe concentration from baseline.

When Policy Topic is not covered

The use of Kuvan is considered investigational for all other indications.

Considerations

Kuvan requires prior authorization through the Clinical Pharmacy Department.

This Blue Cross and Blue Shield of Kansas City policy Statement was developed using available resources such as, but not limited to: Food and Drug Administration (FDA) approvals, Facts and Comparisons, National specialty guidelines, Local medical policies of other health plans, Medicare (CMS), Local providers.

Description of Procedure or Service

Kuvan (sapropterin) is indicated to reduce blood phenylalanine (Phe) levels in patients with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin-(BH4) responsive phenylketonuria (PKU).¹ The medication should be used with a Phe-restricted diet. Kuvan works by increasing phenylalanine hydroxylase (PAH). It is a synthetic preparation of naturally occurring BH4, which is a cofactor for the enzyme PAH.¹ PAH hydroxylates Phe in an oxidative reaction to form tyrosine. In patients with PKU,
PAH activity is deficient or absent. Treatment with BH4 can activate residual PAH enzyme, improve the normal oxidative metabolism of Phe, and decrease Phe levels in some patients. In patients with PKU who are responsive to treatment, blood Phe levels decrease within 24 hours after administration, although maximal effect on Phe levels may take up to 1 month. The recommended starting dose of Kuvan is 10 mg/kg/day taken once daily (QD). Therapy response is determined by changes in blood Phe after treatment for a period of 1 month. Blood Phe levels should be checked after 1 week of treatment and periodically for 1 month. If blood Phe does not decrease from baseline at the recommended dose, the dose may be increased to 20 mg/kg/day. Patients whose blood Phe does not decrease after 1 month of treatment at 20 mg/kg/day are non-responders and treatment with Kuvan should be discontinued. Once responsiveness has been determined, the dose may be adjusted within the range of 5 to 20 mg/kg/day. Tablets and oral solution are given orally with food to increase absorption, preferably at the same time each day. The tablets may be swallowed either as whole tablets or dissolved in 4 to 8 ounces of water or apple juice and taken within 15 minutes of dissolution. Kuvan powder for oral solution should be dissolved in 4 to 8 ounces of water or apple juice and taken orally within 30 minutes of dissolution. The powder should dissolve rapidly and completely. Both the Kuvan tablets and one unit dose packet of powder for oral solution contain the same amount of drug (equivalent to 76.8 mg sapropterin base). The therapy should be administered by a physician knowledgeable in the management of PKU.

**Rationale**

PKU is the most prevalent disorder due to an inborn error in amino acid metabolism. It is caused by mutations in the PAH gene. The annual incidence is about 1:15,000 births in the US. Genotypes of the disease range from a mild increase in blood Phe concentrations to a severe classic phenotype with very pronounced increases in HPA, which if not treated, can result in profound and irreversible mental disability. Other manifestations of PKU, if untreated, can include eczematous rash, autism, seizures, motor defects, developmental problems, impaired memory, behavioral issues (e.g., attention deficit hyperactivity disorder [ADHD]) and psychiatric behavior. Early diagnosis and prompt intervention is important and routine screening programs are in place for newborns. Women with untreated or poorly treated PKU who are pregnant pose a particular health concern due to fetal exposure to teratogenic concentrations of Phe. Dietary restrictions in Phe are a mainstay in PKU management. Patients with PKU have to intake PHE-free formula and avoid foods that are protein-rich (e.g., meats, fish, eggs, standard bread, most cheeses, nuts and seeds). Other foods and beverages that contain aspartame, flour, soy, beer, or cream should be avoided. Low-protein foods that are natural may be consumed in restricted amounts, such as potatoes, some vegetables, and most cereals. During infancy, adherence to dietary restrictions is more manageable but as children grow older and become adults the dietary limitations can become burdensome.

In general, response to Kuvan treatment was defined as ≥ 30% decrease in blood Phe concentration from baseline. However, in some cases (e.g., patients with mild HPA, neonates or children < 4 years of age, or pregnant women), a 20% reduction in blood Phe concentration may be sufficient. Studies suggest that a ≥ 30% reduction in mean plasma Phe concentrations have been demonstrated in about 44% of patients. Other data noted responses generally within this range.

**References:**


Other References Utilized


**Billing Coding/Physician Documentation Information**

N/A Kuvan is considered a specialty pharmacy benefit.

**Additional Policy Key Words**

Policy Number: 5.01.543

**Policy Implementation/Update Information**

<table>
<thead>
<tr>
<th>Date</th>
<th>Change</th>
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<tbody>
<tr>
<td>6/2013</td>
<td>New policy titled Kuvan</td>
</tr>
<tr>
<td>6/2014</td>
<td>Reviewed – no changes made</td>
</tr>
<tr>
<td>6/2015</td>
<td>Reviewed—Added Kuvan powder for oral solution to PA; updated references</td>
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<tr>
<td>6/2016</td>
<td>Reviewed – no changes made</td>
</tr>
<tr>
<td>6/2017</td>
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