Kuvan

**Description**

Kuvan (sapropterin)

**Background**

Prolonged high blood phenylalanine (Phe) levels are neurotoxic and lead to impairment of intelligence and other brain functions (such as attentiveness). Reduction of blood Phe levels through dietary control is an important determinant of long-term neurologic outcome in phenylketonuria (PKU) patients, and reduction of blood Phe levels in patients with PKU has been shown to decrease the long-term risk of neurologic injury. It is difficult for many patients to maintain reduced blood Phe, and many patients with PKU experience some degree of neurological impairment despite efforts to maintain dietary Phe control (1).

Response to treatment cannot be pre-determined by laboratory testing (e.g., genetic testing), and can only be determined by a therapeutic trial of Kuvan. Although long-term assessment of neurologic function in patients with PKU receiving Kuvan for the treatment of elevated blood Phe has not been done, Kuvan may help maintain reduced blood Phe levels as an adjunct to a Phe-controlled diet (1).

**Regulatory Status**

FDA-approved indication: Kuvan is indicated to reduce blood phenylalanine (Phe) levels in patients with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin- (BH4-) responsive phenylketonuria (PKU). Kuvan is to be used in conjunction with a Phe-restricted diet (1).
The most common side effects of Kuvan are headache, vomiting, diarrhea, runny nose, cough, and sore throat. Most of these side effects were mild, and did not result in patients stopping Kuvan treatment (1).

During clinical trials, gastritis was reported as a serious adverse reaction. Monitor patients for signs and symptoms of gastritis (1).

Patients with liver impairment have not been evaluated in clinical trials with Kuvan. Monitor liver function tests in patients with liver impairment who are receiving Kuvan because hepatic damage has been associated with impaired Phe metabolism (1).

Pediatric patients with PKU, 1 month to 16 years of age, have been treated with Kuvan in clinical studies (1).

**Related policies**
Palynziq

**Policy**
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Kuvan may be considered medically necessary for the treatment of phenylketonuria in patients 1 month of age and older and if the conditions indicated below are met.

Kuvan may be considered investigational in patients of age 1 month or less and for all other indications.

**Prior-Approval Requirements**

**Age**
1 month of age or older

**Diagnosis**

Patient must have the following:
Phenylketonuria (PKU)

AND ALL of the following:

a. Tetrahydrobiopterin (BH₄) deficiency has been ruled out
b. Phenylalanine-restricted diet
c. Prescriber agrees to monitor phenylalanine levels

d. NOT being used in combination with Palynziq (pegvaliase-pqpz)

Prior – Approval **Renewal** Requirements

**Age**

1 month of age or older

**Diagnosis**

Patient must have the following:

Phenylketonuria (PKU)

AND ALL of the following:

a. Phenylalanine-restricted diet
b. Reduction from baseline phenylalanine levels of 30% or greater
c. NOT being used in combination with Palynziq (pegvaliase-pqpz)

**Policy Guidelines**

**Pre - PA Allowance**

None

**Prior - Approval Limits**

**Duration**

12 weeks

**Prior – Approval **Renewal** Limits**

**Duration**

12 months

**Rationale**

**Summary**

Reduction of blood Phe levels in patients with PKU has been shown to decrease the long-term risk of neurologic injury. In clinical trials of Kuvan in patients with PKU, reductions in blood Phe levels were observed in some patients. Pediatric patients with PKU, 1 month to 16 years of age, have been treated with Kuvan in clinical studies (1).

Prior authorization is required to ensure the safe, clinically appropriate and cost effective use of Kuvan while maintaining optimal therapeutic outcomes.
Section: Prescription Drugs  Effective Date: January 1, 2020
Subsection: Endocrine and Metabolic Drugs  Original Policy Date: December 7, 2011
Subject: Kuvan  Page: 4 of 4

References

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>December 2011</td>
<td>Annual revision</td>
</tr>
<tr>
<td>December 2012</td>
<td>Annual revision</td>
</tr>
<tr>
<td>March 2014</td>
<td>Line-addition of 100mg oral powder packs</td>
</tr>
<tr>
<td>June 2014</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>October 2014</td>
<td>Change of age requirement to include 1 month of age and older</td>
</tr>
<tr>
<td>December 2014</td>
<td>Annual review and reference update</td>
</tr>
<tr>
<td>September 2015</td>
<td>Annual review and reference update</td>
</tr>
<tr>
<td>September 2016</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>December 2017</td>
<td>Policy number change from 5.08.14 to 5.30.14</td>
</tr>
<tr>
<td>September 2018</td>
<td>Annual editorial review, addition of no dual therapy with Palynziq.</td>
</tr>
<tr>
<td></td>
<td>Addition of prescriber agrees to monitor phenylalanine levels for</td>
</tr>
<tr>
<td></td>
<td>initiation. Removal of ruling out BH4 deficiency for continuation</td>
</tr>
<tr>
<td>December 2019</td>
<td>Annual review</td>
</tr>
</tbody>
</table>

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 6, 2019 and is effective January 1, 2020.