



## PRIOR AUTHORIZATION POLICY

- POLICY:** Phenylketonuria – Sapropterin Prior Authorization Policy
- Kuvan™ (sapropterin dihydrochloride tablets and powder for oral solution – BioMarin, generic)
  - Javygtor™ (sapropterin dihydrochloride tablets and powder for oral solution – Dr. Reddy’s Laboratories)

**REVIEW DATE:** 08/28/2024

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### **INSTRUCTIONS FOR USE**

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

## **CIGNA NATIONAL FORMULARY COVERAGE:**

### **OVERVIEW**

Sapropterin (Kuvan, Javygtor, generic), a synthetic form of the cofactor for the enzyme phenylalanine hydroxylase, is indicated to reduce blood phenylalanine levels in patients one month of age and older with hyperphenylalaninemia due to tetrahydrobiopterin-responsive **phenylketonuria (PKU)**.<sup>1</sup>

The medication should be used with a phenylalanine-restricted diet. Of note, some patients do not show a biochemical response to sapropterin. Per the prescribing information, biochemical response cannot be predetermined by laboratory testing and should be determined through a therapeutic trial (evaluation) of sapropterin response.

### **Dose Titration**

The initial starting dose of sapropterin is either 10 mg/kg per day or 20 mg/kg per day. If a 10 mg/kg per day starting dose is used, the dose should be increased to 20 mg/kg if the patient's blood phenylalanine does not decrease after 1 month of treatment. If blood phenylalanine does not decrease after 1 month of treatment on 20 mg/kg per day, sapropterin should be discontinued.

### **Guidelines**

According to the European guidelines for PKU (2017), there is consensus in the literature that patients with blood phenylalanine concentration > 600 micromol/L should be treated.<sup>8</sup> There is also consensus that patients with blood phenylalanine concentration < 360 micromol/L can remain untreated but should be monitored. Patients with blood phenylalanine concentration between 360 to 600 micromol/L should be treated until 12 years of age. Treatment for life is recommended for any patient with PKU; however, it is also noted that patients ≥ 12 years of age with blood phenylalanine concentration < 600 micromol/L do not require treatment. All adults with PKU should have lifelong systematic follow-ups in specialized metabolic centers, due to specific risks which may occur during adulthood. With regards to target phenylalanine levels, in treated PKU patients up to 12 years of age, the target levels should be 120 to 360 micromol/L; in treated PKU patients ≥ 12 years of age, the target levels should be 120 to 600 micromol/L.

The American College of Medical Genetics and Genomics (ACMG) published practice guidelines (2014) for the diagnosis and management of phenylalanine hydroxylase (PAH) deficiency.<sup>9</sup> The guidelines recommend initiating treatment as early as possible, preferably within the first week of life with a goal of having blood phenylalanine levels in the treatment range within the first 2 weeks. Dietary restriction of phenylalanine intake is the mainstay of therapy for PKU. Blood phenylalanine levels in all patients should be maintained in the range of 120 to 360 micromol/L. The guidelines state that approximately 25% to 50% of patients with PAH deficiency are responsive to sapropterin. A significant decline in blood phenylalanine level is expected in responders once treatment is initiated (with phenylalanine-restricted diet); however, patients in the lower end of the treatment range (≤ 180 micromol/L) rarely show a decrease in blood phenylalanine level even if they are responsive to sapropterin. In these patients, responsiveness is determined by adding phenylalanine to the diet in a stepwise method. An improvement in neuropsychiatric symptoms or increase in phenylalanine tolerance without a decrease in blood phenylalanine levels is sufficient reasoning to continue therapy. According to the guidelines, there is strong evidence to support life-long treatment and maintenance of metabolic control in patients with PAH deficiency.

#### **POLICY STATEMENT**

Prior Authorization is recommended for prescription benefit coverage of sapropterin (Kuvan, Javygtor, generic). Because of the specialized skills required for evaluation and diagnosis of patients treated with sapropterin as well as the monitoring required for adverse events and long-term efficacy, initial approval requires sapropterin to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration noted below.

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**is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):**

#### **FDA-Approved Indication**

- 1. Phenylketonuria.** Approve for the duration noted if the patient ONE of meets the following (A or B):
  - A) Initial Therapy.** Approve for 12 weeks if the patient meets BOTH of the following (i and ii):

- i. Sapropterin is prescribed in conjunction with a phenylalanine-restricted diet; AND
  - ii. The medication is prescribed by or in consultation with a metabolic disease specialist (or specialist who focuses on the treatment of metabolic diseases).
- B) Patients is Currently Receiving Sapropterin (Kuvan, Javygtor, generic).** Approve for 1 year if the patient meets BOTH of the following (i and ii):
- Note: A patient who has received < 12 weeks of therapy or who is restarting therapy with sapropterin should be considered under Initial Therapy.
- i. Patient meets ONE of the following (a, b, or c):
    - a) Patient has had a clinical response (e.g., cognitive, and/or behavioral improvements) as determined by the prescriber; OR
    - b) Patient has achieved a  $\geq 20\%$  reduction in blood phenylalanine concentration from pre-treatment baseline (i.e., blood phenylalanine concentration before starting sapropterin therapy); OR
    - c) Treatment with sapropterin has resulted in an increase in dietary phenylalanine tolerance, according to the prescriber; AND
  - ii. Patient is not receiving concomitant Palynziq (pegvaliase-pqpz subcutaneous injection) at a stable maintenance dose.
- Note: Concomitant use with Palynziq is permitted during Palynziq dose titration.

#### CONDITIONS NOT COVERED

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**is(are) considered experimental, investigational, or unproven for ANY other use(s).**

#### REFERENCES

1. Kuvan™ tablets and powder for oral solution [prescribing information]. Novato, CA: BioMarin; February 2021.
2. Levy H, Burton B, Cederbaum S, Scriver C. Recommendations for evaluation of responsiveness to tetrahydrobiopterin (BH4) in phenylketonuria and its use in treatment. *Mol Genet Metab.* 2007; 92:287-291.
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4. Feillet F, van Spronsen FJ, MacDonald A, et al. Challenges and pitfalls in the management of phenylketonuria. *Pediatrics.* 2010;126(2):333-341.
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7. Burton BK, Nowacka M, Hennermann JB, et al. Safety of extended treatment with sapropterin dihydrochloride in patients with phenylketonuria: results of a phase 3b study. *Mol Genet Metab.* 2011;103(4):315-322.
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9. Vockley J, Andersson HC, Antshel KM, et al. Phenylalanine hydroxylase deficiency: diagnosis and management guideline. Available at:

[https://www.acmg.net/docs/Phenylalanine\\_Hydrosylase\\_Deficiency\\_Practice\\_Guideline\\_AOP\\_Jan\\_2013.pdf](https://www.acmg.net/docs/Phenylalanine_Hydrosylase_Deficiency_Practice_Guideline_AOP_Jan_2013.pdf). Accessed on August 23, 2024.

**HISTORY**

<b>Type of Revision</b>	<b>Summary of Changes</b>	<b>Review Date</b>
Annual Revision	No criteria changes.	08/30/2023
Annual Revision	No criteria changes.	08/28/2024

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