BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

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KUVAN® (sapropterin dihydrochloride) oral

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

KUVAN® (sapropterin dihydrochloride) oral

Criteria:

- **Criteria for initial therapy:** Kuvan (sapropterin dihydrochloride) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a specialist with knowledge and expertise in metabolic diseases or genetic diseases

  2. Individual is 1 month of age or older

  3. A confirmed diagnosis of hyperphenylalaninemia (HPA) due to tetrahydrobiopterin (BH4) responsive phenylketonuria (PKU)

  4. Individual is on a phenylalanine (PHE)-restricted diet

  5. **ALL** of the following baseline tests have been completed before initiation of treatment:
     a. Phenylalanine (PHE) level is above the recommended level for the individual's age or condition (baseline value must be submitted with the request)
     b. Liver function tests

  6. Will not be used concurrently with Palynziq (pegvaliase-pqpz)

  Initial approval duration: 2 months

- **Criteria for continuation of coverage (renewal request)**: Kuvan (sapropterin dihydrochloride) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a specialist with knowledge and expertise in metabolic diseases or genetic diseases

  2. PHE-restricted diet was not changed in any way during the initial trial of therapy with Kuvan in order to determine responsiveness

  3. Individual's condition responded while on therapy
     a. Response is defined as:
        i. Baseline PHE level and the most recent PHE level show at least a 30% decrease in PHE while on Kuvan (levels must be submitted when requesting continued treatment)

  4. Individual has been adherent with the medication

  5. Will not be used concurrently with Palynziq (pegvaliase-pqpz)

  6. There are no significant interacting drugs

  Renewal duration: 12 months

KUVAN® (sapropterin dihydrochloride) oral

Description:

Kuvan (sapropterin dihydrochloride) is an orally administered phenylalanine (PHE) hydroxylase activator approved to reduce blood PHE levels in patients with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin (BH4)-responsive phenylketonuria (PKU). Left untreated the condition can lead to profound neurocognitive and developmental defects. Neurologic damage can include severe mental retardation, microcephaly, delayed speech, seizures, and behavioral abnormalities. Conversely, prolonged low levels of blood PHE have been associated with catabolism and protein breakdown.

The underlying defect seen is a deficiency or a decrease in activity of the hepatic enzyme phenylalanine hydroxylase (PAH). PAH deficiency is an autosomal-recessive disorder. The gene is located on chromosome 12. More than 500 different mutations in the PAH gene have been described.

Kuvan (sapropterin dihydrochloride) is a biologically active synthetic form of naturally occurring BH4. It reduces blood PHE levels in patients with HPA by improving the normal metabolism of PHE. BH4 is a cofactor for the enzyme phenylalanine hydroxylase (PAH) that hydroxylates PHE through an oxidative reaction to form tyrosine (TYR). PAH activity is absent or deficient among patients with PKU. While these individuals are not deficient in endogenous BH4, some patients with PAH deficiency, who have some residual enzyme activity respond to administration of Kuvan (sapropterin dihydrochloride) with an increase in the metabolism of PHE to TYR.

The mechanism by which residual PAH activity is enhanced is unclear, but BH4 may act as a pharmacologic chaperone leading to improved folding and increased stability of the mutant protein. In clinical trials, approximately 20–75% of the patients with PAH deficiency are BH4-responsive. Patients whose blood PHE does not decrease after 1 month of treatment at 20 mg/kg per day are considered non-responders and treatment with Kuvan (sapropterin dihydrochloride) should be discontinued in these patients. Current literature cites a 30% reduction in PHE levels as evidence for responsiveness to Kuvan (sapropterin dihydrochloride).

Kuvan (sapropterin dihydrochloride) must be used in conjunction with a PHE restricted diet. Active management of dietary PHE intake is the mainstay of therapy and requires restriction of dietary PHE intake necessitating a decrease in the intake of natural protein and replacing it with a protein (amino acid mixture) source devoid of PHE. A provider experienced in metabolic disorders and a nutritionist team-based approach should manage this therapy. Dietary manipulation will be required to maintain appropriate blood PHE levels with frequent dietary modification to respond to growth, life stages, concurrent illness, and comorbidities.

The American College of Medical Genetics and Genomics 2014 practice guideline suggests blood PHE levels should be maintained in the range of 120–360 µmol/L for all patients, although there is no evidence to suggest normalization of PHE levels is required and lower levels of 60-120 µmol/L should not be viewed as too low. It should be noted that measurement of PHE levels in blood varies and is dependent on the analytical method used; requiring consistency in testing methodology in order to interpret the resultant values.

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Resources:

Kuvan (sapropterin) product information, revised by BioMarin Pharmaceutical, Inc. 03-2020, at DailyMed http://dailymed.nlm.nih.gov accessed January 28, 2021.

Bodamer OA. Overview of phenylketonuria. In: UpToDate, Hahn S, TePas E (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Accessed on January 28, 2021.