Clinical Policy: Sapropterin Dihydrochloride (Kuvan)

Reference Number: CP.PHAR.43
Effective Date: 02/10
Last Review Date: 04/17

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for sapropterin dihydrochloride (Kuvan®).

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that Kuvan is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Phenylketonuria (must meet all):

1. Prescribed by or in consultation with a metabolic or genetic disease specialist;
2. Diagnosis of hyperphenylalaninemia (HPA) due to tetrahydrobiopterin- (BH4-) responsive phenylketonuria (PKU);
3. Recent (within 90 days) phenyalanine (Phe) blood level is > 360 µmols/L;
4. Kuvan is prescribed to be used in conjunction with a Phe-restricted diet;
5. Prescribed dose of Kuvan does not exceed 20 mg/kg/day.

Approval Duration: 2 months

B. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy

II. Continued Approval

A. Phenylketonuria (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Demonstrated clinical response to Kuvan as evidenced by one of the following (a, b, or c):
   a. Reduction of Phe blood levels from baseline;
   b. Increase in dietary Phe tolerance;
   c. Improvement in neuropsychiatric symptoms;
3. Prescribed dose of Kuvan does not exceed 20 mg/kg/day.

Approval Duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy.

Background

Description/Mechanism of Action:
Kuvan (sapropterin dihydrochloride) is a synthetic form of BH4, the cofactor for the enzyme phenylalanine hydroxylase (PAH). PAH hydroxylates Phe through an oxidative reaction to form tyrosine. In patients with PKU, PAH activity is absent or deficient. Treatment with BH4 can activate residual PAH enzyme activity, improve the normal oxidative metabolism of Phe, and decrease Phe levels in some patients.

Formulations:
Tablets: 100 mg
Powder for Oral Solution: 100 mg

FDA Approved Indication:
Kuvan is a phenylalanine hydroxylase activator/oral tablet or powder for oral solution indicated to:

- Reduce blood phenylalanine (Phe) levels in patients with hyperphenylalaninemia (HPA) due to treatment of tetrahydrobiopterin- (BH4-) responsive phenylketonuria (PKU). Kuvan is to be used in conjunction with a Phe-restricted diet.

Appendices

Appendix A: Abbreviation Key

HPA: hyperphenylalaninemia
PAH: phenylalanine hydroxylase
Phe: phenylalanine
PKU: phenylketonuria

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
N/A	

Reviews, Revisions, and Approvals	Date	Approval Date
No criteria changes	04/13	05/13
Converted to Centene policy template	05/13	
Removed dosing and prospective monitoring questions from Figure 1 Updated Table 2 safety concerns	04/14	05/14
Added that PKU is also known as PAH deficiency	02/15	04/15

Reviews, Revisions, and Approvals	Date	Approval Date
Removed Appendix B (Low-Phe diet) and Appendix C (Initiation of treatment) Reauthorization algorithm requires 2-6mg/dl Phe target level		
Policy converted to new template. Initial criteria: Removed requests for documentation; specialist criteria added given complexity of disease state and recommendation for multidisciplinary management[2-4]; added max dose per PI. Removed baseline Phe requirement of >600 µmol/L if >12 years; added contraindications, including two null mutations per guidelines.[2-3] Changed initial approval duration to two months; changed requirement that Phe decrease to 120–360 µmol/l during the Kuvan trial period to "any Phe decrease."	03/16	04/16
Removed contraindication of anaphylaxis to Kuvan due to verification challenges; Added a time frame for which Phe level will be considered valid.	03/17	04/17

References

1. Kuvan Prescribing Information. Novato, CA: BioMarin Pharmaceutical, Inc.; August 2016. Available at www.Kuvan.com. Accessed March 2017.
2. Vockly J, Andersson HC, Antshel KM, et al. ACMG practice guidelines: phenylalanine hydroxylase deficiency: diagnosis and management guideline. Genet Med. 2014; 16(2): 188-200.
3. Camp KM, Parisi MA, Acosta PB, et al. Phenylketonuria scientific review conference: state of the science and future research needs. Mol Genet Metab. June 2014; 112(2): 87-122.
4. van Spronsen FJ. Mild hyperphenylalaninemia: to treat or not to treat. J Inherit Metab Dis. 2011; 34: 651-656.

Important reminder

of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.