Clinical Policy: Sapropterin Dihydrochloride (Kuvan)

Reference Number: PA.CP.PHAR.43
Effective Date: 01/2018
Last Review Date: 04/2023

Coding Implications
Revision Log

Description
Sapropterin dihydrochloride (Kuvan®) is a synthetic form of tetrahydrobiopterin (BH4), the cofactor for the enzyme phenylalanine hydroxylase.

FDA Approved Indication(s)
Kuvan is indicated to reduce blood phenylalanine (Phe) levels in adult and pediatric patients one month of age and older with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin- (BH4-) responsive phenylketonuria (PKU). Kuvan is to be used in conjunction with a Phe-restricted diet.

Policy/Criteria
It is the policy of PA Health & Wellness® that Kuvan is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Phenylketonuria (must meet all):
1. Diagnosis of hyperphenylalaninemia (HPA) due to phenylketonuria (PKU);
2. Prescribed by or in consultation with a metabolic or genetic disease specialist;
3. Recent (within 90 days) phenyalanine (Phe) blood level is > 360 µmols/L;
4. Member is currently on a phenylalanine-restricted diet and will continue this diet during treatment with Kuvan;
5. Kuvan is not prescribed concurrently with Palynziq;
6. Dose does not exceed 20 mg/kg per day.

Approval Duration: 3 months

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Phenylketonuria (must meet all):
1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy as demonstrated by a reduction in Phe blood levels since initiation of therapy;
3. Member is currently on a phenylalanine-restricted diet and will continue this diet during treatment with Kuvan;
4. Dose does not exceed 20 mg/kg per day.

Approval Duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
BH4: tetrahydrobiopterin
HPA: hyperphenylalaninemia
FDA: Food and Drug Administration
Phe: phenylalanine
PKU: phenylketonuria

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information
- According to the prescribing information, if a 10 mg/kg per day starting dose is used, then response to therapy is determined by change in blood Phe following treatment with Kuvan at 10 mg/kg per day for a period of up to 1 month. Blood Phe levels should be checked after 1 week of Kuvan treatment and periodically for up to a month. If blood Phe does not decrease from baseline at 10 mg/kg per day, the dose may be increased to 20 mg/kg per day. Patients whose blood Phe does not decrease after 1 month of treatment at 20 mg/kg per day are non-responders and treatment with Kuvan should be discontinued in these patients.

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
BH4-responsive PKU	Age 1 month to ≤ 6 years (starting dose) 10 mg/kg QD. Age ≥ 7 years (starting dose): 10 to 20 mg/kg QD	20 mg/kg/day

V. Product Availability

Tablets: 100 mg
Powder for oral solution: 100 mg, 500 mg

VII. References

1. Kuvan Prescribing Information. Novato, CA: BioMarin Pharmaceutical, Inc.; February 2021. Available at www.Kuvan.com. Accessed February 9, 2023.
2. Levy HL, Milanowski A, Chakrapani A, et. al. Efficacy of sapropterin dihydrochloride (tetrahydrobiopterin, 6R-BH4) for reduction of phenylalanine concentration in patients with

phenylketonuria: a phase III randomized placebo-controlled study. Lancet. 2007;370(9586):504.
3. 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.
4. 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.
5. van Spronsen FJ. Mild hyperphenylalaninemia: to treat or not to treat. J Inherit Metab Dis. 2011;34:651-656.

Reviews, Revisions, and Approvals	Date	Approval Date
1Q 2018 annual review: Use in conjunction with a Phe-restricted diet is removed. Initial approval duration increased from 2 to 3 months to allow adequate time for follow-up. Continuation criteria that refers to an increase in dietary Phe tolerance or improvement in neuropsychiatric symptoms is deleted leaving reduction of Phe levels per the PI. References reviewed and updated.	02/2018	
1Q 2019 annual review: references reviewed and updated.	01/2019	
1Q 2020 annual review: references reviewed and updated.	01/2020	
1Q 2021 annual review: references reviewed and updated.	01/2021	
2Q 2021 annual review: added requirements for a Phe-restricted diet and excluded coverage of concurrent use of Kuvan and Palynziq; references reviewed and updated.	04/2021	
2Q 2022 annual review: references reviewed and updated.	04/2022	
2Q 2023 annual review: no significant changes; references reviewed and updated.	04/2023	