Clinical Policy: Sapropterin Dihydrochloride (Kuvan)

Reference Number: ERX.SPA.19
Effective Date: 07.01.16
Last Review Date: 05.21
Line of Business: Commercial, Medicaid

Revision Log

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

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 patients with hyperphenylalaninemia (HPA) due to BH4-responsive phenylketonuria (PKU). Kuvan is to be used in conjunction with a Phe-restricted diet.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Kuvan is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Phenylketonuria (must meet all)**:**

1. Diagnosis of HPA due to PKU;
2. Prescribed by or in consultation with a metabolic or genetic disease specialist;
3. Recent (within 90 days) 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

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Phenylketonuria (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
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. If request is for a dose increase, new dose 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 a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BH4: tetrahydrobiopterin
FDA: Food and Drug Administration
HPA: hyperphenylalaninemia
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. Additionally, regardless of starting dose, 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.

V. 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

VI. Product Availability

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

VII. References

1. Kuvan Prescribing Information. Novato, CA: BioMarin Pharmaceutical, Inc.; March 2020. Available at: www.kuvan.com. Accessed February 28, 2021.
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 randomised 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	P&T Approval Date
Added a time frame for which Phe level will be considered valid.	04.17	05.17
1Q18 annual review: The diagnostic description "BH4 responsive" in relation to PKU is deleted as it may not be determined until after a therapeutic trial. 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 updated.	11.17.17	02.18
1Q 2019 annual review: no significant changes; references reviewed and updated.	11.13.18	02.19
1Q 2020 annual review: no significant changes; references reviewed and updated.	11.05.19	02.20
1Q 2021 annual review: no significant changes; references reviewed and updated.	10.28.20	02.21
2Q 2021 annual review: to align with the previously approved approach for the treatment of PKU, added requirements for a Phe-restricted diet and excluded coverage of concurrent use of Kuvan and Palynziq; references reviewed and updated.	02.28.21	05.21

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.