



STANDARD COMMERCIAL DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

SAPROPTERIN DIHYDROCHLORIDE

Generic	Brand	HICL	GCN	Exception/Other
SAPROPTERIN DIHYDROCHLORIDE	KUVAN	35266		ROUTE = ORAL

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of hyperphenylalaninemia (HPA) due to tetrahydrobiopterin (BH4)-responsive phenylketonuria (PKU) and follows a phenylalanine-restricted diet?

If yes, **approve for 1 month by HICL.**

APPROVAL TEXT: Renewal of **SAPROPTERIN DIHYDROCHLORIDE** requires that the patient experiences a $\geq 30\%$ decrease in blood phenylalanine from baseline after taking Kuvan (sapropterin dihydrochloride) and follows a phenylalanine-restricted diet.

If no, do not approve.

DENIAL TEXT: Our guideline for **SAPROPTERIN DIHYDROCHLORIDE** requires a diagnosis of hyperphenylalaninemia (HPA) due to tetrahydrobiopterin (BH4)-responsive phenylketonuria (PKU) and that the patient follows a phenylalanine-restricted diet.

RENEWAL CRITERIA

1. Does the patient have a diagnosis of hyperphenylalaninemia (HPA) due to tetrahydrobiopterin (BH4)-responsive phenylketonuria (PKU) and meets the following criteria?
 - The patient experienced a $\geq 30\%$ decrease in blood phenylalanine from baseline after taking Kuvan (sapropterin dihydrochloride).
 - The patient follows a phenylalanine-restricted diet.

If yes, **approve for 12 months by HICL.**

If no, do not approve.

DENIAL TEXT: Our guideline for **SAPROPTERIN DIHYDROCHLORIDE** renewal requires a diagnosis of hyperphenylalaninemia (HPA) due to tetrahydrobiopterin (BH4)-responsive phenylketonuria (PKU), in addition to the patient experiencing a $\geq 30\%$ decrease in blood phenylalanine from baseline after taking Kuvan (sapropterin dihydrochloride) and continuing to follow a phenylalanine-restricted diet.

RATIONALE

Promote appropriate utilization of sapropterin dihydrochloride based on FDA approved indication and dosing.

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RATIONALE (CONTINUED)

Phenylketonuria (PKU), in most cases, is caused by deficiency of phenylalanine hydroxylase (PAH). PAH is a hepatic enzyme that catalyzes the conversion of the essential amino acid phenylalanine to tyrosine. Tetrahydrobiopterin (BH4) is a cofactor required for PAH activity. PKU results in elevated blood and urine concentrations of phenylalanine and its metabolites, phenylacetate and phenyllactate. Tyrosine concentration is normal or low normal. Occasionally tyrosine concentrations are low.

Complete enzyme deficiency results in classic PKU, in which serum phenylalanine concentration exceeds 20 mg/dL (1200 micromol/L). Residual enzyme activity causes mild PKU (phenylalanine concentration 10 to 20 mg/dL, 600 to 1200 micromol/L) and hyperphenylalaninemia (HPA, phenylalanine concentration 2.5 to 10 mg/dL, 150 to 600 micromol/L).

Kuvan is a synthetic form of the cofactor BH4 (tetrahydrobiopterin) for the enzyme phenylalanine hydroxylase (PAH). BH4 activates residual PAH enzyme, improving normal phenylalanine metabolism and decreasing phenylalanine levels in Kuvan responders. Response to Kuvan treatment was defined in clinical trials as a $\geq 30\%$ decrease in blood Phe from baseline. Approximately 25% to 50% of patients with PAH deficiency are responsive to sapropterin. The prevalence of responsiveness was 79 to 83% in patients with mild HPA, 49 to 60% in patients with mild PKU, and 7 to 10% in patients with classic PKU. Before routine treatment with Kuvan is initiated, a test should be conducted to determine if the patient is responsive.

DOSAGE

Patients 1 month to 6 years

- The recommended starting dose of Kuvan is 10 mg/kg taken once daily.

Patients 7 years and older

- The recommended starting dose of Kuvan is 10 to 20 mg/kg taken once daily.

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 nonresponders and treatment with Kuvan should be discontinued in these patients.

Once responsiveness to Kuvan has been established, the dosage may be adjusted within the range of 5 to 20 mg/kg per day according to response to therapy. Periodic blood Phe monitoring is recommended to assess blood Phe control.

FDA APPROVED INDICATION

Kuvan is indicated to reduce blood phenylalanine (Phe) levels in patients with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin- (BH4-) responsive Phenylketonuria (PKU). Kuvan is to be used in conjunction with a Phe-restricted diet.

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REFERENCES

- Kuvan [Prescribing Information]. BioMarin Pharmaceutical Inc. Novato, CA. May 2015.
- UpToDate, Inc. Overview of phenylketonuria. UpToDate [database online]. Waltham, MA. Available at: <http://www.uptodate.com/home/index.html>. Updated March 20, 2015.
- Kuvan. [Online Drug Database]. Available at: www.factsandcomparisons.com. Updated January 2015.

Library	Commercial	NSA
Yes	Yes	No

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