VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

KUVAN (Sapropterin)

Effective Date: 1/28/14

Date Developed: 1/28/14 by Catherine Sanders, MD

Last Approval Date: 1/26/16, 1/24/17, 1/23/18, 1/22/19

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Kuvan is a synthetic form of the cofactor BH4 (tetrahydrobiopterin) for the enzyme phenylalanine hydroxylase (PAH). PAH hydroxylates phenylalanine to form tyrosine. BH4 activates residual PAH enzyme, improving normal phenylalanine metabolism and decreasing phenylalanine levels in sapropterin responders.

Pre-Authorization Criteria:
Kuvan is prescribed for use as an adjunct to dietary management in the treatment of tetrahydrobiopterin (BH4) responsive phenylketonuria (PKU).

VCHCP requires that Kuvan be prescribed by a physician specializing in the condition being treated.

Dosing: Adult:
PKU: Oral: Initial: 10 mg/kg once daily; adjust after 1 month based on blood phenylalanine levels (if phenylalanine levels do not decrease from baseline, increase dose to 20 mg/kg once daily); discontinue if phenylalanine levels do not decrease after 1 month of treatment at 20 mg/kg/day (nonresponder). Maintenance range: 5-20 mg/kg once daily

Dosing: Pediatric:
PKU: Children ≥4 years: Refer to adult dosing.

Dosing: Geriatric:
Refer to adult dosing.

Dosing: Renal Impairment:
No dosage adjustment provided in manufacturer's labeling (has not been studied). Use with caution.

Dosing: Hepatic Impairment:
No dosage adjustment provided in manufacturer's labeling (has not been studied). Use with caution.

Dosage Forms: U.S.:
Excipient information presented when available (limited, particularly for generics); consult specific product labeling.
Tablet Soluble, Oral, as dihydrochloride:
Kuvan: 100 mg

Administration:
Administer with food, preferably at the same time each day. Dissolve tablets in 120-240 mL (4-8 oz) water or apple juice. May crush or stir to aid in dissolution. Take within 15 minutes of dissolution. Tablets may not dissolve completely; rinse remaining tablet residue (with more water or apple juice) and drink.

Adverse Reactions:
>10%: Headache, rhinorrhea
Other Serious Less Common Reactions: Neutropenia, abdominal pain, agitation,arthralgia, bleeding, dizziness, gastrointestinal bleeding, hyper-reflexia, MI, over stimulation, peripheral edema, respiratory failure, seizure, seizure exacerbation, thrombocytopenia, tremor.

References:

1. Burton BK, Grange DK, Milanowski A, et al, "The Response of Patients With Phenylketonuria and Elevated Serum Phenylalanine to Treatment With Oral Sapropterin Dihydrochloride (6R-Tetrahydrobiopterin): A Phase II, Multicentre, Open-Label, Screening Study," *J Inherit Metab Dis*, 2007, 30(5):700-7. [PubMed 17846916]
2. Koch R, Hanley W, Levy H, et al, "The Maternal Phenylketonuria International Study: 1984-2002," *Pediatrics*, 2003, 112(6 Pt 2):1523-9. [PubMed 14654658]
3. Levy H, Burton B, Cederbaum S, et al, "Recommendations for Evaluation of Responsiveness to Tetrahydrobiopterin (BH4) in Phenylketonuria and its Use in Treatment," *Mol Genet Metab*, 2007, 92(4):287-291. [PubMed 18036498]
4. 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):504-10. [PubMed 17693179]
5. Maillot F, Cook P, Lilburn M, et al, "A Practical Approach to Maternal Phenylketonuria Management," *J Inherit Metab Dis*, 2007, 30(2):198-201.
6. www.uptodate.com: Sapropterin: Drug Information
7. www.epocrates.com: Kuvan Drug information

REVISION HISTORY:

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