MEDICAL MUTUAL®

Drug Policy

Policy:	Kuvan (sapropterin dihydrochloride) Javygtor (sapropterin dihydrochloride)	Annual Review Date: 07/20/2023 Last Revised Date: 07/20/2023

OVERVIEW

Kuvan and Javygtor are indicated to reduce blood phenylalanine (Phe) levels in patients with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin-(BH4) responsive phenylketonuria (PKU). These medications should be used with a Phe-restricted diet. These drugs work by increasing phenylalanine hydroxylase (PAH). In patients with PKU who are responsive to treatment, blood Phe levels decrease within 24 hours after administration, although maximal effect on Phe levels may take up to 1 month. The recommended starting dose of Kuvan and Javygtor is 10 mg/kg taken once daily (QD) for patients 1 month to 6 years of age. For patients ≥ 7 years of age, the recommended starting dose is 10 to 20 mg/kg QD. Therapy response is determined by changes in blood Phe after treatment for a period of 1 month. Blood Phe levels should be checked after 1 week of treatment and periodically for 1 month. Patients whose blood Phe does not decrease after 1 month of treatment at 20 mg/kg/day are non-responders and treatment with Kuvan or Javygtor should be discontinued.

POLICY STATEMENT

This policy involves the use of Kuvan and Javygtor. Prior authorization is recommended for pharmacy benefit coverage of Kuvan and Javygtor. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Kuvan or Javygtor, as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Kuvan or Javygtor be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Kuvan or Javygtor is recommended in those who meet the following criteria:

1. **Hyperphenylalaninemia (HPA) in Patients with Phenylketonuria (PKU)**
   Criteria. *Patient must meet the following criteria*
   - **A.** The drug is prescribed by or in consultation with a metabolic diseases specialist or a provider who specializes in the treatment of PKU and other metabolic diseases; AND
   - **B.** The patient has PKU that is responsive to tetrahydrobiopterin (BH4); AND

C. The patient is using the drug in combination with a phenylalanine (Phe)-restricted diet.
D. If the request is for brand Kuvan or Javygtor, the patient must meet one of the following:
  a. The patient has tried the generic product [documentation in chart notes or claims history required]; OR
  b. The patient cannot take the generic product due to formulation difference in the inactive ingredients [e.g. difference in dyes, fillers, preservatives] between the brand and generic product which would result in a significant allergy or adverse reaction per the prescriber [documentation required]

2. <u>Patient has been started on Kuvan, Javygtor or sapropterin dihydrochloride</u>
Criteria. *Patient must meet the following criteria*

A. The patient has had at least a 20% reduction in Phe levels; OR
B. The patient has responded to use of Kuvan, Javygtor or sapropterin dihydrochloride (e.g. cognitive and/or behavioral improvements), as determined by the prescriber.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 3 months (90 days)
B) *Extended Approval:* 1 year (365 days)

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Kuvan has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Concomitant Therapy with Palynziq.** There are no data available to support the concomitant use of Palynziq and Kuvan or Javygtor. In the Palynziq pivotal studies, patients were required to discontinue use of Kuvan at least 14 days prior to the first dose of Palynziq.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Kuvan [prescribing information]. Novato, CA: BioMarin Pharmaceutical Inc. February 2021.
2. Sapropterin Dihydrochloride. In: DRUGDEX (online database). Truven Health Analytics: Greenwood Village, CO. Last updated 27 December 2019. Accessed on 20 January 2020.
3. Levy H, Burton B, Cederbaum S, Scriver C. Recommendations for evaluation of responsiveness to tetrahydrobiopterin (BH4) in phenylketonuria and its use in treatment. *Mol Genet Metab*. 2007;92:287-291.
4. Burton BK, Nowacka M, Hennermann JB, et al. Safety of extended treatment with sapropterin dihydrochloride in patients with phenylketonuria: results of a phase 3b study. *Mol Genet Metab*. 2011;103(4):315-322.
5. Cunningham A, Bausell H, Brown M, et al. Recommendations for the use of sapropterin in phenylketonuria. *Mol Genet Metab*. 2012;106:269-276.