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5.30.014

Section:	Prescription Drugs	**Effective Date:**	January 1, 2026
Subsection:	Endocrine and Metabolic Drugs	**Original Policy Date:**	December 7, 2011
Subject:	Kuvan Javygtor Zelvysia	**Page:**	1 of 5

Last Review Date: December 12, 2025

Sapropterin

Description

Kuvan, Javygtor, Zelvysia (sapropterin)

Background
Prolonged high blood phenylalanine (Phe) levels are neurotoxic and lead to impairment of intelligence and other brain functions (such as attentiveness). Reduction of blood Phe levels through dietary control is an important determinant of long-term neurologic outcome in phenylketonuria (PKU) patients, and reduction of blood Phe levels in patients with PKU has been shown to decrease the long-term risk of neurologic injury. It is difficult for many patients to maintain reduced blood Phe, and many patients with PKU experience some degree of neurological impairment despite efforts to maintain dietary Phe control (1-3).

Response to treatment cannot be pre-determined by laboratory testing (e.g., genetic testing), and can only be determined by a therapeutic trial of sapropterin. Although long-term assessment of neurologic function in patients with PKU receiving sapropterin for the treatment of elevated blood Phe has not been done, sapropterin may help maintain reduced blood Phe levels as an adjunct to a Phe-controlled diet (1-3).

Regulatory Status
FDA-approved indication: Sapropterin is indicated to reduce blood phenylalanine (Phe) levels in patients with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin- (BH4-) responsive phenylketonuria (PKU). Sapropterin is to be used in conjunction with a Phe-restricted diet (1-3).

The most common side effects of sapropterin are headache, vomiting, diarrhea, runny nose, cough, and sore throat. Most of these side effects were mild and did not result in patients stopping sapropterin treatment (1-3).

During clinical trials, gastritis was reported as a serious adverse reaction. Monitor patients for signs and symptoms of gastritis (1-3).

Pediatric patients with PKU, 1 month to 16 years of age, have been treated with sapropterin in clinical studies (1-3).

Related policies
Palynziq

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Sapropterin may be considered **medically necessary** if the conditions indicated below are met.

Sapropterin may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 1 month of age or older

Diagnosis

Patient must have the following:
Phenylketonuria (PKU)

AND ALL of the following:

a. Tetrahydrobiopterin (BH_4) deficiency has been ruled out
b. Phenylalanine-restricted diet
c. Prescriber agrees to monitor phenylalanine levels
d. **NOT** being used in combination with Palynziq (pegvaliase-pqpz)
e. **Brand Kuvan, Javygtor and Zelvysia ONLY:** Inadequate treatment response, intolerance, or contraindication to generic Kuvan: sapropterin

Prior – Approval *Renewal* Requirements

Age 1 month of age or older

Diagnosis

Patient must have the following:
Phenylketonuria (PKU)

AND ALL of the following:

a. Phenylalanine-restricted diet
b. Reduction from baseline phenylalanine levels of 30% or greater
c. **NOT** being used in combination with Palynziq (pegvaliase-pqpz)
d. **Brand Kuvan, Javygtor and Zelvysia ONLY:** Inadequate treatment response, intolerance, or contraindication to generic Kuvan: sapropterin

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 weeks

Prior – Approval *Renewal* Limits

Duration 12 months

Rationale

Summary

Reduction of blood Phe levels in patients with PKU has been shown to decrease the long-term risk of neurologic injury. In clinical trials of sapropterin in patients with PKU, reductions in blood Phe levels were observed in some patients. Pediatric patients with PKU, 1 month to 16 years of age, have been treated with sapropterin in clinical studies (1-3).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of sapropterin while maintaining optimal therapeutic outcomes.

References

1. Kuvan [package insert]. Novato, CA: BioMarin Pharmaceutical Inc.; August 2024.

2. Javygtor [package insert]. Princeton, NJ: Dr. Reddy's Laboratories Inc.; October 2024.

3. Zelvysia [package insert]. Piscataway, NJ: Aucta Pharmaceuticals, Inc.; April 2025.

Policy History

Date	Action
December 2011	Annual revision
December 2012	Annual revision
March 2014	Line-addition of 100mg oral powder packs
June 2014	Annual editorial review and reference update
October 2014	Change of age requirement to include 1 month of age and older
December 2014	Annual review and reference update
September 2015	Annual review and reference update
September 2016	Annual editorial review and reference update Policy number change from 5.08.14 to 5.30.14
December 2017	Annual review and reference update
September 2018	Annual editorial review, addition of no dual therapy with Palynziq. Addition of prescriber agrees to monitor phenylalanine levels for initiation. Removal of ruling out BH4 deficiency for continuation
December 2019	Annual review
December 2020	Annual review and reference update
June 2021	Annual review and reference update
December 2021	Annual review. Added requirement that brand Kuvan has to t/f the preferred product sapropterin
June 2022	Annual review
January 2023	Changed policy name to Kuvan Javygtor. Addition of Javygtor to policy as a non-preferred medication. Changed policy number to 5.30.014. Removed hepatic monitoring from regulatory status per PI
March 2023	Annual review

March 2024	Annual review
March 2025	Annual review and reference update
December 2025	Annual review. Added Zelvysia. Removed MedEx requirement and switched to t/f

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 12, 2025 and is effective on January 1, 2026.