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Section:	Prescription Drugs	**Effective Date:**	April 1, 2026
Subsection:	Endocrine and Metabolic Drugs	**Original Policy Date:**	September 5, 2025
Subject:	Sephience	**Page:**	1 of 4

Last Review Date: March 6, 2026

Sephience

Description

Sephience (sepiapterin)

Background
Sephience is a precursor of the enzymatic co-factor tetrahydrobiopterin (BH_4) which activates phenylalanine hydroxylase (PAH). Biochemical response to treatment cannot be pre-determined by laboratory testing (e.g., molecular testing), and should be determined by a therapeutic evaluation of Sephience (1).

Regulatory Status
FDA-approved indication: Sephience is a phenylalanine hydroxylase (PAH) activator indicated for the treatment of hyperphenylalaninemia (HPA) in adult and pediatric patients 1 month of age and older with sepiapterin-responsive phenylketonuria (PKU). Sephience is to be used in conjunction with a phenylalanine (Phe)- restricted diet (1).

Sephience carries warnings for increased bleeding, hypophenylalaninemia, and interaction with levodopa. Monitor for signs of bleeding and changes in neurological status in patients receiving levodopa. Obtain baseline blood Phe concentrations before initiating therapy and monitor Phe levels during treatment (1).

The safety and effectiveness of Sephience in pediatric patients less than 1 month of age have not been established (1).

Related policies

Kuvan, 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.

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

Sephience 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. Phenylalanine-restricted diet
b. Inadequate treatment response, intolerance, or contraindication to generic Kuvan: sapropterin
c. Prescriber agrees to monitor phenylalanine levels
d. **NOT** being used in combination with Palynziq (pegvaliase-pqpz) or Kuvan/Javygtor (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. Phenylananine-restricted diet
b. Reduction from baseline phenylalanine levels of 30% or greater
c. **NOT** being used in combination with Palynziq (pegvaliase-pqpz) or Kuvan/Javygtor (sapropterin)

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 weeks

Prior – Approval *Renewal* Limits

Duration 12 months

Rationale

Summary

Sephience is a phenylalanine hydroxylase (PAH) activator indicated for the treatment of hyperphenylalaninemia (HPA) in patients with sepiapterin-responsive phenylketonuria (PKU). Sephience carries warnings for increased bleeding, hypophenylalaninemia, and interaction with levodopa. The safety and effectiveness of Sephience in pediatric patients less than 1 month of age have not been established (1).

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

References

1. Sephience [package insert]. Warren, NJ: PTC Therapeutics, Inc.; July 2025.

Policy History

Date	Action
September 2025	Addition to PA
December 2025	Annual review. Per SME, removed BH4 deficiency requirement, added t/f generic Kuvan: sapropterin

March 2026 Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 6, 2026 and is effective on April 1, 2026.