CareSource Rx Innovations

PHARMACY POLICY STATEMENT
Marketplace

DRUG NAME	Sephience (sepiapterin)
BENEFIT TYPE	Pharmacy
STATUS	Prior Authorization Required

Sephience, approved by the FDA in 2025, 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.
PKU results from a deficiency of phenylalanine hydroxylase (PAH) enzyme, leading to increased concentrations of Phe. If untreated, this excess accumulation causes neuropsychiatric and neurocognitive symptoms. Standard of care for PKU is a Phe-restricted diet.

Sephience (sepiapterin) will be considered for coverage when the following criteria are met:

Phenylketonuria (PKU)

For **initial** authorization:
1. Member is at least 1 month of age; AND
2. Medication must be prescribed by or in consultation with a specialist experienced in metabolic or genetic diseases; AND
3. Member has a diagnosis of PKU; AND
4. Member has documentation of current blood Phe level sustained ≥ 360 µmol/L despite dietary management; AND
5. Provider attests medication will be used in conjunction with a Phe-restricted diet; AND
6. Member has a trial and failure of generic sapropterin. *Note*: trial is not required if member has documentation of 2 null mutations; AND
7. Provider attests medication will not be prescribed in combination with Palynziq and/or sapropterin products.
8. **Dosage allowed/Quantity limit:** administer orally once daily with food per table below. Discontinue after 2 weeks at the dose of 60 mg/kg if Phe has not decreased.

Age	SEPHIENCE (mg/kg) per day
Less than 6 months	7.5 mg/kg
6 months to less than 1 year	15 mg/kg
1 year to less than 2 years	30 mg/kg
2 years and older	60 mg/kg

If all the above requirements are met, the medication will be approved for 2 months.

For **reauthorization**:
1. Chart notes must show at least a 30% reduction of Phe and/or Phe level ≤360 µmol/L; AND
2. Provider attests medication is being used in conjunction with a Phe-restricted diet

If all the above requirements are met, the medication will be approved for an additional 12 months.

CareSource considers Sephience (sepiapterin) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
08/12/2025	New policy for Sephience created.
09/22/2025	Added trial and failure of generic sapropterin unless member has two null mutations Replaced Kuvan with sapropterin products as medications Sephience will not be used with

References:

1. Sephience [prescribing information]. PTC Therapeutics, Inc.; 2025.
2. Nulmans I, Lequeue S, Desmet L, Neuckermans J, De Kock J. Current state of the treatment landscape of phenylketonuria. *Orphanet J Rare Dis.* 2025;20(1):281. Published 2025 Jun 5. doi:10.1186/s13023-025-03840-
3. van Wegberg AMJ, MacDonald A, Ahring K, et al. European guidelines on diagnosis and treatment of phenylketonuria: First revision. *Mol Genet Metab*. 2025;145(2):109125. doi:10.1016/j.ymgme.2025.109125
4. Smith WE, Berry SA, Bloom K, et al. Phenylalanine hydroxylase deficiency diagnosis and management: A 2023 evidence-based clinical guideline of the American College of Medical Genetics and Genomics (ACMG). *Genet Med*. 2025;27(1):101289. doi:10.1016/j.gim.2024.101289

Effective date: 01/01/2026
Revised date: 09/22/2025