UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2025 P 2384-1
Program	Prior Authorization/Medical Necessity
Medication	Sephience™ (sepiapterin)
P&T Approval Date	11/2025
Effective Date	2/1/2026

1. Background:

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.

2. Coverage Criteria[a]:

A. Initial Authorization

1. **Sephience** will be approved based on **all** of the following criteria:

   a. Diagnosis of phenylketonuria (PKU)

   -AND-

   b. Patient is actively on a phenylalanine(Phe)-restricted diet

   -AND-

   c. **One** of the following:

      (1) Patient has a contraindication to sapropterin (list reason)

      -OR-

      (2) History of failure or intolerance to sapropterin therapy (document date of trial and list reason for therapeutic failure or intolerance) as determined by a trial of sapropterin

      -OR-

      (3) Patient is not an appropriate candidate for sapropterin due to two null mutations in *trans*

      -AND-

   d. Physician attestation that the patient will not be receiving Sephience in combination with sapropterin dihydrochloride or Palynziq (pegvaliase-pqpz)

Authorization will be issued for 12 months.

B. Reauthorization

1. **Sephience** will be approved based on **all** of the following criteria:

   a. Patient is actively on a Phe-restricted diet

   -AND-

   b. Blood Phe levels continue to remain lower than baseline level

   -AND-

   c. Submission of medical records (e.g., chart notes, laboratory values) documenting that the patient is not receiving Sephience in combination with sapropterin dihydrochloride or Palynziq (pegvaliase-pqpz) [Prescription claim history that does not show any concomitant sapropterin dihydrochloride or Palynziq (pegvaliase-pqpz) claim within 60 days of reauthorization request may be used as documentation.]

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may also be in place.

4. References:

1. Sephience [package insert]. Warren, NJ: PTC Therapeutics, Inc.; July 2025.
2. Thomas J, Levy H, Amato S, et al. Pegvaliase for the treatment of phenylketonuria: Results of a long-term phase 3 clinical trial program (PRISM). Mol Genet Metab. 2018;124(1):27-38.
3. Vockley et al. Phenylalanine hydroxylase deficiency: diagnosis and management guideline. American College of Medical Genetics and Genomics Practice Guidelines. Genetics in Medicine 2014;16 (2):188-200.
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

Program	Prior Authorization/Medical Necessity - Sephience (sepiapterin)
Change Control	
11/2025	New program.