

UnitedHealthcare Pharmacy  
Clinical Pharmacy Programs

Program Number	2025 P 3199-1
Program	Step Therapy
Medication	Sephience™ (sepiapterin)
P&T Approval Date	11/2025
Effective Date	2/1/2026

**1. Background:**

Step therapy programs are utilized to encourage use of lower cost alternatives for certain therapeutic classes. This program requires a member to try sapropterin dihydrochloride before providing coverage for Sephience.

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.

Sapropterin dihydrochloride (generic Kuvan) is a phenylalanine hydroxylase activator indicated to reduce blood phenylalanine levels in adult and pediatric patients one month of age and older with hyperphenylalaninemia due to tetrahydrobiopterin-responsive Phenylketonuria and is to be used in conjunction with a phenylalanine-restricted diet.

Members currently on Sephience as documented in claims history will be allowed continued coverage of their current therapy. Members new to therapy will be required to meet the coverage criteria below.

**2. Coverage Criteria<sup>a</sup>:****A. Sephience** will be approved based on the following criteria:

1. History of failure, contraindication, or intolerance to sapropterin dihydrochloride (document date of trial and list reason for therapeutic failure, contraindication, or intolerance)

**-OR-**

2. Patient is not an appropriate candidate for sapropterin due to two null mutations in *trans*

**Authorization will be issued for 12 months.**

<sup>a</sup> 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.
- Medical Necessity, Supply Limits and/or Notification may be in place.

### 4. References:

1. Sephience [package insert]. Warren, NJ: PTC Therapeutics, Inc.; July 2025.
2. Kuvan [package insert]. Novato, CA: BioMarin Pharmaceutical Inc.; August 2024.
3. Sapropterin Dihydrochloride [package insert]. Malvern, PA: Endo USA. July 2024.
4. Sapropterin Dihydrochloride [package insert]. Piscataway, NJ: Camber Pharmaceuticals, Inc.; September 2022.
5. 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.
6. 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	Step Therapy – Sephience (sepiapterin)
<b>Change Control</b>	
11/2025	New program.