| Effective Date: 02/2026 |
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| Reviewed: 11/2025 |
| Scope: Medicaid |

# SEPHIENCE (sepiapterin)

## POLICY

### I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met, and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Indicated for the treatment of hyperphenylalaninemia (HPA) in adult and pediatric members 1 month of age and older with sepiapterin-responsive phenylketonuria (PKU). Sephience is to be used in conjunction with a phenylalanine (Phe)- restricted diet.

All other indications are considered experimental/investigational and not medically necessary.

### II. CRITERIA FOR INITIAL APPROVAL

**Phenylketonuria (PKU)**
Authorization of 2 months may be granted when all of the following criteria are met:

A. The medication is prescribed by, or in consultation with, a physician who specializes in the treatment of metabolic disease and/or phenylketonuria (PKU).
B. Member is one month of age or older.
C. Member has been diagnosed with phenylketonuria and meets both of the following criteria:
    a. Member has a clinical diagnosis of hyperphenylalaninemia (HPA) with documentation of a past medical history of at least 2 blood phenylalanine measurements greater than or equal to 600 µmol/L.
    b. Member has documentation of baseline phenylalanine level greater than or equal to 360 µmol/L prior to starting treatment with the requested medication.
D. Member has not been diagnosed with hyperphenylalaninemia due to pathogenic variants in GCH1, PTS, QDPR, SPR, or PCBD1, consistent with a diagnosis of primary $BH_4$ deficiency.
E. Documentation that the member does not have any abnormal physical examination or laboratory findings indicative of signs or symptoms of renal disease including calculated glomerular filtration rate (GFR) <60 mL/min/1.73 $m^2$.
F. The requested medication will be used in conjunction with a phenylalanine (Phe)-restricted diet.
G. Documentation that the requested medication will not be used in combination with sapropterin products (e.g., sapropterin, Javygtor, Kuvan) or Palynziq (pegvaliase-pqpz).
H. Documentation of the member's most recent weight.
I. Medication is being prescribed at the appropriate FDA approved dose based on the member's weight and the dose does not exceed 60 mg/kg.
J. Member has had a documented inadequate treatment response or intolerance to a formulary sapropterin product (Note: inadequate response is defined as a blood Phe ≥360 µmol/L, despite consistent use in combination with dietary Phe restriction)

## III. CONTINUATION OF THERAPY

**Phenylketonuria (PKU)**
Authorization of 6 months may be granted for when all of the following criteria are met:

A. Member continues to meet all initial criteria; **AND**
B. Chart notes or medical records demonstrate achievement or maintenance of a 30% decrease in phenylalanine levels from baseline; **OR**
C. Chart notes or medical records demonstrate phenylalanine levels are in an acceptable range (less than 360 µmol/L; **OR**
D. Chart notes or medical records demonstrate an improvement in neuropsychiatric symptoms.

## IV. COVERAGE DURATION

- Initial: 2 months
- Renewal: 6 months

## V. REFERENCES

1. Sephience [package insert]. Warren, NJ: PTC Therapeutics, Inc.; July 2025.
2. 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. Published online December 2, 2024. doi:10.1016/j.gim.2024.101289
3. Singh RH, Rohr F, Frazier D, et al. Recommendations for the nutrition management of phenylalanine hydroxylase deficiency. Genet Med. 2014;16(2):121-131.