Reference number(s)
7115-A

Specialty Guideline Management Sephience

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Sephience	sepiapterin

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 Indications[1]

Sephience is 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.

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

Documentation

Submission of the following information is necessary to initiate the prior authorization review:

Initial Requests

Chart notes or medical record documentation documenting all of the following:

- Past medical history of at least 2 blood phenylalanine measurements greater than or equal to 600 micromol/L.

- Baseline phenylalanine level greater than or equal to 360 micromol/L prior to starting treatment with the requested medication.
- Baseline renal function assessments (e.g., glomerular filtration rate (GFR)).

Continuation Requests

Chart notes or medical records demonstrating achievement or maintenance of a 30% decrease in phenylalanine levels from baseline, phenylalanine levels that are in an acceptable range (less than 360 micromol/L), or an improvement in neuropsychiatric symptoms.

Prescriber Specialties

This medication must be prescribed by or in consultation with a physician who specializes in the treatment of metabolic disease and/or phenylketonuria (PKU).

Coverage Criteria

Phenylketonuria (PKU) [1-3]

Authorization of 60 days may be granted when all of the following criteria are met:

- Member is one month of age or older.
- Member has been diagnosed with phenylketonuria and meets both of the following criteria:
    - Member has a clinical diagnosis of hyperphenylalaninemia (HPA) documented by past medical history of at least 2 blood phenylalanine measurements greater than or equal to 600 micromol/L.
    - Member has a baseline phenylalanine level greater than or equal to 360 micromol/L prior to starting treatment with the requested medication.
- 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.
- 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.
- The requested medication will be used in conjunction with a phenylalanine (Phe)-restricted diet.
- The requested medication will not be used in combination with sapropterin products.

Note: If Sephience is initiated in a member currently receiving Palynziq for phenylketonuria (PKU), then Palynziq will be discontinued after an appropriate period of overlap.

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Continuation of Therapy

Phenylketonuria (PKU) [1-3]

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for phenylketonuria (PKU) who meet any of the following criteria:

- Achieve or maintain a 30% decrease in phenylalanine levels from baseline; or
- Phenylalanine levels are in an acceptable range (less than 360 micromol/L); or
- Demonstrate an improvement in neuropsychiatric symptoms.

Note: Sephience should not be used concomitantly with Palynziq or sapropterin products for phenylketonuria (PKU).

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.