AETNA BETTER HEALTH® Coverage Policy/Guideline					
Name:	Sephience			Page:	1 of 3
Effective Date:	11/6/2025			Last Review Date:	10/2025
Applies to:	☒Illinois ☒New Jersey ☒Pennsylvania Kids	☐Florida ☒Maryland ☒Virginia		☒Florida Kids ☐Michigan ☐Kentucky PRMD	

Intent:

The intent of this policy/guideline is to provide information to the prescribing practitioner outlining the coverage criteria for Sephience under the patient's prescription drug benefit.

Description:

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.

Applicable Drug List:

Sephience

Policy/Guideline:

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.
- Patient is unable to take generic sapropterin dihydrochloride for the given diagnosis due to a trial and inadequate treatment response or intolerance, or a contraindication. Documentation is required for approval.

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.

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).

Approval Duration and Quantity Restrictions:

Approval:
Initial approval: 60 days
Renewal Approval: 6 months

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.