MEDICATION POLICY:
Sephience (sepiapterin)

Applicable Drugs: Sephience (sepiapterin)

Preferred: N/A

Non-preferred: N/A

Date of Origin: 10/24/2025

Date Last Reviewed / Revised: 10/24/2025

Prior Authorization Criteria

(May be considered medically necessary when criteria I through V are met)

I. Documented diagnosis of hyperphenylalaninemia (HPA) due to phenylketonuria (PKU) and meets criteria A through C:
   A. Elevated blood phenylalanine (Phe) concentrations >360 µmol/L (6 mg/dL) at baseline.
   B. Documented trial of a phenylalanine-restricted diet in combination with generic sapropterin, demonstrating treatment failure or contraindication with persistent Phe blood levels ≥360 µmol/L.
   C. The requested medication will be used as an adjunct to a phenylalanine-restricted diet.

II. Minimum age requirement: ≥1 month of age.

III. Treatment must be prescribed by or in consultation with an endocrinologist, metabolic disease specialist, or genetic disease specialist.

IV. Medication is prescribed in accordance with FDA labeling and is supported by current clinical practice guidelines.

V. Refer to the plan document for the list of preferred products. If the requested agent is not listed as a preferred product, must have a documented failure, intolerance, or contraindication to a preferred product(s).

Exclusion Criteria

- Concurrent use with sapropterin (Kuvan, Javygtor) or pegvaliase-pqpz (Palynziq)
- Primary BH_4 deficiency (variants in GCH1, PTS, QDPR, SPR, PCBD1)

Other Criteria

- N/A

Quantity / Days Supply Restrictions

- Adults and pediatric patients (≥1 month of age): Maximum dose of 60 mg/kg/day, not to exceed the FDA-recommended limits; dispense up to a 30-day supply

- Pediatric patients (≥1 month to <2 years): Recommended starting doses are outlined in Appendix Table 1 and should be dispensed for a 30-day supply in accordance with weight-based dosing.

APPROVAL LENGTH

- **Authorization:** 3 months
- **Re-Authorization:** 1 year, with an updated letter of medical necessity or progress notes showing sustained clinical benefit from therapy, including maintenance of at least a 30% reduction in blood Phe levels from baseline OR achievement of Phe levels <360 µmol/L.

APPENDIX

Table 1. Recommended Starting Dosage

Age	SEPHIENCE (mg/kg) per day
Less than 6 months	7.5 mg/kg
6 months to less than 1 year	15 mg/kg
1 year to less than 2 years	30 mg/kg
2 years and older	60 mg/kg

REFERENCES

1. SEPHIENCE (sepiapterin) oral powder. Prescribing Information. PTC Therapeutics, Inc.; revised July 2025. US Food and Drug Administration. Accessed October 6, 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219666s000lbl.pdf
2. Muntau AC, Longo N, Ezgu F, et al. Effects of oral sepiapterin on blood Phe concentration in a broad range of patients with phenylketonuria (APHENITY): results of an international, phase 3, randomised, double-blind, placebo-controlled trial. Lancet. 2024;404(10460):1333-1345. doi:10.1016/S0140-6736(24)01556-3
3. 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). Genetics in Medicine. Published online December 4, 2024:101289. doi:https://doi.org/10.1016/j.gim.2024.101289
4. A.M.J. van Wegberg, MacDonald A, Ahring K, et al. European guidelines on diagnosis and treatment of phenylketonuria: First revision. Molecular Genetics and Metabolism. Published online April 1, 2025:109125-109125. doi:https://doi.org/10.1016/j.ymgme.2025.109125

DISCLAIMER: Medication Policies are developed to help ensure safe, effective and appropriate use of selected medications. They offer a guide to coverage and are not intended to dictate to providers how to practice medicine. Refer to Plan for individual adoption of specific Medication Policies. Providers are expected to exercise their medical judgement in providing the most appropriate care for their patients.