Mass General Brigham
Health Plan

Sephience (sepiapterin)
Effective 03/01/2026

Plan	☐ MassHealth UPPL ☒ Commercial/Exchange	**Program Type**	☒ Prior Authorization ☐ Quantity Limit ☐ Step Therapy
Benefit	☒ Pharmacy Benefit ☐ Medical Benefit		
Specialty Limitations	These medications have been designated specialty and must be filled at a contracted specialty pharmacy.		
Contact Information	**Medical Benefit** **Pharmacy Benefit**	Phone: 833-895-2611 Phone: 800-711-4555	Fax: 888-656-6671 Fax: 844-403-1029
Exceptions	N/A		

Overview
Sephience (sepiapterin) is a phenylalanine hydroxylase (PAH) activator indicated for the treatment of hyperphenylalanemia (HPA) in adult and pediatric patients 1 month of age and older with sepiapterin-responsive phenylketonuria (PKU).

Sephience should be used in conjunction with a phenylalanine (Phe)-restricted diet. Sephience should be discontinued in patients who blood Phe does not decrease after 2 weeks of treatment at the maximum dosage of 60 mg/kg.

Coverage Guidelines
Authorization may be granted for members new to the plan within the past 90 days who are currently receiving treatment with the requested medication, excluding when the product is obtained as samples or via manufacturer's patient assistance programs
OR
Authorization may be granted when all of the following criteria are met:

1. Member has a diagnosis of phenylketonuria
2. Member is 1 month of age or older
3. Requested medication will be used in conjunction with a phenylalanine (Phe)-restricted diet
4. **For members starting therapy:** Member will have Phe blood levels measured within two weeks of therapy and periodically for up to 3 months of therapy to determine response
5. Member meets ONE of the following:
    a. Member has a diagnosis of classic PKU (untreated serum phenylalanine concentrations > 1200 micromol/L)
    b. Member has had a trial and failure, contraindication, or intolerance to sapropterin (Kuvan)
6. Requested medication will not be used in combination with another PKU drug, including a sapropterin-containing product and Palynziq (pegvaliase-pqpz)

<u>Continuation of Therapy</u>
Requests for reauthorization will be approved when the following criteria are met:

1. Documentation member has had at least a 15% decrease in phenylalanine blood levels compared to baseline

2. Requested medication continues to be used in conjunction with a phenylalaine (Phe)-restricted diet
3. Member continues to have blood Phe levels measured periodically during therapy

Limitations

1. Initial approvals will be granted for 3 months
2. Reauthorizations will be granted for 12 months

References

1. Bratkovic D, Margvelashvili L, Tchan MC, Nisbet J, Smith N. PTC923 (sepiapterin) lowers elevated blood phenylalanine in subjects with phenylketonuria: a phase 2 randomized, multi-center, three-period crossover, open-label, active controlled, all-comers study. *Metabolism*. 2022; 128:155116.
2. Elhawary NA, AlJahdali IA, Abumansour IS, et al. Genetic etiology and clinical challenges of phenylketonuria. *Hum Genomics*. 2022;16(22): 1-17.
3. Harding CO, Amato RS, Stuy M, et al. Pegvaliase for the treatment of phenylketonuria: A pivotal, double-blind randomized discontinuation phase 3 clinical trial. *Mol Genet Metab*. 2018;124(1):20-26.
4. Hillert A, Anikster Y, Belanger-Quintana A, et al. The genetic landscape and epidemiology of phenylketonuria. *AJHG*. 2020;107: 234-250.
5. Levy HL, Milanowski A, Chakrapani A, et al. Efficacy of sapropterin dihydrochloride (tetrahydrobiopterin, 6R-BH_4) for reduction of phenylalanine concentration in patients with phenylketonuria: a phase III randomised placebo-controlled study. *Lancet*. 2007;370(9586):504-510
6. Muntau AC, Longo N, Ezgu F, et al. Effects of oral sepiapterin on blood Phe concentration in a
7. broad range of patients with phenylketonuria (APHENITY): results of an international, phase 3, randomised, double-blind, placebo-controlled trial. *Lancet*.2024;404: 1333-1345.
8. Sephience. Package insert. PTC Therapeutics, Inc.; July 2025.
9. 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.
10. Stone WL, Basit H, Los E. Phenylketonuria. StatPearls [Internet]. Updated August 8, 2023. Accessed September 28, 2025. https://www.ncbi.nlm.nih.gov/books/NBK535378/
11. Thomas J, Levy H, Amato S, et al. Pegvaliase for the treatment of phenylketonuria: Results of a long-term phase 3 clinical trial program (PRISM). *Mol Genet Metab*. 2018;124(1):27-38.
12. Trefz FK, Burton BK, Longo N, et al. Efficacy of sapropterin dihydrochloride in increasing phenylalanine tolerance in children with phenylketonuria: a phase III, randomized, double-blind, placebo-controlled study. *J Pediatr*. 2009;154(5):700-707.

Review History

01/14/2026 – Reviewed at December P&T. Effective 03/01/2026.