HAP CareSource™

PHARMACY POLICY STATEMENT
HAP CareSource™ Marketplace

DRUG NAME	**Sodium Phenylbutyrate (Buphenyl, Pheburane, Olpruva)**
BENEFIT TYPE	Pharmacy
STATUS	Prior Authorization Required

Sodium phenylbutyrate (NaPB) is indicated as adjunctive therapy in the chronic management of patients with urea cycle disorders involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS). It is indicated in all patients with neonatal-onset deficiency (complete enzymatic deficiency, presenting within the first 28 days of life). It is also indicated in patients with late-onset disease (partial enzymatic deficiency, presenting after the first month of life) who have a history of hyperammonemic encephalopathy. Treatment must be combined with dietary protein restriction and, in some cases, essential amino acid supplementation.
The first NaPB product was approved as Buphenyl (tablets and powder) in 1996. The 505b2 formulations of NaPB, Pheburane (granules) and Olpruva (suspension), were developed to improve palatability compared to the characteristic bitterness of Buphenyl. Another available option with favorable palatability is Ravicti (glycerol phenylbutyrate). These phenylbutyrate derivatives act as nitrogen scavengers to remove excess nitrogen and ammonia from the body by an alternate pathway.
The urea cycle clears nitrogen waste from the body as urea. Urea cycle disorders (UCDs) are rare inherited deficiencies in any of the enzymes involved in the urea cycle. The enzyme deficiency makes ureagenesis defective and causes ammonia to accumulate. Hyperammonemia is a marker of inadequate nitrogen detoxification, and its severity strongly correlates with brain damage. Signs and symptoms can present at any age and are mainly neurologic. The only curative option is liver transplant.

Sodium phenylbutyrate will be considered for coverage when the following criteria are met:

Urea Cycle Disorders (UCDs)

For **initial** authorization:

1. If the request is for Olpruva, member must weigh at least 20 kg and have a body surface area (BSA) of 1.2 m^2 or greater; if the request is for Buphenyl tablets, member must weigh at least 20 kg; AND
2. Medication must be prescribed by or in consultation with a metabolic specialist or geneticist; AND
3. Member has a documented diagnosis of a UCD (e.g., involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS)); AND
4. The diagnosis has been confirmed by genetic testing or enzyme activity assay results; AND
5. The member has a history of hyperammonemia (150 µmol/L (>260 µg/dl) or higher in neonates or > 100 µmol/l (175 µg/dl) in older children and adults); AND
6. Medication is prescribed as an adjunctive therapy to dietary protein restriction; AND
7. If the request is for Pheburane or Olpruva, documentation of intolerance to generic Buphenyl tablets or powder is required; AND
8. Medication will NOT be used in combination with Ravicti.

HAP CareSource™

9. **Dosage allowed/Quantity limit:**
   Weight < 20 kg: 450-600 mg/kg/day
   Weight 20 kg or greater: 9.9–13.0 g/m2/day. MAX 20 g/day.

   QL Buphenyl: 1200 tablets per 30 days (40 tablets/day) or 2 bottles of powder per 25 days
   QL Pheburane: 7 bottles of oral granules per 28 days
   QL Olpruva: 1 kit (90 dosage envelopes) per 30 days

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:
1. Documentation of ongoing dietary management; AND
2. Chart notes must include documentation of a positive response to therapy such as normalized ammonia levels or reduced number of hyperammonemic crises.

If all the above requirements are met, the medication will be approved for an additional 12 months.

HAP CareSource considers sodium phenylbutyrate not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
01/09/2023	New policy for sodium phenylbutyrate created.

References:

1. Buphenyl [prescribing information]. Horizon Therapeutics USA, Inc.; 2022.
2. Pheburane [prescribing information]. Medunik USA, Inc.; 2022.
3. Olpruva [prescribing information]. Acer Therapeutics Inc.; 2022.
4. Peña-Quintana L, Llarena M, Reyes-Suárez D, Aldámiz-Echevarria L. Profile of sodium phenylbutyrate granules for the treatment of urea-cycle disorders: patient perspectives. *Patient Prefer Adherence*. 2017;11:1489-1496. Published 2017 Sep 6. doi:10.2147/PPA.S136754
5. Kibleur Y, Dobbelaere D, Barth M, Brassier A, Guffon N. Results from a Nationwide Cohort Temporary Utilization Authorization (ATU) survey of patients in france treated with Pheburane(®) (Sodium Phenylbutyrate) taste-masked granules. *Paediatr Drugs*. 2014;16(5):407-415. doi:10.1007/s40272-014-0081-5
6. NIH Rare Diseases Clinical Research Network (RDCRN): Urea Cycle Disorders Consortium (UCDC). Urea Cycle Treatment Guidelines. Available from: https://www1.rarediseasesnetwork.org/cms/ucdc/Healthcare-Professionals/Urea-Cycle-Treatment-Guidelines
7. Ah Mew N, Simpson KL, Gropman AL, et al. Urea Cycle Disorders Overview. 2003 Apr 29 [Updated 2017 Jun 22]. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1217/
8. Häberle J, Burlina A, Chakrapani A, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders: First revision. *J Inherit Metab Dis*. 2019;42(6):1192-1230. doi:10.1002/jimd.12100
9. Häberle J, Boddaert N, Burlina A, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders. *Orphanet J Rare Dis*. 2012;7:32. Published 2012 May 29. doi:10.1186/1750-1172-7-32

Effective date: 01/01/2025
Revised date: 01/09/2023