Clinical Policy: Sodium Phenylbutyrate (Buphenyl, Pheburane, Olpruva)

Reference Number: CP.PHAR.208
Effective Date: 05.01.16
Last Review Date: 02.26
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Sodium phenylbutyrate (Buphenyl®, Pheburane®, Olpruva®) is a nitrogen-binding agent.

FDA Approved Indication(s)

Buphenyl is indicated as adjunctive therapy in the chronic management of patients with urea cycle disorders (UCDs) involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS).

Pheburane is indicated as adjunctive therapy to standard of care, which includes dietary management, for the chronic management of adult and pediatric patients with UCDs, involving deficiencies of CPS, OTC or AS.

Olpruva is indicated as adjunctive therapy to standard of care, which includes dietary management, for the chronic management of adult and pediatric patients 1 year of age and older weighing 7 kg or greater, with UCDs involving deficiencies of CPS, OTC, or AS.

Limitation(s) of use:

- Buphenyl, Pheburane, and Olpruva should not be used to manage acute hyperammonemia, which is a medical emergency.
- Olpruva is not recommended for patients younger than 1 year of age due to the volume of free water required for daily administration.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Buphenyl, Pheburane, and Olpruva are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Urea Cycle Disorder: CPS, OTC, AS (must meet all)**:**

1. Diagnosis of a UCD caused by one or more of the following, confirmed by enzymatic, biochemical, or genetic analysis:
   a. CPS deficiency;
   b. OTC deficiency;
   c. AS deficiency;
2. Prescribed by or in consultation with a physician experienced in treating metabolic disorders;

3. If request is for Olpruva, member meets both of the following (a and b):
   a. Weight ≥ 7 kg;
   b. Age ≥ 1 year;
4. Member must use generic sodium phenylbutyrate tablets or powder, unless contraindicated or clinically significant adverse events are experienced;
5. Member must currently be on dietary protein restriction;
6. Dose does not exceed 20 grams per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Approval

A. Urea Cycle Disorder: CPS, OTC, AS (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. If request is for Olpruva, member meets both of the following (a and b):
   a. Weight ≥ 7 kg;
   b. Age ≥ 1 year;
3. Member must use generic sodium phenylbutyrate tablets or powder, unless contraindicated or clinically significant adverse events are experienced;
4. Member is responding positively to therapy;
5. Member must currently be on dietary protein restriction;
6. If request is for a dose increase, new dose does not exceed 20 grams per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ASL: argininosuccinate lyase
AS: argininosuccinate synthetase
BSA: body surface area
CPSI: carbamyl phosphate synthetase 1
CTLN1: type I citrullinemia
FDA: Food and Drug Administration
NAGS: N-acetyl glutamate synthetase
OTC: ornithine transcarbamylase
UCD: urea cycle disorder

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): should not be used to manage acute hyperammonemia (Buphenyl only)
- Boxed warning(s): none reported

Appendix D: Urea Cycle Disorders

UCDs are caused by a deficiency in any of the below enzymes in the pathway that transforms nitrogen to urea:

- Carbamyl phosphate synthetase 1 (CPS1) deficiency
- Ornithine transcarbamylase (OTC) deficiency

- Argininosuccinate synthetase (AS) deficiency (also known as classic citrullinemia or type I citrullinemia, CTLN1)
- Argininosuccinate lyase (ASL) deficiency (also known as argininosuccinic aciduria)
- N-acetyl glutamate synthetase (NAGS) deficiency
- Arginase deficiency

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Sodium phenylbutyrate (Buphenyl, Pheburane)	• Weight < 20 kg: 450-600 mg/kg/day PO in three to six equally divided doses with each meal or feeding • Weight ≥ 20 kg: 9.9-13 g/m^2/day PO in three to six equally divided doses with each meal or feeding	20 grams/day
Sodium phenylbutyrate (Olpruva)	• Weight ≥ 7 kg to < 20 kg: 450 to 600 mg/kg/day of sodium phenylbutyrate • Weight ≥ 20 kg: 9.9-13 g/m^2/day PO in three to six equally divided doses with food	20 grams/day

VI. Product Availability

Drug Name	Availability
Sodium phenylbutyrate (Buphenyl)	• Tablet: 500 mg • Powder: 250 grams (each level tablespoon dispenses 8.6 grams of Buphenyl)
Sodium phenylbutyrate (Pheburane)	Oral pellet: 84 g of sodium phenylbutyrate per bottle
Sodium phenylbutyrate (Olpruva)	Oral suspension pellets in packets for reconstitution: 0.5g, 1 g, 2 g, 3 g, 4 g, 5 g, 6 g, and 6.67 g

VII. References

1. Buphenyl Prescribing Information. Lake Forest, IL: Horizon Pharma USA, Inc.; July 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/020572s025,020573s022lbl.pdf. Accessed: November 12, 2025.
2. Pheburane Prescribing Information. Bryn Mawr, PA: Medunik USA, Inc; June 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/216513s000lbl.pdf. Accessed November 12, 2025.
3. Olpruva Prescribing Information. Newton, MA: Acer Thereapeutics Inc; October 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/214860s007lbl.pdf. Accessed: November 12, 2025.
4. Haberle 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2022 annual review: no significant changes; references reviewed and updated.	09.16.21	02.22
RT4: added Pheburane oral pellets dosage formulation. Template changes applied to other diagnoses/indications.	08.29.22	
1Q 2023 annual review: RT4: added Olpruva oral solution dosage formulation; updated "CPSI" with "CPS1" to clarify the enzyme name; references reviewed and updated.	01.09.23	02.23
Per August SDC, added redirection to generic sodium phenylbutyrate in initial approval criteria and continued approval section.	08.22.23	11.23
1Q 2024 annual review: no significant changes; references reviewed and updated.	11.12.23	02.24
1Q 2025 annual review: no significant changes; references reviewed and updated.	11.12.24	02.25
1Q 2026 annual review: RT4: added pediatric age extension to 1 year old for Olpruva; added requirement for dietary protein restriction per labeling; extended initial approval duration from 6 to 12 months; references reviewed and updated.	11.07.25	02.26

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or

regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.