

Clinical Policy: Sodium Phenylbutyrate (Buphenyl)

Reference Number: CP.PHAR.208

Effective Date: 05.01.16

Last Review Date: 02.21

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[®]) 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 (ASS).

Limitation(s) of use: Buphenyl should not be used to manage acute hyperammonemia, which is a medical emergency.

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 is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria**A. Urea Cycle Disorder: CPS, OTC, ASS (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. ASS deficiency;
2. Prescribed by or in consultation with a physician experienced in treating metabolic disorders;
3. Dose does not exceed 20 g per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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, ASS (must meet all):**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 20 g per day.

Approval duration: 12 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy;
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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

ASS: argininosuccinate synthetase

CPSI: carbamyl phosphate synthetase I

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
- 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 I (CPSI) deficiency
- Ornithine transcarbamylase (OTC) deficiency
- Argininosuccinate synthetase (ASS) 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

Indication	Dosing Regimen	Maximum Dose
UCD	<ul style="list-style-type: none"> Weight < 20 kg: 450-600 mg/kg/day PO in equally divided doses with each meal or feeding Weight ≥ 20 kg: 9.9-13 g/m²/day PO in equally divided doses with each meal or feeding 	20 g/day

VI. Product Availability

- Tablet: 500 mg
- Powder: 250 g

VII. References

1. Buphenyl Prescribing Information. Lake Forest, IL: Horizon Pharma USA, Inc.; February 2020. Available at <https://www.hzndocs.com/BUPHENYL-Prescribing-Information.pdf>. Accessed October 28, 2020.
2. 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
Specific UCDs are added to initial criteria; positive response to therapy is added to renewal criteria; duration of approval changed to 6 and 12 months for initial and continued approval, respectively.	04.17	05.17
1Q18 annual review: - Converted to new template. - Removed dietary protein restriction requirements as this cannot be confirmed - References reviewed and updated	11.15.17	02.18
1Q 2019 annual review: added Commercial line of business; references reviewed and updated	10.25.18	02.19
1Q 2020 annual review: no significant changes; added HIM line of business; references reviewed and updated	10.20.19	02.20
1Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	10.28.20	02.21

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.

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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.

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