

## Clinical Policy: Sodium Phenylbutyrate (Buphenyl)

Reference Number: ERX.SPA.21

Effective Date: 07.01.16

Last Review Date: 02.22

Line of Business: Commercial, Medicaid

[Revision Log](#)

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

### Description

Sodium phenylbutyrate (Buphenyl<sup>®</sup>) 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.*

*Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.*

It is the policy of health plans affiliated with Envolve Pharmacy Solutions<sup>™</sup> that Buphenyl is **medically necessary** when the following criteria are met:

#### I. Initial Approval Criteria

##### A. Urea Cycle Disorders: 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 grams per day.

**Approval duration: 6 months**

##### B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

#### II. Continued Therapy

##### A. Urea Cycle Disorders: CPS, OTC, ASS (must meet all):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions 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 grams per day.

**Approval duration: 12 months**

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

- Approval duration: Duration of request or 6 months (whichever is less);** or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

**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 – ERX.PA.01 or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

- |                                       |                                     |
|---------------------------------------|-------------------------------------|
| ASL: argininosuccinate lyase          | FDA: Food and Drug Administration   |
| ASS: argininosuccinate synthetase     | NAGS: N-acetyl glutamate synthetase |
| CPSI: carbamyl phosphate synthetase I | OTC: ornithine transcarbamylase     |
| CTLN1: type I citrullinemia           | 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"> <li>• Weight &lt; 20 kg: 450-600 mg/kg/day PO in equally divided doses with each meal or feeding</li> <li>• Weight ≥ 20 kg: 9.9-13 g/m<sup>2</sup>/day PO in equally divided doses with each meal or feeding</li> </ul>	20 grams/day

**VI. Product Availability**

- Tablet: 500 mg
- Powder: 250 grams (each level teaspoon dispenses 8.6 grams of Buphenyl)

**VII. References**

1. Buphenyl Prescribing Information. Lake Forest, IL: Horizon Pharma USA, Inc.; March 2021. Available at <https://www.horizontherapeutics.com>. Accessed September 16, 2021.
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
1Q18 annual review: Removed dietary protein restriction requirements as this cannot be confirmed.	11.15.17	02.18
1Q 2019 annual review: no significant changes; references reviewed and updated.	10.25.18	02.19
1Q 2020 annual review: no significant changes; references reviewed and updated.	10.20.19	02.20
1Q 2021 annual review: no significant changes; references reviewed and updated.	10.28.20	02.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	09.16.21	02.22

**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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

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