Clinical Policy: Sodium phenylbutyrate (Buphenyl)

Reference Number: PA.CP.PHAR.208
Effective Date: 01/18
Last Review Date: 01/19

Coding Implications
Revision Log

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
It is the policy of Pennsylvania Health and Wellness that Buphenyl is **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. 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: Refer to PA.CP.PMN.53

II. Continued Approval

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. Prescribed dose does not exceed 20 grams of sodium phenylbutyrate per day;

Approval duration: 12 months

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PMN.53

Background

Description/Mechanism of Action:

Sodium phenylbutyrate is a pro-drug and is rapidly metabolized to phenylacetate. Phenylacetate is a metabolically-active compound that conjugates with glutamine via acetylation to form phenylacetylglutamine. Phenylacetylglutamine then is excreted by the kidneys. On a molar basis, it is comparable to urea (each containing two moles of nitrogen). Therefore, phenylacetylglutamine provides an alternate vehicle for waste nitrogen excretion. Sodium phenylbutyrate is an oral product that provides an alternative vehicle for nitrogen waste removal in patients with UCDs.

III. 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

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
UCD	• 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/m^2/day PO in equally divided doses with each meal or feeding	20 g/day

V. Product Availability

Tablet: 500 mg
Powder: 250 g

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
N/A	

Reviews, Revisions, and Approvals	Date	Approval Date
Removed dietary protein restriction requirements as this cannot be confirmed. References reviewed and updated	02/18	
1Q 2019 annual review: references reviewed and updated	01/19	

References

1. Buphenyl Prescribing Information. Lake Forest, IL: Horizon Pharma USA, Inc.; April 2016. Available at http://www.horizonpharma.com/wp-content/uploads/2016/06/BUPHENYL_PI_April-2016.pdf. Accessed October 25, 2018.