Clinical Policy: Sodium Phenylbutyrate (Buphenyl)
Reference Number: ERX.SPA.21
Effective Date: 07.01.16
Last Review Date: 05/17
Line of Business: Commercial [Prescription Drug Plan] Revision Log

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

Description
Sodium phenylbutyrate (Buphenyl®) is a pro-drug of phenylacetate that conjugates with glutamine to provide an alternate vehicle for waste nitrogen excretion.

FDA approved indication
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 of use: Buphenyl should not be used to manage acute hyperammonemia, which is a medical emergency.

Policy/Criteria
Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 one of the following urea cycle disorders (UCDs) confirmed by enzymatic, biochemical or genetic analysis:
   a. Carbamyl phosphate synthetase (CPS) deficiency;
   b. Ornithine transcarbamylase (OTC) deficiency;
   c. Argininosuccinic acid synthetase (ASS) deficiency;
2. Prescribed by or in consultation with a physician experienced in treating metabolic disorders;
3. Inadequate response to dietary protein restriction or amino acid supplementation alone;
4. Buphenyl will be used in conjunction with dietary protein restriction;
5. Dose does not exceed 20 g/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 (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. Documentation of positive response to therapy;
3. If request is for a dose increase, new dose does not exceed 20 g/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 12 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
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
PBA: phenylbutyrate
UCD: urea cycle disorder

Appendix B: Urea Cycle Disorders

Deficiency of an enzyme in the pathway causes a urea cycle disorder (UCD):

- 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
Urea cycle disorder	• Weight ≤ 20 kg: 450-600 mg/kg/day orally in equally divided doses with each meal or feeding • Weight > 20 kg: 9.9-13 g/m^2/day orally 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.; April 2016. Available at http://www.horizonpharma.com/wp-content/uploads/2016/06/BUPHENYL_PI_April-2016.pdf. Accessed March 15, 2017.
2. Lee B. Urea cycle disorders: Clinical features and diagnosis. In: UpToDate, Waltham, MA Wolters Kluwer Health; 2017. Available at UpToDate.com. Accessed March 15, 2017.
3. Lee B. Urea cycle disorders: Management. In: UpToDate, Waltham, MA Wolters Kluwer Health; 2017. Available at UpToDate.com. Accessed March 15, 2017.
4. Sodium phenylbutyrate: Drug information. In: UpToDate (Lexicomp), Waltham, MA Wolters Kluwer Health; 2017. Available at UpToDate.com. Accessed March 15, 2017.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	05/16	06/16
Specific UCDs are added to initial criteria per PI. Positive response to therapy is added to renewal criteria. List of UCD disorders is added at Appendix B. Duration of approval changed to 6 and 12 months for initial and continued approval respectively. PI updated.	04/17	05/17

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.