

Clinical Policy: Sodium phenylbutyrate (Buphenyl)

Reference Number: CP.PHAR.208

Effective Date: 05/16

Last Review Date: 05/17

[Coding Implications](#)
[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for sodium phenylbutyrate (Buphenyl®).

Policy/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, AS (must meet all):

1. Prescribed by or in consultation with a physician experienced in treating metabolic disorder;
2. Diagnosis of one of the following urea cycle disorders (UCDs) confirmed by enzymatic, biochemical or genetic analysis:
 - a. Carbamylphosphate synthetase (CPS) deficiency;
 - b. Ornithine transcarbamylase (OTC) deficiency;
 - c. Argininosuccinic acid synthetase (AS) deficiency;
3. Inadequate response to dietary protein restriction or amino acid supplementation alone;
4. Buphenyl will be used in conjunction with dietary protein restriction;
5. Prescribed dose does not exceed 20 grams of sodium phenylbutyrate per day.

Approval duration: 6 months

B. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

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

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
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 Centene benefit and documentation supports positive response to therapy;

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to CP.PHAR.57 - Global Biopharm Policy.

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.

Formulations:

Buphenyl is supplied as

- Oral tablets containing 500 mg of sodium phenylbutyrate;
- Oral powder containing 3.0 grams of sodium phenylbutyrate per level teaspoon.

Sodium phenylbutyrate is supplied as

- Oral powder containing 3.0 grams of sodium phenylbutyrate per level teaspoon.

FDA Approved Indications:

Buphenyl is a urea substitute/oral tablet or powder formulation indicated as:

- Adjunctive therapy in the chronic management of patients with urea cycle disorders involving deficiencies of CPS, OTC, or AS.
 - It is indicated in all patients with neonatal-onset deficiency (complete enzymatic deficiency, presenting within the first 28 days of life).
 - It is also indicated in patients with late-onset disease (partial enzymatic deficiency, presenting after the first month of life) who have a history of hyperammonemic encephalopathy.
 - It is important that the diagnosis be made early and treatment initiated immediately to improve survival. Any episode of acute hyperammonemia should be treated as a life-threatening emergency. Buphenyl must be combined with dietary protein restriction and, in some cases, essential amino acid supplementation.

Appendices

Appendix A: Abbreviation Key

AS: argininosuccinate synthetase

CPS: carbamylphosphate synthetase

OTC: ornithine transcarbamylase

UCD: urea cycle disorder

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-

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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
Policy split from CP.PHAR.113 and converted to new template. Added requirement that agent should be prescribed/or ordered in consultation with a physician experienced in treating metabolic disorder; Added dosing restriction per package insert.	03/16	05/16
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

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.

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

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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.

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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.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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