Clinical Policy: Sodium Phenylbutyrate (Buphenyl)
Reference Number: CP.PHAR.208
Effective Date: 05.01.16
Last Review Date: 02.19
Line of Business: Commercial, Medicaid

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 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 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 and CP.PMN.53 for Medicaid or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASL</td>
<td>argininosuccinate lyase</td>
</tr>
<tr>
<td>ASS</td>
<td>argininosuccinate synthetase</td>
</tr>
<tr>
<td>CPSI</td>
<td>carbamyl phosphate synthetase I</td>
</tr>
<tr>
<td>CTLN1</td>
<td>type I citrullinemia</td>
</tr>
<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
</tr>
<tr>
<td>NAGS</td>
<td>N-acetyl glutamate synthetase</td>
</tr>
<tr>
<td>OTC</td>
<td>ornithine transcarbamylase</td>
</tr>
<tr>
<td>UCD</td>
<td>urea cycle disorder</td>
</tr>
</tbody>
</table>

*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

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
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<tbody>
<tr>
<td>UCD</td>
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<tr>
<td></td>
<td>• Weight &lt; 20 kg: 450-600 mg/kg/day PO in equally divided doses with each meal or feeding</td>
<td>20 g/day</td>
</tr>
<tr>
<td></td>
<td>• Weight ≥ 20 kg: 9.9-13 g/m²/day PO in equally divided doses with each meal or feeding</td>
<td></td>
</tr>
</tbody>
</table>

VI. Product Availability

Tablet: 500 mg
Powder: 250 g

VII. References


<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
<td>03.16</td>
<td>05.16</td>
</tr>
<tr>
<td>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.</td>
<td>04.17</td>
<td>05.17</td>
</tr>
<tr>
<td>1Q18 annual review: - Converted to new template. - Removed dietary protein restriction requirements as this cannot be confirmed - References reviewed and updated</td>
<td>11.15.17</td>
<td>02.18</td>
</tr>
<tr>
<td>1Q 2019 annual review: added Commercial line of business; references reviewed and updated</td>
<td>10.25.18</td>
<td>02.19</td>
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</table>

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.

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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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