MEDICAL MUTUAL®

Drug Policy

Policy:	Metabolic Disorders – Phenylbutyrate Products Prior Authorization Policy • Ravicti (glycerol phenylbutyrate) • Buphenyl (sodium phenylbutyrate) • Olpruva (sodium phenylbutyrate) • Pheburane (sodium phenylbutyrate)	**Annual Review Date:** **03/21/2024** **Last Revised Date:** **03/21/2024**

OVERVIEW

Phenylbutyrate products are indicated in combination with dietary management for treatment of **urea cycle disorders**.

- **Sodium phenylbutyrate** is indicated as adjunctive therapy in the chronic management of patients with urea cycle disorders involving deficiencies of carbamylphosphate synthetase, ornithine transcarbamylase, or argininosuccinic acid synthetase.[1]
  - **Buphenyl** and **Pheburane** can be administered orally in pediatric patients weighing less than 20 kg.
  - Buphenyl powder is compatible with feeding tube administration.
  - **Olpruva** is indicated for use in patients weighing ≥ 20 kg and with a body surface area of ≥ 1.2 m^2.

  Limitation of use: Sodium phenylbutyrate products are not indicated for the treatment of acute hyperammonemia, which can be a life-threatening medical emergency that requires rapid acting interventions to reduce plasma ammonia levels.
- **Ravicti** is indicated for chronic management patients with urea cycle disorders that cannot be managed by dietary protein restriction and/or amino acid supplementation alone.[2]
  Limitation of use: Ravicti is not indicated for treatment of acute hyperammonemia in patients with urea cycle disorders. Safety and efficacy for treatment of N-acetylglutamate synthetase deficiency has not been established.

POLICY STATEMENT

This policy involves the use of Ravicti, Buphenyl, Olpruva and Pheburane. Prior authorization is recommended for pharmacy benefit coverage of Ravicti, Buphenyl, Olpruva and Pheburane. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Ravicti, Buphenyl, Olpruva and Pheburane as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Ravicti, Buphenyl, Olpruva, Pheburane be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

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Coverage of Ravicti, Buphenyl, Pheburane or Olpruva is recommended in those who meet the following criteria:

1. **Urea Cycle Disorder**
   Criteria. *Patient must meet the following criteria (A, B, and C):*
   A. The patient is following a protein-restricted diet; AND
   B. The drug is prescribed by or in consultation with a provider specializing in metabolic disorders, a genetic specialist, or a physician experienced in the management of urea cycle disorders; AND
   C. The patient meets one of the following (a *or* b):
      i. If the request is for Buphenyl or Olpruva the patient meets one of the following (1 *or* 2):
         1. Patient has tried generic sodium phenylbutyrate; OR
         2. Patient has tried Pheburane.
      ii. If the request is for Ravicti the patient meets one of the following (1, 2, 3, *or* 4):
         1. Patient has tried generic sodium phenylbutyrate; OR
         2. Patient has tried Pheburane; OR
         3. Patient is on a sodium-restricted diet OR, according to the prescriber, a high sodium diet is contraindicated [documentation required]; OR
         4. Patient is unable to eat soft food and does NOT have a feeding tube (e.g. young infant).

Initial Approval/ Extended Approval.
A) *Initial Approval:* 1 year
B) *Extended Approval:* 1 year

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Ravicti has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Concomitant Therapy with Another Phenylbutyrate Product.** There are no data available to support concomitant use.
   Note: Examples of phenylbutyrate products include sodium phenylbutyrate, Pheburane, and Ravicti.

2. **N-acetylglutamate synthase (NAGS) deficiency.** Safety and efficacy for treatment of N-acetylglutamate synthase (NAGS) deficiency has not been established.

3. **Acute hyperammonemia.** Oral phenylbutyrate products are not indicated for treatment of acute hyperammonemia in patients with UCDs.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:
The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Buphenyl® tablets and powder for oral solution [prescribing information]. Lake Forest, IL: Horizon; May 2021.
2. Ravicti [package insert]. Lake Forest, IL: Horizon Therapeutics, LLC.; Nov 2019
3. Pheburane® oral pellets [prescribing information]. Bryn Mawr, PA; June 2022.
4. Glycerol phenylbutyrate. In: DRUGDEX [online database]. Truven Health Analytics; Greenwood Village, CO. Last updated 06 December 2019. Accessed on 20 January 2020.
5. Diaz GA, Krivitzky LS, Mokhtarani M, et al. Ammonia control and neurocognitive outcome among urea cycle disorder patients treated with glycerol phenylbutyrate. *Hepatology*. 2013;57(6):2171-2179.
6. Hereditary urea cycle abnormality. Medline Plus. A service of the U.S. National Library of Science, National Institutes of Health (NIH). Updated February 18, 2022. Available at: http://www.nlm.nih.gov/medlineplus/ency/article/000372.htm. Accessed on March 4, 2022.
7. Summar M. Urea cycle disorders. National Organization of Rare Disorders [Website]. Available at: https://rarediseases.org/physician-guide/urea-cycle-disorders/. Accessed on March 4, 2022.