PREFERRED SPECIALTY MANAGEMENT POLICY

POLICY: Metabolic Disorders – Phenylbutyrate Products Preferred Specialty Management Policy

- Buphenyl® (sodium phenylbutyrate tablets and powder for oral solution – Horizon, generic)
- Olpruva® (sodium phenylbutyrate for oral suspension – Acer)
- Pheburane® (sodium phenylbutyrate oral pellets – Medunik)
- Ravicti® (glycerol phenylbutyrate oral liquid – Horizon)

REVIEW DATE: 10/23/2024

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Phenylbutyrate products are indicated in combination with dietary management for treatment of **urea cycle disorders (UCDs)**. Of the available agents, only Ravicti does not contain sodium.

- **Sodium phenylbutyrate** products are indicated as adjunctive therapy in the chronic management of adult and pediatric patients with UCDs involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS).[1-3]
  - **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 $\geq$ 20 kg and with a body surface area of $\geq$ 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 the chronic management of patients with UCDs that cannot be managed by dietary protein restriction and/or amino acid supplementation alone.[4]
  Limitation of use: Ravicti is not indicated for treatment of acute hyperammonemia in patients with UCDs. Safety and efficacy for treatment of N-acetylglutamate synthetase deficiency has not been established.

POLICY STATEMENT

This Preferred Specialty Management program has been developed to encourage the use of Preferred Products. For all medications (Preferred and Non-Preferred), the patient is required to meet the respective standard *Prior Authorization Policy* criteria. The program also directs the patient to try one Preferred Product prior to the approval of a Non-Preferred Product. Requests for Non-Preferred Products will also be reviewed using the exception criteria (below). All approvals are provided for the duration noted below. If the patient meets the standard *Metabolic Disorders – Phenylbutyrate Products Prior Authorization Policy* criteria, but has not tried a Preferred Product, a review will be offered for the Preferred Product using the respective standard *Prior Authorization Policy* criteria.

Documentation: Documentation will be required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, prescription claims records, and prescription receipts.

Preferred Products:	generic sodium phenylbutyrate (tablets or powder), Pheburane
Non-Preferred Products:	Brand Buphenyl (tablets or powder), Olpruva, Ravicti

Metabolic Disorders – Phenylbutyrate Products Preferred Specialty Management Policy non-preferred product(s) is(are) covered as medically necessary when the following non-preferred product exception criteria is(are) met. Any other exception is considered not medically necessary.

NON-PREFERRED PRODUCT EXCEPTION CRITERIA

Non-Preferred Product	Exception Criteria
Buphenyl, Olpruva	**1.** Approve for 1 year if the patient meets ALL of the following (A and B): **A)** Patient meets the standard *Metabolic Disorders – Phenylbutyrate Products Prior Authorization Policy* criteria; AND **B)** Patient meets ONE of the following (i or ii): **i.** Patient has tried generic sodium phenylbutyrate; OR **ii.** Patient has tried Pheburane. **2.** If the patient has met criteria 1A but NOT 1B, offer to review for one of the Preferred Products using the standard *Metabolic Disorders – Phenylbutyrate Products Prior Authorization Policy* criteria.
Ravicti	**1.** Approve for 1 year if the patient meets ALL of the following (A and B): **A)** Patient meets the standard *Metabolic Disorders – Phenylbutyrate Products Prior Authorization Policy* criteria; AND **B)** Patient meets ONE of the following (i, ii, iii, or iv): **i.** Patient has tried generic sodium phenylbutyrate; OR **ii.** Patient has tried Pheburane; OR **iii.** Patient is on a sodium-restricted diet OR, according to the prescriber, a high sodium diet is contraindicated **[documentation required]**; OR **iv.** Patient is unable to eat soft food and does NOT have a feeding tube (e.g. young infant) **2.** If the patient has met criteria 1A, but NOT 1B, offer to review for one of the Preferred Products using the standard *Metabolic Disorders – Phenylbutyrate Products Prior Authorization Policy* criteria.

REFERENCES

1. Buphenyl® tablets and powder for oral solution [prescribing information]. Lake Forest, IL: Horizon; July 2022.
2. Olpruva® oral powder for suspension [prescribing information]. Newton, MA: Acer; December 2022.
3. Pheburane® oral pellets [prescribing information]. Bryn Mawr, PA: Medunik; June 2022.
4. Ravicti® oral liquid [prescribing information]. Lake Forest, IL: Horizon; September 2021.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	Effective 01/01/2024	10/18/2023
Selected Revision	**Ravicti:** Requirement for documentation of a sodium-restricted diet or contraindication to a high sodium diet was added.	02/21/2024

Annual Revision	No criteria changes.	10/23/2024