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, generic)

REVIEW DATE: 10/22/2025; selected revision 11/19/2025

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 WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. 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 ≥ 1 year of age and weighing ≥ 7 kg.

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.

Preferred Products:	generic sodium phenylbutyrate (tablets or powder), glycerol phenylbutyrate, 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, 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 has tried ONE of generic sodium phenylbutyrate, glycerol phenylbutyrate, or 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.

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; October 2025.
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
Annual Revision	No criteria changes.	10/22/2025
Selected Revision	Glycerol phenylbutyrate was added as a Preferred product. **Buphenyl, Olpruva**: Added an option of approval for a patient that has tried generic glycerol phenylbutyrate. **Ravicti**: Removed the following exceptions: The patient has tried Pheburane, the patient has tried generic sodium phenylbutyrate, the patient is on a sodium-restricted diet, or according to the prescriber, a high sodium diet is contraindicated, or the patient is unable to eat soft food and does not have a feeding tube. Documentation requirements were also removed. Ravicti now shares the same exception criteria as the other Non-Preferred products.	11/19/2025