CareSource Rxinnovations

PHARMACY POLICY STATEMENT
Indiana Medicaid

DRUG NAME	Ravicti (glycerol phenylbuytyrate)
BENEFIT TYPE	Pharmacy
STATUS	Prior Authorization Required

Ravicti, approved by the FDA in 2013, is indicated for use as a nitrogen-binding agent for chronic management of patients with urea cycle disorders (UCDs) who cannot be managed by dietary protein restriction and/or amino acid supplementation alone. Ravicti must be used with dietary protein restriction and, in some cases, dietary supplements (e.g., essential amino acids, arginine, citrulline, protein-free calorie supplements). It is not indicated for treatment of acute hyperammonemia, and it is not indicated for treatment of N-acetylglutamate synthase (NAGS) deficiency.
The urea cycle clears nitrogen waste from the body as urea. Urea cycle disorders (UCDs) are rare inherited deficiencies in any of the enzymes involved in the urea cycle. The enzyme deficiency makes ureagenesis defective and causes ammonia to accumulate. Hyperammonemia is a marker of inadequate nitrogen detoxification, and its severity strongly correlates with brain damage. Signs and symptoms can present at any age and are mainly neurologic. The only curative option is liver transplant.
Compared to Buphenyl (available as generic sodium phenylbutyrate; NaPB), Ravicti is more palatable and contains no sodium. Both are phenylbutyrate derivatives which act as nitrogen scavengers to remove excess nitrogen and ammonia from the body by an alternate pathway. Other formulations of NaPB are Pheburane and Olpruva.

Ravicti (glycerol phenylbuytyrate) will be considered for coverage when the following criteria are met:

Urea Cycle Disorders (UCDs)

For **initial** authorization:

1. Medication must be prescribed by, or in consultation with a metabolic or genetic specialist; AND
2. Member has a documented diagnosis of a UCD (e.g., involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS)); AND
3. The diagnosis has been confirmed by genetic testing or enzyme activity assay results; AND
4. The member has a history of hyperammonemia (150 µmol/L (>260 µg/dl) or higher in neonates or > 100 µmol/l (175 µg/dl) in older children and adults); AND
5. Ravicti is prescribed as an adjunctive therapy to dietary protein restriction; AND
6. Member has had a trial of sodium phenylbutyrate with documentation of one of the following:
   a) Intolerance due to taste disturbance severe enough to induce vomiting or interfere with adherence
   b) Contraindication such as congestive heart failure, severe renal insufficiency, or a clinical state in which there is sodium retention with edema
   c) Failure to normalize ammonia levels despite optimized dosing; AND
7. Member does NOT have N-acetylglutamate synthase (NAGS) deficiency; AND
8. Ravicti is NOT being used to treat acute hyperammonemia; AND
9. Ravicti is NOT being used concomitantly with any formulation of sodium phenylbutyrate.
10. **Dosage allowed/Quantity limit:** 4.5 to 11.2 mL/m^2/day (5 to 12.4 g/m^2/day) in 3 equally divided doses. The maximum total daily dosage is 17.5 mL (19 g).
    If switching from sodium phenylbutyrate, see prescribing information.
    QL: 525 mL per 30 days

If all the above requirements are met, the medication will be approved for 12 months.

For **reauthorization**:
1. Documentation of ongoing dietary management; AND
2. Chart notes must include documentation of a positive response to therapy such as normalized ammonia levels or reduced number of hyperammonemic crises.

If all the above requirements are met, the medication will be approved for an additional 12 months.

CareSource considers Ravicti (glycerol phenylbuytyrate) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
05/20/2019	New policy for Ravicti created.
01/11/2023	Transferred to new template. Updated and added references. Added confirmatory diagnostics. Split hyperammonemia and UCD into separate bullets and added ammonia values. Removed valproate/haloperidol/steroid restriction; may be acceptable if closely monitored. Added restriction for concomitant sodium phenylbutyrate. Rephrased dietary requirement as adjunctive. Specified dietary treatment as protein restriction. Removed requirement for dietary failure alone. Changed Buphenyl trial to sodium phenylbutyrate and condensed to 3 options. Added max dose and QL Edited renewal criteria.

References:

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3. Ah Mew N, Simpson KL, Gropman AL, et al. Urea Cycle Disorders Overview. 2003 Apr 29 [Updated 2017 Jun 22]. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1217/
4. Häberle J, Burlina A, Chakrapani A, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders: First revision. J Inherit Metab Dis. 2019;42(6):1192-1230. doi:10.1002/jimd.12100
5. Häberle J, Boddaert N, Burlina A, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders. Orphanet J Rare Dis. 2012;7:32. Published 2012 May 29. doi:10.1186/1750-1172-7-32
6. 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. doi:10.1002/hep.26058
7. Smith W, Diaz GA, Lichter-Konecki U, et al. Ammonia control in children ages 2 months through 5 years with urea cycle disorders: comparison of sodium phenylbutyrate and glycerol phenylbutyrate. *J Pediatr*. 2013;162(6):1228-1234.e1. doi:10.1016/j.jpeds.2012.11.084

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