CareSource

PHARMACY POLICY STATEMENT **Marketplace**	
DRUG NAME	Ravicti (glycerol phenylbuytyrate)
BILLING CODE	Must use valid NDC code
BENEFIT TYPE	Pharmacy
SITE OF SERVICE ALLOWED	Home
COVERAGE REQUIREMENTS	Prior Authorization Required (Non-Preferred Product) Alternative preferred product includes Buphenyl QUANTITY LIMIT— 11.2 mL/m^2/day
LIST OF DIAGNOSES CONSIDERED **NOT** MEDICALLY NECESSARY	Click Here

Ravicti (glycerol phenylbuytyrate) is a **non-preferred** product and will only be considered for coverage under the **pharmacy** benefit when the following criteria are met:

Members must be clinically diagnosed with one of the following disease states and meet their individual criteria as stated.

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 documented history of hyperammonemia associated with diagnosis of a UCD as one of the following:
   a) Carbamoyl phosphate synthetase 1 deficiency (CPS1D);
   b) Orthinine transcarbamylase deficiency (OTCD);
   c) Argininosuccinate synthetase deficiency (ASSD/classic citrullinemia/type 1 citrullinemia);
   d) Argininosuccinate lyase deficiency (ASLD/argininosuccinic aciduria);
   e) Arginase deficiency (ARG1D/argininemia); AND
3. Member must currently be treated with, and adherent to dietary protein restriction, and when appropriate, dietary supplements (e.g., essential amino acids, arginine, citrulline, protein-free calorie supplements) as documented in chart notes, or evident in pharmacy claims history (*Note:* Arginine supplementation should be used in all UCDs except ARG1D, citrulline supplementation should be used in OTCD and CPSID); AND
4. Dietary treatment has been insufficient to maintain plasma ammonia levels below the upper limit of normal (ULN), 35 µmol/L, despite treatment adherence; AND
5. Member tried and failed treatment with Buphenyl except one of the following:
   a) Not tolerated Buphenyl due to severe adverse effects;
   b) Has contraindication to Buphenyl (e.g., hypersensitivity, pregnancy, breastfeeding);
   c) Failed to maintain ammonia levels below ULN (35 µmol/L) despite optimized dosing (13 g/m^2/day, max: 20 g/day) and treatment adherence;
   d) Treatment was complicated by a clinical state where there is sodium retention and edema (e.g., congestive heart failure, severe renal insufficiency); AND
6. Member does **not** have ANY of the following:
   a) *N*-acetylglutamate synthase (NAGS) deficiency;
   b) Concomitant use of drugs known to increase ammonia levels (e.g., valproate, haloperidol, systemic corticosteroids); AND
7. Ravicti is NOT being used to treat acute hyperammonemia.
8. **Dosage allowed:** 4.5 to 11.2 mL/m^2/day (5 to 12.4 g/m^2/day).

If member meets all the requirements listed above, the medication will be approved for 12 months.

For **reauthorization**:
1. Member meets all initial authorization requirements; AND
2. Chart notes have been provided that show the member has shown improvement of signs and symptoms of disease (e.g., normalized plasma ammonia levels).

If member meets all the reauthorization requirements above, the medication will be approved for an additional 12 months.

CareSource considers Ravicti (glycerol phenylbuytyrate) not medically necessary for the treatment of the following disease states based on a lack of robust clinical controlled trials showing superior efficacy compared to currently available treatments:

- Byler disease (progressive familial intrahepatic cholestasis 1 (PFIC-1))
- Cirrhosis, hepatic encephalopathy
- Cystic fibrosis
- Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency

DATE	ACTION/DESCRIPTION
05/20/2019	New policy for Ravicti created.
11/17/2021	Annual review, no changes

References:

1. Ravicti [package insert]. Lake Forest, IL: Horizon Therapeutics; 2018 Dec.
2. Buphenyl (sodium phenylbutyrate) [prescribing information]. Deerfield, IL: Horizon Pharma; June 2015.
3. ClinicalTrials.gov. Identifier: NCT00992459. Efficacy and Safety of HPN-100 for the Treatment of Adults With Urea Cycle Disorders. Available: clinicaltrials.gov/ct2/show/NCT00992459.
4. ClinicalTrials.gov. Identifier: NCT01347073. Study of the Safety, Pharmacokinetics and Efficacy of HPN-100, in Pediatric Subjects With Urea Cycle Disorders (UCDs). Available: clinicaltrials.gov/ct2/show/NCT01347073.
5. ClinicalTrials.gov. Identifier: NCT 00999167. A Study of Safety and Efficacy of HPN-100 in Subjects With Cirrhosis and Episodic Hepatic Encephalopathy (HALT-HE). Available: clinicaltrials.gov/ct2/show/NCT00999167.
6. ClinicalTrials.gov. Identifier: NCT01881984. Use of Ravicti™ in Patients With MCAD Deficiency With the 985A>G (K304E) Mutation. Available: clinicaltrials.gov/ct2/show/NCT01881984.
7. Häberle J, et al. Suggested Guidelines for the Diagnosis and Management of Urea Cycle Disorders. Orphanet Journal of Rare Diseases. 2012 Dec;7(1):32. Available: ncbi.nlm.nih.gov/pmc/articles/PMC3488504.
8. National Organization for Rare Diseases. rarediseases.org/physician-guide/urea-cycle-disorders.
9. NIH Rare Diseases Clinical Research Network: Urea Cycle Disorders Consortium. Urea Cycle Treatment Guidelines. Available: rarediseasesnetwork.org/cms/ucdc/healthcare-professionals/treatment-guidelines.
10. Ah Mew N, et al. Urea cycle disorders overview. In: Adam MP, et al., eds. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2019. 2003 Apr 29 [updated 2017 Jun 22].

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