Clinical Policy: Glycerol phenylbutyrate (Ravicti)

Reference Number: PA.CP.PHAR.207
Effective Date: 01/18
Last Review Date: 05/17

Coding Implications
Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness® clinical policy for glycerol phenylbutyrate (Ravicti®).

Policy/Criteria
It is the policy of Pennsylvania Health and Wellness that Ravicti is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Urea Cycle Disorder (must meet all)**:**

1. Prescribed by or in consultation with a physician experienced in treating metabolic disorders;
2. Age ≥ 2 months;
3. Diagnosis of one of the following urea cycle disorders (UCDs) caused by one or more of the following, confirmed by enzymatic, biochemical or genetic analysis:
   a. Carbamyl phosphate synthetase I (CPSI) deficiency;
   b. Ornithine transcarbamylase (OTC) deficiency;
   c. Argininosuccinate synthetase (ASS) deficiency (also known as classic citrullinemia or type I citrullinemia, CTLN1);
   d. Argininosuccinate lyase (ASL) deficiency (also known as argininosuccinic aciduria);
   e. Arginase deficiency;
4. Inadequate response to dietary protein restriction or amino acid supplementation;
5. Ravicti is prescribed to be used in conjunction with dietary protein restriction with or without dietary supplements (e.g., essential amino acids, arginine, citrulline, protein-free calorie supplements);
6. Inadequate response, intolerance or contraindication to sodium phenylbutyrate, unless member has urea cycle disorders with deficiencies involving of any of the following:
   a. Argininosuccinate lyase (ASL);
   b. Arginase deficiency;
7. Prescribed dose does not exceed 17.5 mL (19 g) of Ravicti per day.

Approval duration: 6 months

B. Other diagnoses/indications: Refer to PA.CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

A. Urea Cycle Disorder (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;

3. Prescribed dose does not exceed 17.5 mL (19 g) of Ravicti per day.

Approval duration: 6 months

B. Other diagnoses/indications (1 or 2)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PHAR.57 - Global Biopharm Policy.

Background
Description/Mechanism of Action:
UCDs are inherited deficiencies of enzymes or transporters necessary for the synthesis of urea from ammonia (NH3, NH4+). Absence of these enzymes or transporters results in the accumulation of toxic levels of ammonia in the blood and brain of affected patients. Ravicti is a triglyceride containing 3 molecules of phenylbutyrate (PBA). PAA, the major metabolite of PBA, is the active moiety of Ravicti. PAA conjugates with glutamine (which contains 2 molecules of nitrogen) via acetylation in the liver and kidneys to form PAGN, which is excreted by the kidneys. On a molar basis, PAGN, like urea, contains 2 moles of nitrogen and provides an alternate vehicle for waste nitrogen excretion.

Formulations:
Ravicti is supplied as an oral liquid (1.1 g/mL of glycerol phenylbutyrate) in a multi-use, 25-mL glass bottle.

FDA Approved Indications:
Ravicti is a nitrogen-binding agent/oral liquid formulation is indicated for:
- Chronic management of patients 2 years of age and older 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).

Limitations of use:
- Ravicti is not indicated for the treatment of acute hyperammonemia in patients with UCDs because more rapidly acting interventions are essential to reduce plasma ammonia levels.
- The safety and efficacy of Ravicti for the treatment of N-acetylglutamate synthase (NAGS) deficiency has not been established.

Appendices
Appendix A: Abbreviation Key
ASL: argininosuccinate lyase ASS: argininosuccinate synthetase

CPSI: carbamyl phosphate synthetase I
CTLN1: type I citrullinemia
NAGS: N-acetyl glutamate synthetase
OTC: ornithine transcarbamylase
PBA: phenylbutyrate
UCD: urea cycle disorder

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services

HCPCS Codes	Description
N/A	

Reviews, Revisions, and Approvals	Date	Approval Date

References
1. Ravicti prescribing information. Lake Forest, IL: Horizon Pharma USA, Inc.; September 2016. Available at https://www.rivicti.com Accessed March 15, 2017.
2. Lee B. Urea cycle disorders: Clinical features and diagnosis. In: UpToDate, Waltham, MA Wolters Kluwer Health; 2017. Available at UpToDate.com. Accessed March 15, 2017.
3. Lee B. Urea cycle disorders: Management. In: UpToDate, Waltham, MA Wolters Kluwer Health; 2017. Available at UpToDate.com. Accessed March 15, 2017.