Ravicti (glycerol phenylbutyrate)
Policy Number: C7041-A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DATE
3/2015	6/2019	6/2020
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL/VERSION**
J8499 (NOC)- Prescription drug, oral, non chemotherapeutic, nos	RxPA	Q3 2019 20190828C7041-A

PRODUCTS AFFECTED:
Ravicti (glycerol phenylbutyrate)

DRUG CLASS:
Urea Cycle Disorder - Agents

ROUTE OF ADMINISTRATION:
Oral

PLACE OF SERVICE:
Specialty Pharmacy
The recommendation is that medications in this policy will be for pharmacy benefit coverage and patient self-administered.

AVAILABLE DOSAGE FORMS:
Ravicti LIQD 1.1GM/ML (25ml bottle)

FDA-APPROVED USES:
For long-term management of patients 2 years and older with urea cycle disorders who cannot be managed by dietary protein restriction and/or amino acid supplementation alone.
Ravicti is not indicated for the treatment of acute hyperammonemia in patients with UCD 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

COMPENDIAL APPROVED OFF-LABELED USES: None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS: Chronic hyperammonemia with enzymatic and or genetic diagnosis.

REQUIRED MEDICAL INFORMATION:
A. CHRONIC HYPERAMMONEMIA:

1. Documentation of a diagnosis of chronic hyperammonemia that has been cofirmed with enzymatic and/or genetic diagnosis. Documentation of enzymatic, biohemical or genetic testing confirmation required.
   AND
2. Prescriber attests that patient does NOT have acute hyperammonemia
   AND

3. Prescriber attests that member's condition has failed to be managed with dietary protein restriction and/or amino acid supplementation alone (i.e. essential amino acids, arginine, citrulline, protein-free calorie supplements).
   AND
4. Documented therapeutic failure or ineffectiveness, contraindications, or clinical intolerance to both of the following. sodium phenylbutyrate powder or Buphenyl powder AND Buphenyl tablet
   AND
5. Prescriber attests that Ravicti (glycerol phenylbutyrate) therapy will be used concomitantly with dietary protein restriction and, in some cases, dietary supplements (e.g., essential amino acids, arginine, citrulline, protein-free calorie supplements).

DURATION OF APPROVAL: Initial authorization: 3 months, Continuation of therapy: 6 months

QUANTITY: 525 mL/30 days [maximum total daily dose is 17.5 mL (19 g)]

PRESCRIBER REQUIREMENTS: Prescribed by, or in consultation with, a board-certified geneticist/metabolic specialist or physician experienced in the management of urea cycle disorder. Submit consultation notes if applicable. Prescribed with active involvement of a nutritionist to maximize caloric intake with neutral nitrogen balance

AGE RESTRICTIONS: 2 MONTHS of age or older

GENDER:
Male and female

CONTINUATION OF THERAPY:
A. CHRONIC HYPERAMMONEMIA:

1. Member currently meets ALL initial coverage criteria
   AND
2. Documentation of stabilization or improvement to Ravicti therapy as evaluated by a board-certified geneticist/metabolic specialist or physician experienced in the management of urea cycle disorder, including decreased fasting plasma ammonia levels which are indicative of efficacy.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION: All other uses of Ravicti (glycerol phenylbutyrate oral liquid) that are not an FDA-approved indication or not included in this policy are considered experimental/investigational or not a covered benefit of this policy. This subject to change based on research and medical literature, or at the discretion of Molina Healthcare.

OTHER SPECIAL CONSIDERATIONS:
PREFERRRED: Sodium Phenylbutyrate (Buphenyl)

- Glycerol phenylbutyrate and sodium phenylbutyrate are similar drugs used for the chronic management of adult and pediatric patients with Urea Cycle Disorders (UCDs) that cannot be managed by dietary protein restriction and/or amino acid supplementation alone. The active metabolite for both drugs is Phenylacetate (PAA).
- Buphenyl (available as oral tablets and as a powder for oral, nasogastric, or gastrostomy tube administration) may be administered to pediatric patients over 20 kg; Ravicti (available in an oral liquid) is indicated for patients 2 years and older with UCDs and contraindicated in patients younger than 2 months.
- Notable difference of Buphenyl is the unpleasant smell/taste profile and a higher daily sodium load than the recommended daily allowance (2,400 mg vs 2,300 mg/day) than Ravicti. Ravicti

has no sodium and has a mild smell/taste profile compared to Buphenyl. However, there is no evidence that Ravicti is safer or more efficacious than Buphenyl. Furthermore, Buphenyl has a longer track record of clinical experience.

- There is insufficient evidence that Ravicti is more efficacious than Buphenyl:
  The major study supporting Ravicti's safety and efficacy involved 44 adults who were randomly assigned to receive Buphenyl or Ravicti for two weeks before being switched to the other product for two weeks. Blood testing showed Ravicti was as effective as Buphenyl in controlling ammonia levels.
  Pooled data from the pivotal trial and additional phase II studies suggest that Ravicti may be superior to Buphenyl in the control of ammonia levels. This data, however, is considered preliminary due to the small number of subjects included. [12]

Long-term studies in pediatric patients suggest Ravicti may improve neurocognitive function as defined by the BRIEF (Behavior Rating Inventory of Executive Function) score. This data, however, is considered exploratory and hypothesis-generating due to lack of a control group and no prespecified endpoints related to neurocognitive function

BACKGROUND:

Ravicti is indicated for the management of urea cycle disorders in patients 2 months of age and older who cannot be managed solely by dietary protein restriction and/or amino acid supplementation. Ravicti is a nitrogen- binding agent.

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).

Ravicti is not indicated for treatment of acute hyperammonemia in patients with UCDs.

The safety and efficacy for treatment in N-acetylglutamate synthase (NAGS) deficiency has not been established

APPENDIX: None

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