Urea Cycle Disorder Products
Approved July 2019

Buphenyl® (sodium phenylbutyrate)
Ravicti® (glycerol phenylbutyrate)
Carbaglu® (carglumic acid)

Background:

Sodium phenylbutyrate (Buphenyl) Is indicated as adjunctive therapy in the chronic management of patients with urea cycle disorders (UCDs). It is indicated in all patients with neonatal-onset deficiency (complete enzymatic deficiency, presenting within the first 28 days of life). It is also indicated in patients with late-onset disease (partial enzymatic deficiency, presenting after the first month of life) who have a history of hyperammonemic encephalopathy.

Glycerol phenylbutyrate (Ravicti) is a nitrogen-binding agent indicated for chronic management of adults and pediatric patients with UCDs who cannot be managed by dietary protein restriction and/or amino acid supplementation alone.

Safety and efficacy of Ravicti in the treatment of N-acetylglutamate synthase (NAGS) deficiency has not been established.

Carglumic acid (Carbaglu) is indicated as adjunctive therapy for the treatment of acute hyperammonemia due to acetylglutamate synthase (NAGS) enzyme deficiency with other ammonia lowering therapies (e.g., alternative pathway drugs, hemodialysis, and dietary protein). It is also indicated as maintenance therapy for the treatment of chronic hyperammonemia due to NAGs deficiency and may be used with other ammonia lowering therapies and protein restriction.

Criteria for approval:

1. Diagnosis was confirmed by enzymatic, biochemical, or genetic testing
2. Medication is prescribed by or in consultation with a geneticist or a physician experienced in treating metabolic disorders
3. Weight must be received for drugs that have weight-based dosing. Height and weight must be received for drugs that have dosing based on body surface area.
4. Medication is prescribed in accordance with Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, or national guidelines.

Initial Approval Duration: 6 months

Continuation of therapy

a. Submission of lab results within the past 6 months indicating a normal or improved ammonia level.

A. For Buphenyl® requests

a. Patient has a diagnosis of UCD AND
b. The medication is not being used for the treatment of acute hyperammonemia in patients with UCD AND

c. Medication will be used in conjunction with dietary protein restriction

B. For Ravicti® requests

a. Patient has a diagnosis of UCD AND
b. The medication is not being used for the treatment of acute hyperammonemia in patients with UCD AND
c. Medication will be used in conjunction with dietary protein restriction AND
d. Physician has determined that Ravicti is preferable over sodium phenylbutyrate for ONE of the following reasons:
    i. Patient has a history of intolerance to sodium phenylbutyrate
    ii. Patient has tried sodium phenylbutyrate and had suboptimal control of hyperammonemia
    iii. Patient is currently using Ravicti and has shown a positive response
    iv. There is significant concern for potential complications from excess sodium intake associated with high doses of sodium phenylbutyrate
e. Medication is not being used for the treatment of N-acetylglutamate synthase (NAGS) deficiency

C. For Carbaglu® requests

a. Medication will only be approved for the treatment of hyperammonemia due to NAGS deficiency
b. For treatment of acute hyperammonemia, the medication will be used in conjunction with other ammonia lowering therapies (e.g., alternative pathway drugs, hemodialysis, and dietary protein).

Renewal Approval Duration: 6 months

References:

1. Buphenyl [package insert]. Lake Forest, IL. Horizon Pharma USA, Inc.; Mar 2018.
2. Ravicti [package insert]. Lake Forest, IL. Horizon Pharma USA, Inc.; Dec 2018
3. Carbaglu [package insert]. Lebanon, NJ. Recordati Rare Disease Inc.; Nov 2017
4. Clinical Pharmacology® Gold Standard Series [Internet database]. Tampa FL. Elsevier 2018. Updated periodically
5. Longo N, Holt RJ. Glycerol phenylbutyrate for the maintenance treatment of patients with deficiencies in enzymes of the urea cycle. Expert Opinion on Orphan Drugs, 2017; 5(12):999-1010
6. Pena-Quintana L et al. Profile of sodium phenylbutyrate granules for the treatment of urea-cycle disorders: patient perspectives. Patient Preference and Adherence 2017;11:1489-1496