Pharmacy Policy Bulletin

Title: Carglumic acid (Carbaglu®)

Policy #: Rx.01.10

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for **carglumic acid (Carbaglu®)** as provided under the member's prescription drug benefit.

Description:

Hyperammonemia is a urea cycle disorder due to a deficiency of an enzyme in the pathway that can cause life-threatening metabolic decompensations in infancy. Survivors frequently have severe neurologic injury. Frequent vomiting and poor appetite with food refusal and protein aversion are common in patients with UCD. In newborns, central hyperventilation leading to respiratory alkalosis is an early sign of hyperammonemia. Infants become symptomatic after feeding in which initial signs include somnolence, inability to maintain normal body temperature, poor feeding followed by vomiting lethargy and coma.

N-acetylglutamate synthetase (NAGS) deficiency is a rare, autosomal, recessive genetic disorder in which lack of NAGS enzyme leads to hyperammonemia (excess ammonia). NAGS deficiency is one of several urea cycle disorders.

Carglumic acid (Carbaglu®) is a synthetic structural analogue of N-acetylglutamate (NAG), which is produced from glutamate and acetyl-CoA in a reaction catalyzed by N-acetylglutamate synthase (NAGS), a mitochondrial liver enzyme. NAG acts as an essential allosteric activator of carbamoyl phosphate synthetase 1 (CPS 1) in liver mitochondria. CPS 1 catalyzes the first reaction of the urea cycle, . NAG is the product of NAGS, a mitochondrial liver enzyme. Carglumic acid acts as a CPS 1 activator in NAGS deficiency patients, thereby facilitating ammonia detoxification and urea production by removing the block in the urea cycle

Carglumic Acid (Carbaglu®) is indicated for adjunctive therapy in the treatment of acute hyperammonemia and maintenance therapy of chronic hyperammonemia due to the deficiency of the hepatic enzyme NAGS.

Policy:

Carglumic Acid (Carbaglu®) is approved when there is a diagnosis of N-acetylglutamate synthase (NAGS) deficiency.

Black Box Warning as shown in the drug Prescribing Information:

N/A

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Carbaglu® [package insert]. Lebanon NJ. Recordati Rare Diseases, Inc. December 2019. Available at: https://www.carbaglu.com/wp-content/uploads/2020/01/carbaglu-prescribing-information.pdf. Accessed August 27, 2020.

N-acetylglutamate synthetase deficiency. National organization for rare disorders. Available at: http://rarediseases.org/rare-diseases/n-acetylglutamate-synthetase-deficiency/. Accessed August 27, 2020.

Lee B. Urea cycle disorders: clinical features and diagnosis. UpToDate website. Last updated June 11th, 2019. Available at http://www.uptodate.com/. Accessed August 27, 2020.

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Carbaglu®	Carglumic Acid

Cross References:

Off-Labe Use Rx01.33

Policy Version Number:	11.00
P&T Approval Date:	July 09, 2020
Policy Effective Date:	October 01, 2020
Next Required Review Date:	July 09, 2021