ROCKY MOUNTAIN HEALTH PLANS®
We understand Colorado. We understand you.

UNIFORM PHARMACY PRIOR AUTHORIZATION REQUEST FORM

CONTAINS CONFIDENTIAL PATIENT INFORMATION

Complete this form in its entirety and send to Rocky Mountain Health Plans at 858-357-2538

☐ **Initial Request** ☐ **Renewal** ☐ **Appeal/Redetermination**[1]

☐ **Urgent**[2] ☐ **Non-Urgent**

Requested Drug Name: Carbaglu™ (carglumic acid) – Medicare Part D

Patient Information:	**Prescribing Provider Information:**
Patient Name:	Prescriber Name:
Member/Subscriber Number:	Prescriber Fax:
Policy/Group Number:	Prescriber Phone:
Patient Date of Birth (MM/DD/YYYY):	Prescriber Pager:
Patient Address:	Prescriber Address:
Patient Phone:	Prescriber Office Contact:
Patient Email Address:	Prescriber NPI:
	Prescriber DEA:
Prescription Date:	Prescriber Tax ID:
	Specialty/Facility Name (If applicable):
	Prescriber Email Address:

Prior Authorization Request for Drug Benefit

Patient Diagnosis and ICD Diagnostic Code(s):

Drug(s) Requested (with J-Code, if applicable):

Strength/Route/Frequency:

Unit/Volume of Named Drug(s):

Start Date and Length of Therapy:

Location of Treatment: (e.g. provider office, facility, home health, etc.) including name, Type 2 NPI (if applicable), address and tax ID:

Clinical Criteria for Approval, Including other Pertinent Information to Support the Request, other Medications Tried, Their Name(s), Duration, and Patient Response:

Carbaglu™ (carglumic acid)

Diagnosis (documentation supportive of diagnosis required)

☐ Maintenance therapy for **chronic** hyperammonemia in patients with NAGS (N-acetylglutamate synthase) deficiency
☐ Other (please state):_____

****Note:** Treatment for **acute** hyperammonemia due to NAGS deficiency **does not** require prior authorization

Physician Specialty (diagnosis made by)

☐ Physician experienced in metabolic disorders
☐ Other (please state):_____

☐ For use in clinical trial? (If yes, provide trial name and registration number):			
Drug Name (Brand Name and Scientific Name)/Strength:			
Dose:	Route:	Frequency:	
Quantity:	Number of Refills:		
Product will be delivered to: ☐ Patient's Home ☐Physician Office		Other:	
Prescriber or Authorized Signature:		Date:	
Dispensing Pharmacy Name and Phone Number:			
☐ **Approved** ☐ **Denied**			
If denied, provide reason for denial, and include other potential alternative medications, if applicable, that are found in the formulary of the carrier:			

1. Appeal/redetermination requests can be made for this medication within 60 calendar days from the date on the faxed/written denial notice you received at the time of the original request.

2. A request for prior authorization that if determined in the time allowed for non-urgent requests could seriously jeopardize the life or health of the covered person or the ability of the covered person to regain maximum function, or subject the person to severe pain that cannot be adequately managed without the drug benefit contained in the prior authorization request.

RMHP Formulary Coverage Policy

THIS INFORMATION IS NOT ALL-INCLUSIVE AND IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY

Carbaglu™ (carglumic acid)

CLASSIFICATION

- *N*-acetylglutamate (NAG) analogue

DESCRIPTION

- Carbaglu is a synthetic structural analogue of *N*-acetylglutamate (NAG), which is an essential allosteric activator of carbamoyl phosphate synthetase 1 (CPS 1) in liver mitochondria. CPS 1 is the first enzyme of the urea cycle, which converts ammonia into urea. NAG is the product of N-acetylglutamate synthase (NAGS), an essential mitochondrial enzyme for the function of the urea cycle. Carbaglu acts as a replacement for NAG in patients with NAGS deficiency by activating CPS 1.
- Indicated in pediatric and adult patients, both as an adjunctive therapy for the treatment of acute hyperammonemia, and for maintenance therapy for chronic hyperammonemia, due to the deficiency of the hepatic enzyme *N*-acetylglutamate synthase (NAGS).
- NAGS deficiency is one of the rarest urea cycle disorders. Carbaglu with its unique indication, mechanism of action, and place in therapy appears to provide a specific treatment for patients with NAGS deficiency and improves available treatment options for patients with this extremely rare disease.
- The neonatal-onset phenotype usually reflects complete absence of NAGS activity. Symptoms result primarily from hyperammonemia. If newborns survive the acute hyperammonemic episode, they usually tend to exhibit significant developmental delays, residual neurologic impairments, and seizure disorders. The degree of neurologic impairment in urea cycle disorders has been shown to correlate with peak levels of ammonia and the duration of hyperammonemic coma.
- Late-onset NAGS deficiency has a variable age of onset, and the degree of residual enzyme activity is heterogeneous.
- Two other products, both of which are nitrogen scavengers, are approved for hyperammonemia in urea cycle disorders (not specifically NAGS deficiency): Ammonul® (sodium phenylacetate and sodium benzoate injection) and Buphenyl® (sodium phenylbutyrate for oral administration). Limited data are available on the use of these agents in patients with NAGS deficiency. In clinical practice, other interventions are used in conjunction with nitrogen scavenging therapies to treat hyperammonemia secondary to NAGS deficiency.
- The efficacy of Carbaglu was evaluated in a retrospective review of the clinical course of 23 patients with NAGS deficiency that all began Carbaglu treatment during infancy or childhood. There are no apparent differences in clinical response between adults and pediatric patients with NAGS deficiency treated with Carbaglu; however, data are limited.
- DNA testing is used to confirm a diagnosis of NAGS deficiency.
- Common adverse reactions include infection, vomiting, abdominal pain, pyrexia, tonsillitis, anemia, ear infection, diarrhea, nasopharyngitis, and headache.

FORMULARY COVERAGE

Prior authorization:	Required (See coverage criteria)
Good Health Formulary:	Tier 5
Commercial Formulary:	Tier 4
Medicare Part D coverage:	Tier 5

COVERAGE CRITERIA

Carbaglu™ (carglumic acid) meets the definition of **medical necessity** for all FDA-approved indications not otherwise excluded from Part D, including the following:

- **Acute** hyperammonemia due to deficiency of the hepatic enzyme N-acetylglutamate synthase (NAGS) does not require prior authorization. Given this is a potentially life-threatening situation; access will not be restricted for the initial claim.
- Continued maintenance therapy for chronic hyperammonemia in patients with NAGS deficiency will require prior authorization. Documentation of NAGS deficiency required.

Carbaglu™ (carglumic acid) is considered **experimental** for the following:

- Any indication that is not FDA approved or Compendia supported.

Required Provider Specialty:

- Diagnosis and treatment should be initiated by a physician experienced in metabolic disorders.

DOSAGE/ADMINISTRATION:

Hyperammonemia due to *N*-acetylglutamate synthase (NAGS) deficiency:

- Initial dose for **acute hyperammonemia** is 100mg/kg/day to 250mg/kg/day divided into two to four doses administered immediately before meals or feedings.
- Concomitant administration of other ammonia lowering therapies is recommended.
- Dosing should be titrated based on individual patient plasma ammonia levels and clinical symptoms.
- Maintenance dose for **chronic hyperammonemia** should be titrated to target normal plasma ammonia level for age. Based on limited data in 22 patients receiving maintenance treatment with Carbaglu in a retrospective case series, maintenance doses were usually less than 100 mg/kg/day.
- For adults, the divided dose should be rounded to the nearest 100 mg (i.e., half a Carbaglu tablet).
- Tablet should NOT be swallowed whole or crushed – each 200mg tablet should be dispersed in a minimum of 2.5mL of water immediately before use.
- Mixing a 200mg tablet in 2.5mL of water yields a concentration of 80mg/mL. Shake gently. The tablet does not dissolve completely. To ensure complete delivery of the dose, the mixing container should be rinsed with additional volumes of water and the contents swallowed immediately.
- Use in other foods and liquids has not been studied clinically and therefore is not recommended.
- Preparation for nasogastric tube administration and oral syringe administration is detailed in the product labeling.

PRECAUTIONS:

- **Hyperammonemia:** Prolonged exposure to elevated plasma ammonia levels can rapidly result in injury to the brain or death and should be treated as a life-threatening emergency. Prompt use of all therapies necessary to reduce plasma ammonia levels is essential. This may require dialysis, preferably hemodialysis, to remove a large burden of ammonia.
- **Therapeutic monitoring:** Plasma ammonia levels should be maintained within normal range for age via individual dose adjustment.
- **Nutritional management:** In the initial treatment of NAGS deficiency, protein restriction and hypercaloric intake is recommended to block ammonia generating catabolic pathways. When plasma ammonia levels have normalized, protein intake can usually be increased with the goal of unrestricted protein intake.
- No drug interaction studies have been performed.

Billing/Coding information

Associated HCPCS Codes:

J8499	Prescription drug, oral, non-chemotherapeutic, Not otherwise specified

COST

- AWP (January 2015): Dose is weight-based. Cost of 5 – 200mg tablets is $1,016
- AWP (January 2012): Dose is weight-based. Cost of 5 – 200mg tablets is $798.00

COMMITTEE APPROVAL:

- March 2012

GUIDELINE UPDATE INFORMATION:

January 2012	Coverage Policy created
May 2015	Coverage policy reviewed; AWP updated

REFERENCES:

- DRUGDEX®, accessed 01/12/12, 05/22/15.
- Product Information: CARBAGLU™ tablet, carglumic acid tablet. Orphan Europe SARL. Paris, France. 2010.