Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 02/01/2021**
Policy Number: PA.CP.PHAR.206	**Effective Date: 01/01/2018** **Revision Date: 01/2021**
Policy Name: Carglumic Acid (Carbaglu)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

1Q 2021 annual review: added maximum initial and maintenance dose requirement; references reviewed and updated.

Name of Authorized Individual (Please type or print): **Auren Weinberg, MD**	**Signature of Authorized Individual:** 

Clinical Policy: Carglumic Acid (Carbaglu)

Reference Number: PA.CP.PHAR.206
Effective Date: 01/2018
Last Review Date: 01/2021

Coding Implications
Revision Log

Description
Carglumic acid is a carbamyl phosphate synthetase I (CPSI) activator.

FDA Approved Indication(s)
Carbaglu is indicated for:

- Adjunctive therapy in pediatric and adult patients for the treatment of acute hyperammonemia due to the deficiency of the hepatic enzyme N-acetylglutamate synthase (NAGS). During acute hyperammonemic episodes concomitant administration of Carbaglu with other ammonia lowering therapies such as alternate pathway medications, hemodialysis, and dietary protein restriction are recommended.
- Maintenance therapy in pediatric and adult patients for the treatment of chronic hyperammonemia due to the deficiency of the hepatic enzyme NAGS. During maintenance therapy, the concomitant use of other ammonia lowering therapies and protein restriction may be needed based on plasma ammonia levels.

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

I. Initial Approval Criteria

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

1. Diagnosis of a urea cycle disorder (UCD) caused by NAGS deficiency;
2. NAGS deficiency is confirmed by enzymatic, biochemical, or genetic analysis;
3. Prescribed by or in consultation with a physician experienced in treating metabolic disorders;
4. Dose does not exceed 250 mg per kg per day initially, followed by a maintenance dose of 100 mg per kg per day.

Approval duration: 6 months

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Urea Cycle Disorder: NAGS (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; or
2. Member is responding positively to therapy;
3. If request is for a dose increase, dose does not exceed a maintenance dose of 100 mg per kg per day.

Approval duration: 12 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.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ASL: argininosuccinate lyase
ASS: argininosuccinate synthetase
CPSI: carbamyl phosphate synthetase I
CTLN1: type I citrullinemia
FDA: Food and Drug Administration
NAGS: N-acetyl glutamate synthetase
OTC: ornithine transcarbamylase
UCD: urea cycle disorder

Appendix B: Therapeutic Alternatives

Not applicable.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hyperammonemia, monitor during treatment as prolonged exposure can result in brain injury or death
- Boxed warning(s): none reported

Appendix D: Urea Cycle Disorders

UCDs are caused by a deficiency in any of the below enzymes in the pathway that transforms nitrogen to urea:

- N-acetyl glutamate synthetase (NAGS) deficiency
- Carbamyl phosphate synthetase I (CPSI) deficiency
- Ornithine transcarbamylase (OTC) deficiency
- Argininosuccinate synthetase (ASS) deficiency (also known as classic citrullinemia or type I citrullinemia, CTLN1)
- Argininosuccinate lyase (ASL) deficiency (also known as argininosuccinic aciduria)
- Arginase deficiency

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NAGS	For acute hyperammonemia, initial dose of 100-250 mg/kg/day in 2-4 divided doses, then adjust to maintain normal plasma ammonia levels based on age (typically 10-100 mg/kg/day) For daily maintenance of hyperammonemia, recommended dose is 10-100 mg/kg/day in 2-4 divided doses, then titrate to normal plasma ammonia level for age.	Based on clinical response

V. Product Availability

Tablet for oral suspension: 200 mg

VI. References

1. Carbaglu Prescribing Information. Lebanon, NJ: Recordati Rare Diseases, Inc.; December 2019. Available at https://www.carbaglu.net/. Accessed November 11, 2020.

Reviews, Revisions, and Approvals	Date	Approval Date
Removed requirement for confirmation that Carbaglu is prescribed to treat acute or chronic hyperammonemia as this is characteristic of the condition itself. References reviewed and updated.	02/18	
1Q 2019 annual review: references reviewed and updated.	01/19	
1Q 2020 annual review: added dosing for maintenance hyperammonemia; references reviewed and updated.	01/20	
1Q 2021 annual review: added maximum initial and maintenance dose requirement; references reviewed and updated.	01/21	