Clinical Policy: Carglumic Acid (Carbaglu)

Reference Number: PA.CP.PHAR.206
Effective Date: 01/18
Last Review Date: 01/19

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 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. Prescribed by or in consultation with a physician experienced in treating metabolic disorders;
3. NAGS deficiency is confirmed by enzymatic, biochemical, or genetic analysis;

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.

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

Background

Description/Mechanism of Action:

Carglumic acid 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), a mitochondrial enzyme. Carglumic acid acts as a replacement for NAG in NAGS deficiency patients by activating CPS 1.

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	Based on clinical response

Indication	Dosing Regimen	Maximum Dose
	maintain normal plasma ammonia levels based on age (typically 10-100 mg/kg/day)	

V. Product Availability

Tablet for oral suspension: 200 mg

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
N/A	

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	

References

1. Carbaglu Prescribing Information. Lebanon, NJ: Recordati Rare Diseases, Inc.; November 2017. Available at https://www.carbaglu.net/. Accessed October 25, 2018.