

Clinical Policy: Carglumic Acid (Carbaglu)

Reference Number: CP.PHAR.206

Effective Date: 05.01.16

Last Review Date: 02.21

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Carglumic acid is a carbamyl phosphate synthetase 1 (CPS1) activator.

FDA Approved Indication(s)

Carbaglu is indicated as:

- 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

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation[®] that Carbaglu 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:

Medicaid/HIM – 6 months

Commercial – Length of Benefit

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is

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NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy**A. Urea Cycle Disorder: NAGS (must meet all):**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
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:

Medicaid/HIM – 12 months

Commercial – Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information*Appendix A: Abbreviation/Acronym Key*

ASL: argininosuccinate lyase

ASS: argininosuccinate synthetase

CPS1: carbamyl phosphate synthetase 1

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): none reported
- Boxed warning(s): none reported

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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 1 (CPS1) 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

V. 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

VI. Product Availability

Tablet for oral suspension: 200 mg

VII. 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	P&T Approval Date
Positive response to therapy added to renewal criteria. Duration changed to 6 and 12 months for initial and continued approval, respectively.	04.17	05.17
1Q18 annual review: - Added HIM line of business to criteria. - 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.	11.14.17	02.18

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2019 annual review: added Commercial line of business with length of benefit authorization consistent with criteria for other UCD therapies; references reviewed and updated.	10.25.18	02.19
1Q 2020 annual review: no significant changes; added dosing for maintenance hyperammonemia; references reviewed and updated.	10.21.19	02.20
1Q 2021 annual review: no significant changes; added maximum initial and maintenance dose requirement; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	11.11.20	02.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible

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for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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