Clinical Policy: Carglumic acid (Carbaglu)

Reference Number: CP.PHAR.206
Effective Date: 05/16
Last Review Date: 05/17

Coding Implications
Revision Log

See Important Reminder **at the end of this policy for important regulatory and legal information.**

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for carglumic acid (Carbaglu®)

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that carglumic acid is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Urea Cycle Disorder: N-acetylglutamate synthase deficiency (must meet all):

1. Prescribed by or in consultation with a physician experienced in metabolic disorders;
2. Diagnosis of a urea cycle disorder (UCD) caused by deficiency of the enzyme N-acetylglutamate synthase (NAGS);
3. NAGS deficiency is confirmed by enzymatic or genetic analysis;
4. Carbaglu is prescribed to treat acute or chronic hyperammonemia due to NAGS deficiency.

Approval duration: 6 months

B. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

A. Urea Cycle Disorder: N-acetylglutamate synthase deficiency (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy.

Approval duration: 12 months

B. Other diagnoses/indications (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 CP.PHAR.57 - Global Biopharm Policy**.**

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.

Formulations:
Carbaglu is supplied as scored tablets containing 200 mg of carglumic acid.

FDA-Approved Indications:
Carbaglu is a carbamoyl phosphate synthetase 1 (CPS 1) activator/oral tablet formulation with the following indications:

- Acute hyperammonemia in patients with NAGS deficiency
  - Adjunctive therapy in pediatric and adult patients for the treatment of acute hyperammonemia due to the deficiency of the hepatic enzyme 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 for chronic hyperammonemia in patients with NAGS deficiency
  - 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 reduced or discontinued based on plasma ammonia levels.

Appendices
Appendix A: Abbreviation Key
NAGS: N-acetyl glutamate synthetase
UCD: urea cycle disorder

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
Policy split from CP.PHAR.113 and converted to new template Added requirement that agent should be prescribed/or ordered in consultation with a physician experienced in treating metabolic disorder	03/16	05/16

Reviews, Revisions, and Approvals	Date	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

References

1. Carbaglu prescribing information, Lebanon, NJ: Recordati Rare Diseases, Inc.; November 2015. Available at https://www.carbaglu.net/wp-content/uploads/2016/04/carbaglu-pi-nov-2015-final.pdf. Accessed March 15, 2017.
2. Lee B. Urea cycle disorders: Clinical features and diagnosis. In: UpToDate, Waltham, MA Wolters Kluwer Health; 2017. Available at UpToDate.com. Accessed March 15, 2017.
3. Lee B. Urea cycle disorders: Management. In: UpToDate, Waltham, MA Wolters Kluwer Health; 2017. Available at UpToDate.com. Accessed March 15, 2017.

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

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.