Reference number(s)
2122-A

Specialty Guideline Management carglumic acid-Carbaglu

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Carbaglu	carglumic acid

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indications[1]

Acute Hyperammonemia due to N-acetylglutamate Synthase (NAGS) Deficiency

Carbaglu is indicated in pediatric and adult patients as adjunctive therapy to standard of care for the treatment of acute hyperammonemia due to N-acetylglutamate synthase (NAGS) deficiency. During acute hyperammonemic episodes, concomitant administration of Carbaglu with other ammonia lowering therapies, such as alternate pathway medications, hemodialysis, and dietary protein restriction is recommended.

Chronic Hyperammonemia due to N-acetylglutamate Synthase (NAGS) Deficiency

Carbaglu is indicated in pediatric and adult patients as maintenance therapy for the treatment of chronic hyperammonemia due to NAGS deficiency. During maintenance therapy, the concomitant use of other ammonia lowering therapies and protein restriction may be needed based on plasma ammonia levels.

Acute Hyperammonemia due to Propionic Acidemia (PA) or Methylmalonic Acidemia (MMA)

Carbaglu is indicated in pediatric and adult patients as adjunctive therapy to standard of care for the treatment of acute hyperammonemia due to PA or MMA.

All other indications are considered experimental/investigational and not medically necessary.

Documentation

Submission of the following information is necessary to initiate the prior authorization review:

Initial requests:

- Enzyme assay, biochemical, or genetic testing results supporting diagnosis.
- Lab results documenting baseline plasma ammonia levels.

Continuation of therapy requests:

- Lab results documenting a reduction in plasma ammonia levels from baseline.

Prescriber Specialties

This medication must be prescribed by or in consultation with a physician who specializes in the treatment of enzyme or metabolic disorders.

Coverage Criteria

N-acetylglutamate Synthase (NAGS) Deficiency[1,9]

Authorization of 12 months may be granted for members with a diagnosis of NAGS deficiency when both of the following criteria are met:

- The diagnosis is confirmed by enzymatic, biochemical, or genetic testing.
- The member has elevated plasma ammonia levels at baseline.

Methylmalonic Acidemia[1-4,7-9]

Authorization of 12 months may be granted for members with a diagnosis of methylmalonic acidemia when both of the following criteria are met:

- The diagnosis is confirmed by enzymatic, biochemical, or genetic testing.
- The member has elevated plasma ammonia levels at baseline.

Propionic Acidemia[1-3,5-9]

Authorization of 12 months may be granted for members with a diagnosis of propionic acidemia when both of the following criteria are met:

- The diagnosis is confirmed by enzymatic, biochemical, or genetic testing.
- The member has elevated plasma ammonia levels at baseline.

Continuation of Therapy

N-acetylglutamate Synthase (NAGS) Deficiency, Methylmalonic Acidemia, or Propionic Acidemia

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for NAGS deficiency, methylmalonic acidemia, or propionic acidemia who are experiencing benefit from therapy as evidenced by a decrease in ammonia levels from baseline and disease stability or disease improvement.

References

1. Carbaglu [package insert]. Lebanon, NJ: Recordati Rare Diseases, Inc.; January 2024.
2. Filippi L, Gozzini E, Fiorini P, et al. N-carbamylglutamate in emergency management of hyperammonemia in neonatal acute onset propionic and methylmalonic aciduria. *Neonatology*. 2010;97(3):286-290.
3. Levrat V, Forest I, Fouilhoux A, et al. Carglumic acid: an additional therapy in the treatment of organic acidurias with hyperammonemia. *Orphanet* J Rare Dis. 2008;3:2.
4. Gebhardt B, Vlaho S, Fischer D, et al. N-carbamylglutamate enhances ammonia detoxification in a patient with decompensated methylmalonic aciduria. *Mol Genet Metab.* 2003:79(4):303-304.
5. Gebhardt B, Dittrich S, Parbel S, et al. N-carbamylglutamate protects patients with decompensated propionic aciduria from hyperammonaemia. *J Interit Metab Dis*. 2005;28(2):241-244.
6. Schwahn BC, Pleterse L, Bisset WM, et al. Biochemical efficacy of N-carbamylglutamate in neonatal severe hyperammonaemia due to propionic acidaemia. *Eur J Pediatr.* 2010;169(1):133-134.
7. Valayannopoulos V, Baruteau J, Delgado MB, et. al. Carglumic acid enhances rapid ammonia detoxification in classical organic acidurias with a favourable risk-benefit profile: a retrospective observational study. *Orphanet J Rare Dis.* 2016;11:32.
8. Baumgartner MR, Hörster F, Dionisi-Vici C, et. al. Proposed guidelines for the diagnosis and management of methylmalonic and propionic acidemia. Orphanet J Rare Dis. 2014; 9:130.

9. carglumic acid [package insert]. Deer Park, IL; Eton Pharmaceuticals, Inc.; January 2024.