Reference number(s)
2122-A

SPECIALTY GUIDELINE MANAGEMENT

CARBAGLU (carglumic acid)

POLICY

I. 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.

A. FDA-Approved Indications

1. Acute hyperammonemia in patients with NAGS deficiency
   Carbaglu is indicated as an 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 is recommended.

2. Chronic hyperammonemia in patients with NAGS deficiency
   Carbaglu is indicated for 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.

3. 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.

II. DOCUMENTATION

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

A. Initial requests:
   1. Enzyme assay, biochemical or genetic testing results supporting diagnosis of NAGS deficiency; and
   2. Lab results documenting baseline plasma ammonia levels.
B. Continuation of therapy requests: lab results documenting a reduction in plasma ammonia levels from baseline.

III. CRITERIA FOR INITIAL APPROVAL

A. N-acetylglutamate synthase (NAGS) Deficiency

Authorization of 12 months may be granted for members with diagnosis of NAGS deficiency when both of the following criteria are met:
1. The diagnosis is confirmed by enzymatic, biochemical, or genetic testing.
2. The member has elevated plasma ammonia levels at baseline.

B. Methylmalonic Acidemia
Authorization of 12 months may be granted for members who have a diagnosis of methylmalonic acidemia.

C. Propionic Acidemia
Authorization of 12 months may be granted for members who have a diagnosis of propionic acidemia.

IV. CONTINUATION OF THERAPY

A. N-acetylglutamate synthase (NAGS) Deficiency
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for NAGS deficiency who are experiencing benefit from therapy as evidenced by a decrease in ammonia levels from baseline.

B. Methylmalonic Acidemia or Propionic Acidemia
Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for methylmalonic acidemia or propionic academia who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

V. REFERENCES

1. Carbaglu [package insert]. Lebanon, NJ: Recordati Rare Diseases, Inc.; January 2021.
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.