

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 are recommended.
2. **Maintenance therapy for chronic hyperammonemia in patients with NAGS deficiency**
Carbaglu is indicated for 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.

B. Compendial Uses

1. Methylmalonic acidemia
2. Propionic acidemia

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. **NAGS Deficiency**

Authorization of indefinite approval may be granted for members with diagnosis of NAGS deficiency confirmed by enzymatic or genetic testing.

B. **Methylmalonic Acidemi**

Authorization of indefinite approval may be granted for members who have a diagnosis of methylmalonic acidemia.

C. **Propionic Acidemia**

Authorization of indefinite approval may be granted for members who have a diagnosis of propionic acidemia.

I. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

III. REFERENCES

1. Carbaglu [package insert]. Memphis, TN: Accredo Health Group, Inc.; April 2015.
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 Inher 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.