



Policy Title Carglumic Acid (Carbaglu)

Policy Number

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification and age, gender or quantity restrictions. Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. If the Medical/Pharmacy Reviewer is aware of any new information on the subject of this document, please provide it promptly to the Medical/Pharmacy Policy Department. This information may include new FDA approved indications, withdrawals or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Policy **Carglumic Acid (Carbaglu)** is indicated for Adjunctive therapy in the treatment of acute hyperammonemia and maintenance therapy of chronic hyperammonemia due to the deficiency of the hepatic enzyme N-acetylglutamate synthase (NAGS).

The use of Carglumic Acid (Carbaglu) requires prior authorization (i.e. clinical pharmacy and/or medical director review).

Policy description **Carglumic acid (Carbaglu)** 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 NAGS, a mitochondrial enzyme. Carglumic acid acts as a replacement for NAG in NAGS deficiency patients by activating CPS 1.

Policy guideline inclusion **Carglumic Acid (Carbaglu)** is approved when the following inclusion criteria is met:

- Documentation of a diagnosis of N-acetylglutamate synthase (NAGS) deficiency

Policy guideline exclusion **Carglumic Acid (Carbaglu)** is denied when the following exclusion criteria is present:

- No documentation of a diagnosis of N-acetylglutamate synthase (NAGS) deficiency

Policy List of Applicable Drugs

Brand Name	Generic Name
Carbaglu	Carglumic Acid

Dosing and administration Refer to the specific manufacturer's prescribing information for administration and dosage details for each specific agent.

Policy references Carbaglu [package insert]. Paris, France: Orphan Europe SARL; March 2010.

Caldovic L, Ah Mew NA, Shi D, Morizono H, Yudkoff M, Tuchman M. N-acetylglutamate synthase: structure, function and defects [published online ahead of print February 26, 2010]. *Mol Genet Metab*.2010;100(suppl1):S13-S19.doi: 10.1016/j.ymgme.2010.02.018.

Guffon N, Schiff M, Chellan D, Wermuth B, Haberle J, Vianey-Saban C. Neonatal hyperammonemia: the N-carbamoyl-L-glutamic acid test. *J Pediatr*. 2005;147(2):260-262.

Nordenstrom A, Halldin M, Hallberg B, Alm J. A trial with N-carbamylglutamate may not detect all patients with NAGS deficiency and neonatal onset. *J Inherit Metab Dis*. 2007;30(3):400.

Caldovic L, Morizono H, Daikhin Y, et al. Restoration of ureagenesis in N-acetylglutamate synthase deficiency by N-carbamylglutamate. *J Pediatr*. 2004;145(4):552-554.

Hinnie J, Colombo JP, Wermuth B, Dryburgh FJ. N-acetylglutamate synthetase deficiency responding to carbamylglutamate. *J Inherit Metab Dis*. 1997;20(6):839-840.

Plecko B, Erwa W, Wermuth B. Partial N-acetylglutamate synthetase deficiency in a 13-year-old girl: diagnosis and response to treatment with N-carbamylglutamate. *Eur J Pediatr*. 1998;157(12):996-998.

Morris AA, Richmond SW, Oddie SJ, Pourfarzam M, Worthington V, Leonard JV. N-acetylglutamate synthetase deficiency: favorable experience with carbamylglutamate. *J Inherit Metab Dis*. 1998;21(8):867-868.

Tuchman M, Caldovic L, Daikhin Y, et al. N-carbamylglutamate markedly enhances ureagenesis in N-acetylglutamate deficiency and propionic acidemia as measured by isotopic incorporation and blood biomarkers. *Pediatr Res*. 2008;64(2):213-217.

Gessler P, Buchal P, Schwenk HU, Wermuth B. Favourable long-term outcome after immediate treatment of neonatal hyperammonemia due to N-acetylglutamate synthase deficiency. *Eur J Pediatr*. 2010;169(2):197-199.

Levrat V, Forest I, Fouilhoux A, Acquaviva C, Vianey-Saban C, Guffon N. Carglumic acid: an additional therapy in the treatment of organic acidurias with hyperammonemia? *Orphanet J Rare Dis*. 2008;3:2. doi: 10.1186/1750-1172-3-2.

Schwahn BC, Pieterse L, Bisset WM, Galloway PG, Robinson PH. Biochemical efficacy of N-carbamylglutamate in neonatal severe hyperammonaemia due to propionic acidaemia. *Eur J Pediatr*. 2010;169(1):133-134.

Gebhardt B, Dittrich S, Parbel S, Vlaho S, Matsika O, Bohles H. N-carbamylglutamate protects patients with decompensated propionic aciduria from hyperammonaemia. *J Inherit Metab Dis*. 2005;28(2):241-244.

Jones S, Reed CA, Vijay S, Walter JH, Morris AA. N-carbamylglutamate for neonatal hyperammonaemia in propionic acidaemia [published online ahead of print February 21, 2008]. *J Inherit Metab Dis*. doi: 10.1007/s10545-008-0777-1.

Drug details: Carbaglu (NDA 022562). Drugs@FDA Web site. <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails>. Published March 18, 2010. Accessed April 6, 2010.

FDA advisory committee backs approval of orphan drug without controlled clinical trial. Available at www.thepinksheet.com. Accessed February 28, 2011.

Policy link to related policies

Version effective date 07/01/2011

The Policy Bulletins on this web site were developed to assist Independence Blue Cross (IBC) in administering the provisions of the respective benefit programs, and do not constitute a contract. If you are an IBC member, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. IBC does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of IBC. If you have a specific medical condition, please consult with your doctor. IBC reserves the right at any time to change or update its Policy Bulletins. © 2011 Independence Blue Cross. All Rights Reserved.

Independence Blue Cross is an independent licensee of the Blue Cross and Blue Shield Association
