Clinical Policy: Carglumic Acid (Carbaglu)

Reference Number: PA.CP.PHAR.206
Effective Date: 01/2018
Last Review Date: 01/2026

Description
Carglumic acid is a carbamyl phosphate synthetase I (CPSI) activator.

FDA Approved Indication(s)
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.
- Maintenance therapy for the treatment of chronic hyperammonemia due to NAGS deficiency.
- Adjunctive therapy to standard of care for the treatment of acute hyperammonemia due to propionic acidemia (PA) or methylmalonic acidemia (MMA).

Policy/Criteria
It is the policy of PA Health & Wellness that carglumic acid and Carbaglu are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Urea Cycle Disorder: NAGS (must meet all):

1. Diagnosis of a urea cycle disorder (UCD) caused by NAGS deficiency;
2. NAGS deficiency is confirmed by enzymatic, biochemical, or genetic analysis;
3. Prescribed by or in consultation with a physician experienced in treating metabolic disorders;
4. If request is for treatment of acute hyperammonemia, prescribed as adjunctive therapy with other ammonia lowering therapies (e.g., alternative pathway drugs, hemodialysis, and dietary protein restriction);
5. If request is for brand Carbaglu, member must use generic carglumic acid, unless contraindicated or clinically significant adverse effects are experienced;
6. Documentation of member's current weight (in kg);
7. Dose does not exceed 250 mg per kg per day initially, followed by a maintenance dose of 100 mg per kg per day.

Approval duration: 12 months

B. Organic Acidemias: Propionic Acidemia, Methylmalonic Acidemia (must meet all):

1. Diagnosis of PA or MMA;
2. Diagnosis is confirmed by urine organic acid, genetic, or enzymatic analysis;
3. Prescribed by or in consultation with a physician experienced in treating metabolic disorders;
4. Plasma ammonia level ≥ 70 micromol/L despite standard of care treatment (e.g., intravenous hydration and nutritional support);
5. Prescribed as adjunctive therapy to standard of care (e.g., intravenous glucose, insulin, L-carnitine, protein restriction, dialysis);
6. If request is for brand Carbaglu, member must use generic carglumic acid, unless contraindicated or clinically significant adverse effects are experienced;

7. Documentation of member's current weight (in kg);
8. If member's weight is > 15 kg, documentation of member's current body surface area (BSA);
9. Dose does not exceed one of the following (a or b):
   a. Weight ≤ 15 kg: 150 mg/kg/day for 7 days;
   b. Weight > 15 kg: 3.3 g/m^2/day for 7 days.

Approval duration: 7 days

C. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Urea Cycle Disorder: NAGS (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.PHARM.01) applies; or
2. Member is responding positively to therapy;
3. If request is for brand Carbaglu, member must use generic carglumic acid, unless contraindicated or clinically significant adverse effects are experienced;
4. Documentation of member's current weight (in kg);
5. If request is for a dose increase, dose does not exceed a maintenance dose of 100 mg per kg per day.

Approval duration: 12 months

B. Organic Acidemias: Propionic Acidemia, Methylmalonic Acidemia:

1. Re-authorization is not permitted. Members must meet the initial approval criteria.

Approval duration: Not applicable

C. Other diagnoses/indications (1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.PHARM.01) applies;

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ASL: argininosuccinate lyase
ASS: argininosuccinate synthetase
BSA: body surface area
CPS1: carbamyl phosphate synthetase 1
CTLN1: type I citrullinemia
FDA: Food and Drug Administration
MMA: methylmalonic acidemia
NAGS: N-acetyl glutamate synthetase
OTC: ornithine transcarbamylase
PA: propionic acidemia
UCD: urea cycle disorder

Appendix B: Therapeutic Alternatives

Not applicable.

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): none reported
- Boxed warning(s): none reported

Appendix D: Urea Cycle Disorders
UCDs are caused by a deficiency in any of the below enzymes in the pathway that transforms nitrogen to urea:
- N-acetyl glutamate synthetase (NAGS) deficiency
- Carbamyl phosphate synthetase I (CPSI) deficiency
- Ornithine transcarbamylase (OTC) deficiency
- Argininosuccinate synthetase (ASS) deficiency (also known as classic citrullinemia or type I citrullinemia, CTLN1)
- Argininosuccinate lyase (ASL) deficiency (also known as argininosuccinic aciduria)
- Arginase deficiency

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NAGS	For acute hyperammonemia, initial dose of 100-250 mg/kg/day in 2-4 divided doses (round to the nearest 100 mg (i.e., half tablet). During acute hyperammonemic episodes, administer Carbaglu with other ammonia lowering therapies such as alternate pathway medications, hemodialysis, and protein restriction. For daily maintenance of hyperammonemia, recommended dose is 10-100 mg/kg/day in 2-4 divided doses (round to the nearest 100 mg (i.e., half tablet). During maintenance therapy, the concomitant use of other ammonia lowering therapies and protein restriction may be needed based on plasma ammonia levels. Titrate dosage to maintain the plasma ammonia level within the normal range for the patient's age, taking into consideration their clinical condition (e.g., nutritional requirements, protein intake, growth parameters, etc.).	Based on clinical response
PA, MMA	150 mg/kg/day for patients ≤ 15 kg 3.3 g/m^2/day for patients > 15 kg Divide the daily dosage into two equal doses and round up to the next multiple of 50 mg; administer each dose 12 hours apart.	See dosing regimen

Indication	Dosing Regimen	Maximum Dose
	Continue treatment until ammonia level is less than 50 micromol/L and for a maximum duration of 7 days. During acute hyperammonemic episodes, administer Carbaglu with other ammonia lowering therapies, such as intravenous glucose, insulin, L-carnitine, protein restriction, and dialysis.	

V. Product Availability

Tablet for oral suspension: 200 mg

VI. References

1. Carbaglu Prescribing Information. Lebanon, NJ: Recordati Rare Diseases, Inc.; January 2024. Available at https://www.carbaglu.net/. Accessed October 22, 2025.
2. Forny P, Hörster F, Ballhausen D, et al. Guidelines for the diagnosis and management of methylmalonic acidaemia and propionic acidaemia: First revision. J Inherit Metab Dis. 2021 May; 44(3): 566-592.

Reviews, Revisions, and Approvals	Date
Removed requirement for confirmation that Carbaglu is prescribed to treat acute or chronic hyperammonemia as this is characteristic of the condition itself. References reviewed and updated.	02/2018
1Q 2019 annual review: references reviewed and updated.	01/2019
1Q 2020 annual review: added dosing for maintenance hyperammonemia; references reviewed and updated.	01/2020
1Q 2021 annual review: added maximum initial and maintenance dose requirement; references reviewed and updated.	01/2021
Added new indication as adjunctive therapy for acute hyperammonemia due to PA or MMA.	04/2021
1Q 2022 annual review: updated dosing in Section V; references reviewed and updated.	01/2022
1Q 2023 annual review: added generic redirection for brand requests; references reviewed and updated.	01/2023
1Q 2024 annual review: no significant changes; for PA and MMA added examples of adjunctive therapy to standard of care; references reviewed and updated.	01/2024
1Q 2025 annual review: for NAGS deficiency, added requirement if request is for treatment of acute hyperammonemia, prescribed as adjunctive therapy with other ammonia lowering therapies (e.g., alternative pathway drugs, hemodialysis, and dietary protein restriction); to support weight based dosing added requirement for documentation of member's current weight and/or BSA; references reviewed and updated.	01/2025
1Q 2026 annual review: no significant changes; for UCD initial approval revised from 6 to 12 months; references reviewed and updated.	01/2026