

Carbaglu[®]
(carglumic acid) tablets for oral suspension
200mg

Ordering CARBAGLU

for Acute and Chronic
Hyperammonemia
due to **NAGS Deficiency**



& Acute Hyperammonemia
due to **Propionic Acidemia**
or **Methylmalonic Acidemia**

INDICATIONS AND USAGE

CARBAGLU[®] (carglumic acid) tablets for oral suspension 200mg is a carbamoyl phosphate synthetase 1 (CPS 1) activator 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 N-acetylglutamate synthase (NAGS) deficiency.
- Adjunctive therapy to standard of care for the treatment of acute hyperammonemia due to propionic acidemia (PA) or methylmalonic acidemia (MMA).

IMPORTANT SAFETY INFORMATION

- **NAGS deficiency:** Most common adverse reactions ($\geq 13\%$) are: vomiting, abdominal pain, pyrexia, tonsillitis, anemia, diarrhea, ear infection, infections, nasopharyngitis, hemoglobin decreased, and headache.
- **PA and MMA:** Most common adverse reactions ($\geq 5\%$) are neutropenia, anemia, vomiting, electrolyte imbalance, decreased appetite, hypoglycemia, lethargy/stupor, encephalopathy and pancreatitis/lipase increased.

NAGS Deficiency: Treating Hyperammonemia with CARBAGLU®

Treatment Guidelines

- Initiate CARBAGLU as soon as the diagnosis of NAGS deficiency is suspected, which may be as soon as at birth.
- CARBAGLU treatment should be managed by a physician and medical team experienced in metabolic disorders.
- During acute hyperammonemic episodes, administer CARBAGLU with other ammonia lowering therapies, such as alternate pathway medications, hemodialysis, and protein restriction.
- During maintenance therapy, the concomitant use of other ammonia lowering therapies and protein restriction may be needed based on plasma ammonia levels. Closely monitor plasma ammonia levels. Titrate the CARBAGLU 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.).

Preparation and Administration

- Disperse CARBAGLU tablets in water. Do not swallow whole or crushed. Mix each whole or partial 200 mg tablet in a minimum of 2.5 mL of water.
- CARBAGLU can be taken orally via a cup or oral syringe or via a nasogastric or gastrostomy tube.

IMPORTANT SAFETY INFORMATION

- Most common adverse reactions ($\geq 13\%$) are: vomiting, abdominal pain, pyrexia, tonsillitis, anemia, diarrhea, ear infection, infections, nasopharyngitis, hemoglobin decreased, and headache.
- **To report SUSPECTED ADVERSE REACTIONS, contact Recordati Rare Diseases Inc. at 1-888-575-8344, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**
- If CARBAGLU is administered during pregnancy to women with NAGS deficiency, health care providers should report CARBAGLU exposure to the pregnancy pharmacovigilance program by calling 1-888-575-8344.

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NAGS Deficiency: Treating Hyperammonemia with CARBAGLU®

NAGS Deficiency Dosing and Administration

Patient Type	Recommended Dose	Frequency & Timing	Dose Titration - Yes/No
Acute Hyperammonemia Pediatric & Adult Patients	100 mg/kg/day to 250 mg/kg/day	Divide total daily dose into 2 to 4 doses to be given immediately before meals or feedings. Round dose to the nearest 100 mg (i.e., half of a CARBAGLU tablet).	No.
Maintenance for Chronic Hyperammonemia Pediatric & Adult Patients	10 mg/kg/day to 100 mg/kg/day	Divide total daily dose into 2 to 4 doses to be given immediately before meals or feedings. Round dose to the nearest 100 mg (i.e., half of a CARBAGLU tablet).	Yes. Titrate to maintain the plasma ammonia level within the normal range for the patient's age, taking into consideration their clinical condition.

NAGS Deficiency Sample Dosing Guides to Help with Emergency Ordering

Patient – Weight	Acute initial dose (min/max)	Total daily mg	# of 200-mg tablets per day	3-day supply for acute hyperammonemic episode # of 60-tablet and/or 5-tablet bottles
For example: Neonate 4 kg (8.82 lbs)	100 mg/kg	400 mg	2 tablets	2 bottles of 5 tablets
	250 mg/kg	1000 mg	5 tablets	3 bottles of 5 tablets
For example: 4-year-old 16 kg (35.27 lbs)	100 mg/kg	1600 mg	8 tablets	5 bottles of 5 tablets
	250 mg/kg	4000 mg	20 tablets	1 bottle of 60 tablets
For example: Adult 68 kg (149.91 lbs)	100 mg/kg	6800 mg	34 tablets	1 bottle of 60 tablets and 9 bottles of 5 tablets
	250 mg/kg	17000 mg	85 tablets	4 bottles of 60 tablets and 3 bottles of 5 tablets

IMPORTANT SAFETY INFORMATION

- Contraindications: None.

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PA or MMA: Treating Acute Hyperammonemia with CARBAGLU®

Treatment Guidelines

- Initiate CARBAGLU for the treatment of acute hyperammonemia in patients with a suspected or confirmed diagnosis of propionic acidemia (PA) or methylmalonic acidemia (MMA).
- During acute hyperammonemic episodes, administer CARBAGLU with other ammonia lowering therapies, such as intravenous glucose, insulin, L-carnitine, protein restriction, and dialysis.

Preparation and Administration

- Disperse CARBAGLU tablets in water. Do not swallow whole or crushed. Mix each whole or partial 200 mg tablet in a minimum of 2.5 mL of water.
- CARBAGLU can be taken orally via a cup or oral syringe or via a nasogastric or gastrostomy tube.

IMPORTANT SAFETY INFORMATION

- Most common adverse reactions ($\geq 5\%$) are neutropenia, anemia, vomiting, electrolyte imbalance, decreased appetite, hypoglycemia, lethargy/stupor, encephalopathy and pancreatitis/lipase increased.
- **To report SUSPECTED ADVERSE REACTIONS, contact Recordati Rare Diseases Inc. at 1-888-575-8344, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**

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PA or MMA: Treating Acute Hyperammonemia with CARBAGLU®

PA or MMA Dosing and Administration

Patient Type	Recommended Dose	Frequency & Timing	Duration
Acute Hyperammonemia Pediatric & Adult Patients	150 mg/kg/day for patients ≤15 kg 3.3 g/m ² /day for patients >15 kg	Divide the daily dosage into 2 equal doses. Administer doses 12 hours apart. Round up dose to the next multiple of 50 mg (i.e., one quarter of a CARBAGLU tablet).	Continue CARBAGLU treatment until the patient's ammonia level is <50 micromol/L and for a maximum duration of 7 days.

PA or MMA Sample Dosing Guides to Help with Emergency Ordering

Patient – Weight or body surface area	Acute dose	Total daily mg	# of 200-mg tablets per day	3-day supply for acute hyperammonemic episode # of 60-tablet and/or 5-tablet bottles
For example: Neonate 4 kg (8.82 lbs)	150 mg/kg/day	600 mg	3 tablets	2 bottles of 5 tablets
For example: 4-year-old 16 kg (35.27 lbs) 102 cm (40.16 in)	3.3 g/m ² /day	2221.89 mg*†	11.5 tablets	7 bottles of 5 tablets
For example: Adult 68 kg (149.91 lbs) 175 cm (68.90 in)	3.3 g/m ² /day	6000 mg*	30 tablets	1 bottle of 60 tablets and 6 bottles of 5 tablets

*Formula used: Mosteller body surface area (BSA). Online BSA calculators are available. Correlation between formulas is generally high.

†2300 mg when divided into two doses and rounded up to the nearest 50 mg.

IMPORTANT SAFETY INFORMATION

- Contraindications: None.

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Exclusive Distribution Through Accredo

Representatives at Accredo Health Group, Inc. are committed to helping you and your patients through the ordering process. CARBAGLU is not available in retail pharmacies.

Patient Home Delivery

1. Download the CARBAGLU Prescription & Enrollment Form from the Accredo website (www.accredo.com).
2. Complete the CARBAGLU Prescription & Enrollment Form and fax it to the Accredo specialty pharmacy department at 1-888-454-8488.
3. A CARBAGLU specialty pharmacy representative may call to verify information and determine next steps. In some cases, prior authorization may be necessary.
4. Questions? Contact a CARBAGLU specialty pharmacy representative at 1-888-454-8860.

Hospital Orders – Emergency or Inpatient

1. Alert your hospital pharmacy that your patient requires CARBAGLU. Send an order for CARBAGLU to your hospital pharmacy and specify whether it is a STAT order (required in 6 hours or less*).
2. Ask your hospital pharmacy to call the wholesale department at Accredo at 1-877-900-9223 to place the order.
3. The wholesale department at Accredo will work with your hospital pharmacy to obtain payment information, establish shipping timelines, and verify the delivery address.
4. The Accredo specialty pharmacy team will follow up in 1-2 days to help set up patient home delivery of CARBAGLU, if applicable.

*Delivery time frame is weather dependent and is not guaranteed.

Keep a 5-count bottle of CARBAGLU in stock to allow for immediate treatment.

Return policy: All new orders of 5-count unopened bottles of CARBAGLU can be returned for credit any time prior to the expiration date or up to 12 months past the expiration date.†

†Not applicable for CARBAGLU 60-count bottles. Product shipped as an emergency or STAT order is not eligible for credit unless damaged in transit. This policy covers products purchased after July 1, 2019. Unopened bottles have up to a 3-year expiration date and must be refrigerated. Other terms and conditions may apply.

Questions? Contact a CARBAGLU specialty pharmacy representative at 1-888-454-8860.

Financial Assistance Programs

For patients experiencing financial hardship, Recordati Rare Diseases Inc. supports a Patient Assistance Program and a Co-Pay Assistance Program, administered by Accredo. For more information, call: 1-888-454-8860.

FOR MORE INFORMATION ABOUT CARBAGLU, CALL 1-888-454-8860

**Be prepared for patients who may need CARBAGLU in emergency situations.
Keep a 5-count bottle of CARBAGLU in stock to allow for immediate treatment.**



Unopened 5-count bottles of CARBAGLU can be returned for credit any time prior to the expiration date or up to 12 months past the expiration date.*

*Not applicable for CARBAGLU 60-count bottles. Product shipped as an emergency or STAT order is not eligible for credit unless damaged in transit. This policy covers products purchased after July 1, 2019. Unopened bottles have up to a 3-year expiration date and must be refrigerated. Other terms and conditions may apply.

**Please see accompanying Full Prescribing Information,
including Instructions for Use.**

For more information, visit www.CARBAGLU.com

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