RATIONALE FOR INCLUSION IN PA PROGRAM

Background
Carbaglu (carglumic acid) is used to treat a condition that results in too much ammonia in the blood. The condition, N-acetylglutamate synthase or NAGS deficiency, is an extremely rare, genetic disorder that can be present in babies soon after birth. NAGS deficiency causes a partial or complete lack of the liver enzyme called N-acetylglutamate synthase (NAG). NAGS helps to break down and remove nitrogen from the body. When there is not enough NAG nitrogen builds up in the blood in the form of ammonia. The resulting elevated levels of ammonia (hyperammonemia) can be fatal if it is not detected and treated rapidly. Carbaglu treats the root cause of hyperammonemia by acting as a replacement for NAG in the urea cycle of patients with NAGS deficiency (1).

Regulatory Status
FDA-approved indication: Carbaglu (carglumic acid) is a carbamoyl phosphate synthetase 1 (CPS 1) activator indicated as: (1)
- Adjunctive therapy for the treatment of acute hyperammonemia due to the deficiency of the hepatic enzyme N-acetylglutamate synthase (NAGS).
- Maintenance therapy for the treatment of chronic hyperammonemia due to the deficiency of the hepatic enzyme N-acetylglutamate synthase (NAGS).

Management of hyperammonemia due to NAGS deficiency should be done in coordination with medical personnel experienced in metabolic disorders. Ongoing monitoring of plasma ammonia levels, neurological status, laboratory tests and clinical responses in patients receiving Carbaglu is crucial to assess patient response to treatment. Genetic analysis can be used to confirm the diagnosis of NAGS deficiency (1).

Summary
NAGS deficiency is a rare, autosomal recessive disorder characterized by complete or partial lack of the hepatic enzyme N-acetylglutamate synthase (NAGS). NAGS is one of several enzymes that help break down and remove nitrogen from the body, a process called the urea cycle. Carbaglu, a structural analogue of N-acetyl glutamate (NAG), treats the root cause of hyperammonemia by acting as a replacement for NAG in the urea cycle of patients with NAGS deficiency (1).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Carbaglu while maintaining optimal therapeutic outcomes.
References