SmartPA Criteria Proposal

Drug/Drug Class:	Carbamoyl Phosphate Synthetase 1 Activators PDL Edit
First Implementation Date:	January 12, 2023
Revised Date:	January 19, 2023
Prepared For:	MO HealthNet
Prepared By:	MO HealthNet/Conduent
Criteria Status:	☐Existing Criteria ☒Revision of Existing Criteria ☐New Criteria

Executive Summary

Purpose: The MO HealthNet Pharmacy Program will implement a state-specific preferred drug list.

Why Issue Selected: The urea cycle is a metabolic pathway that is ultimately responsible for converting nitrogen to urea for excretion from the body. Any defect in this complex pathway is considered a Urea Cycle Disorder (UCD). Defects in this cycle can cause a buildup of ammonia in the bloodstream, which can be extremely toxic to the central nervous system. Untreated hyperammonemia can cause coma, permanent brain damage, and possibly death. UCDs are estimated to affect approximately 1 in 35,000 livebirths.

There are multiple types of UCDs, all of which involve deficiencies of one of the six specific enzymes or two transporters normally present in the urea cycle. One of these enzymes, N-acetylglutamate synthase (NAGS), catalyzes the formation of N-acetylglutamate (NAG), an activator of carbamyl phosphate synthetase 1 (CPS1), the first enzyme of the urea cycle. NAGS deficiency, an autosomal recessive genetic disorder, was first described in 1981 and is the rarest of the UCDs, affecting approximately 1 in 2,000,000 livebirths. Most patients are diagnosed as neonates using measurements of liver NAGS enzyme activity after displaying symptoms of poor feeding, lethargy, and seizures.

Carbaglu® (carglumic acid) is a synthetic analog of NAG. It activates CPS1, which allows for normal function of the urea cycle for the conversion of nitrogen to urea. It was first approved by the FDA in 2010 for the adjunctive therapy to standard of care for the treatment of acute hyperammonemia due to N-acetylglutamate synthase (NAGS) deficiency as well as maintenance therapy for the treatment of chronic hyperammonemia due to NAGS deficiency. Carbaglu can also be utilized as adjunctive therapy to standard care for the treatment of acute hyperammonemia due to two types of organic acidemias - propionic acidemia (PA) and methylmalonic acidemia (MMA).

Total program savings for the PDL classes will be regularly reviewed.

Program-Specific Information:

Preferred Agents	Non-Preferred Agents
• Carglumic acid **(Eton Pharmaceuticals Mft)**	• Carbaglu® • **Carglumic acid (Non-Eton Pharmaceuticals Mft)**

Type of Criteria:	☐ **Increased risk of ADE**	☒ **Preferred Drug List**
	☐ **Appropriate Indications**	☐ **Clinical Edit**
Data Sources:	☐ **Only Administrative Databases**	☒ **Databases + Prescriber-Supplied**

Setting & Population

- Drug class for review: Carbamoyl Phosphate Synthetase 1 Activators
- Age range: All appropriate MO HealthNet participants

Approval Criteria

- Claim is for a preferred agent **OR**
- Claim for non-preferred agents:
  - Failure to achieve desired therapeutic outcomes with trial on 1 or more preferred agents:
    - Documented trial period for preferred agents **OR**
    - Documented ADE/ADR to preferred agents **AND**
  - Clinical consultant review for medical necessity

Denial Criteria

- Lack of adequate trial on required preferred agents
- Therapy will be denied if all approval criteria are not met

Required Documentation

Laboratory Results:	☐	Progress Notes:	☐
MedWatch Form:	☐	Other:	☐

Disposition of Edit

Denial: Exception Code “0160” (Preferred Drug List)
Rule Type: PDL

Default Approval Period

1 year

References

- CARBAGLU (carglumic acid) [package insert]. Lebanon, NJ: Recordati Rare Diseases Inc.; January 2021.
- Kenneson A, Singh RH. Presentation and management of N-acetylglutamate synthase deficiency: a review of the literature. Orphanet J Rare Dis. 2020 Oct 9;15(1):279. doi: 10.1186/s13023-020-01560-z. PMID: 33036647; PMCID: PMC7545900.
- Stone WL, Basit H, Jaishankar GB. Urea Cycle Disorders. [Updated 2022 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482363/. Accessed November 2022.
- USPDI, Micromedex; 2022.

- Facts and Comparisons eAnswers (online); 2022 Clinical Drug Information, LLC.