SmartPA Criteria Proposal

Drug/Drug Class:	Urea Cycle Disorder Agents PDL Edit
First Implementation Date:	January 12, 2023
Proposed Date:	October 17, 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. Carglumic acid is an analog of N-acetyl glutamate and is indicated for the treatment of acute hyperammonemia due to N-acetylglutamate synthase (NAGS) deficiency, propionic acidemia (PA), or methylmalonic acidemia (MMA), as well as for the treatment of chronic hyperammonemia due to NAGS deficiency. Glycerol phenylbutyrate (Ravicti®) and sodium phenylbutyrate are nitrogen scavengers that lower the amount of nitrogen changed into ammonia. Both these agents are used in the chronic management of UCDs and are not indicated for the treatment of acute hyperammonemia. Sodium phenylbutyrate is the only agent available in multiple formulations: tablets, powder (Buphenyl®), oral pellets (Pheburane®), and oral granules for reconstitution (Olpruva™).

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

Program-Specific Information:

Preferred Agents	Non-Preferred Agents
• Carglumic acid (Eton Pharmaceuticals Mft) • Pheburane® • Sodium phenylbutyrate	• Buphenyl® • Carbaglu® • Carglumic acid (Non-Eton Pharmaceuticals Mft) • Olpruva™ • Ravicti®

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: Urea Cycle Disorder Agents
- Age range: All appropriate MO HealthNet participants

Approval Criteria

- Documented compliance on current therapy regimen **OR**
- For Carglumic acid and Carbaglu:
  - Documented diagnosis of NAGS deficiency
  - For non-preferred agents: Failure to achieve desired therapeutic outcomes with trial on 1 preferred carglumic acid agent
- For Buphenyl, Olpruva, Pheburane, Ravicti, or sodium phenylbutyrate:
  - Documented diagnosis of a urea cycle disorder confirmed by enzymatic, biochemical, or genetic testing **AND**
  - Documentation of trial and failure of dietary protein restriction and/or amino acid supplementation **AND**
  - For non-preferred agents: Failure to achieve desired therapeutic outcomes with trial on Pheburane

Denial Criteria

- Lack of adequate trial on required preferred agents
- Therapy will be denied if all approval criteria are not met
- For Buphenyl/Ravicti/Olpruva/Pheburane: medication is being used for the treatment of acute hyperammonemia

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.

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- 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.
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- Evidence-Based Medicine and Fiscal Analysis: “Agents for Urea Cycle Disorders – Therapeutic Class Review”-, Gainwell Technologies; last updated July 20, 2023.
- Lee B. Urea cycles disorder: management. UpToDate. Last updated August 6, 2021. Urea cycle disorders: Management - UpToDate. Accessed August 16, 2023.
- Buphenyl® (sodium phenylbutyrate) [package insert]. Scottsdale, AZ: Ucyclyd Pharma, Inc.; March, 2009.
- Ravicti® (glycerol phenylbutyrate) [package insert]. Lake Forest, IL: Horizon Therapeutics USA, Inc.; September, 2021.
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