Washington State Health Care Authority

Endocrine and Metabolic Agents: Urea Cycle Disorder Agents- Oral

Medical policy no. 30.90.80-1 Effective Date: TBD

Related medical policies:

Policy Name
N/A

Note: *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

To see the list of the current Apple Health Preferred Drug List (AHPDL), please visit: https://www.hca.wa.gov/assets/billers-and-providers/apple-health-preferred-drug-list.xlsx

Medical necessity

Drug	Medical Necessity
Glycerol phenylbuyrate (Ravicti) Sodium phenylbuyrate (Buphenyl, Olpruva, Pheburane)	**Endocrine and Metabolic Agents: Urea Cycle Disorder Agents- Oral** may be considered medically necessary in patients who meet the criteria described in the clinical policy below. If all criteria are not met, the clinical reviewer may determine there is a medically necessary need and approve on a case-by-case basis. The clinical reviewer may choose to use the reauthorization criteria when a patient has been previously established on therapy and is new to Apple Health.

Clinical policy:

Clinical Criteria	
Disorder of the urea cycle metabolism Glycerol phenylbuyrate (Ravicti) Sodium Phenylbutyrate (Buphenyl, Olpruva, Pheburane)	Sodium Phenylbutyrate (Buphenyl) may be approved when all the following documented criteria are met: 1. Prescribed by, or in consultation with a healthcare provider experienced in the treatment of urea cycle disorders; **AND** 2. Diagnosis of urea cycle disorders involving deficiencies of any of the following: a. Carbamylphosphate synthetase (CPS) b. Ornithine transcarbamylase (OTC) c. Argininosuccinic acid synthetase (AS); **AND**

	3. Diagnosis is confirmed by genetic or enzymatic testing (mutations in the CPS1, OTC, or ASS1 genes); **AND** 4. Documentation of patient's current weight and body surface area (BSA); **AND** 5. Documentation showing baseline plasma ammonia levels; **AND** 6. Provider attestation the patient is following a protein restricted diet Glycerol phenylbuyrate (Ravicti) and non-preferred sodium phenylbutyrate (Olpruva, Pheburane) products may be approved when all the following documented criteria are met: 7. Criteria 1-6 above is met; **AND** 8. Patient has tried a preferred sodium phenylbutyrate product unless contraindicated or not tolerated; **AND** 9. For Olpruva requests: patient weighs ≥ 20 kg and has a BSA ≥ 1.2m^2. If ALL criteria are met, the request will be authorized for **12 months.**
	Criteria (Reauthorization) Glycerol phenylbuyrate (Ravicti) and Sodium Phenylbutyrate (Buphenyl, Olpruva, Pheburane) may be approved when all the following documented criteria are met: 1. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g., plasma ammonia within normal limits); **AND** 2. Patient continues to follow a protein restricted diet. If ALL criteria are met, the request will be authorized for **12 months.**

Dosage and quantity limits

Drug	Indication	Approved Dose	Dosage Form and Quantity Limit
Buphenyl	Disorder of the urea cycle metabolism	9.9-13 g/m^2/day orally. Administer as three-six divided doses. Max= 20g/day	• Powder (3g/dose): BSA based dosing • 500 mg tablet: BSA based dosing
Olpruva	Disorder of the urea cycle metabolism	9.9-13 g/m^2/day orally. Administer as three-six divided doses. Max= 20g/day	• Pellet Pack for reconstitution (2g, 3g, 4g, 5g, 6,g, 6.67g): BSA based dosing
Pheburane	Disorder of the urea cycle metabolism	Patients weighing < 20 kg: 450-600 mg/kg/day Administer as three-six divided doses	• Pellets (84g sodium phenylbutyrate/bottle): BSA/weight based dosing

		Patients weighing ≥ 20 kg: 9.9-13 g/m^2/day orally. Administer as three-six divided doses Max= 20g/day	
Ravicti	Disorder of the urea cycle metabolism	Phenylbutyrate naïve: 4.5-11.2 mL/m^2/day orally given in 3 divided doses. Phenylbutyrate-naïve with residual enzyme activity: 4.5 mL/m^2/day orally given in 3 divided doses. Switching from sodium phenylbutyrate tablets: TDD sodium phenylbutyrate x 0.86= TDD glycerol phenylbutyrate Switching from sodium phenylbutyrate tablets: TDD sodium phenylbutyrate x 0.81= TDD glycerol phenylbutyrate	• Oral liquid (1.1 g/mL): BSA based dosing
Sodium Phenylbutyrate (generic)	Disorder of the urea cycle metabolism	9.9-13 g/m^2/day orally. Administer as three-six divided doses. Max= 20g/day	• Powder (3g/dose): BSA based dosing • 500 mg tablet: BSA based dosing

Coding:

HCPCS Code	Description
N/A	N/A

Background:

The urea cycle clears nitrogen waste from the body as urea. Urea cycle disorders (UCDs) are rare inherited deficiencies in any of the enzymes involved in the urea cycle. UCDs, except for arginase deficiency result in hyperammonemia and life-threatening illnesses. Initial signs may include somnolence, inability to maintain body temperature, and poor feeding. Neurologic abnormalities and impaired cognitive function are significantly correlated with the duration of hyperammonemia and encephalopathy. Normalization of blood ammonia levels is the management priority.

Treatment guidelines for urea cycle disorders recommend chronic treatment with nitrogen-scavenging medications, specifically sodium phenylbutyrate, three to four times daily.

References

1. Urea Cycle Disorders Conference group. Consensus statement from a conference for the management of patients with urea cycle disorders. J Pediatr. 2001 Jan;138(1 Suppl):S1-5. Review. PubMed PMID: 11148543.
2. Kose, M, Canda, E, Kagnici, M, Ucar, SK, Coker, M. A Patient with MSUD: Acute Management with Sodium Phenylacetate/Sodium Benzoate and Sodium Phenylbutyrate. Case reports in pediatrics. 2017;2017:1045031. PMID: 28589054
3. Buphenyl [Prescribing information]. Lake Forest, IL: Horizon Pharma, Inc.; July 2022.
4. Olpruva [Prescribing information]. Newton, MA: Acer Therapeutics.; December 2022.
5. Ravicti [Prescribing information]. Lake Forest, IL: Horizon Pharma.; September 2021.

History

Approved Date	Effective Date	Version	Action and Summary of Changes
MM/DD/YYY	MM/DD/YYYY	30.90.80-1	Pending Approval (draft/unpublished version) -New policy created

Washington State Health Care Authority

Urea Cycle Disorder Agents- Oral

Please provide the information below, please print your answer, attach supporting documentation, sign, date, and return to our office as soon as possible to expedite this request. **Without this information, we may deny the request in seven (7) working days.**

Date of request:	Reference #:	MAS:	
Patient	Date of birth	ProviderOne ID	
Pharmacy name	Pharmacy NPI	Telephone number	Fax number
Prescriber	Prescriber NPI	Telephone number	Fax number
Medication and strength	Directions for use	Qty/Days supply	

1. Is this request for a continuation of existing therapy? ☐ Yes ☐ No
   If yes, is there documentation demonstrating disease stability or a positive clinical response (e.g., plasma ammonia within normal limits)?
   ☐ Yes ☐ No

2. Is this prescribed by, or in consultation with, any of the following? Check all that apply:
   ☐ Healthcare provider experienced in the treatment of urea cycle disorders
   ☐ Other. Specify: _____

3. Indicate if the patient has deficiencies of any of the following. Check all that apply:
   ☐ Carbamylphosphate synthetase (CPS)
   ☐ Ornithine transcarbamylase (OTC)
   ☐ Argininosuccinic acid synthetase (AS)
   ☐ Other. Specify: _____

4. Has diagnosis been confirmed by genetic or enzymatic testing (mutations in the CPS1, OTC, or ASS1 genes)?
   ☐ Yes ☐ No

5. Provide the following for patient:
   Current weight: _____kg Date taken: _____
   Current body surface area (BSA): _____ Date taken: _____

6. Does provider attest patient is following protein restricted diet? ☐ Yes ☐ No

7. Has documentation been submitted showing baseline plasma ammonia levels? ☐ Yes ☐ No

8. If request is non-preferred, has patient had treatment with preferred oral urea cycle disorder agents on the Apple Health Preferred Drug List (AHPDL) that was ineffective, contraindicated or not tolerated?
   ☐ Yes. List each medication and duration of trial:

   Medication Name: _____ Duration: _____
   Medication Name: _____ Duration: _____
   Medication Name: _____ Duration: _____

☐ No. Explain why preferred products have not been tried: _____		
CHART NOTES ARE REQUIRED WITH THIS REQUEST		
Prescriber signature	Prescriber specialty	Date