Clinical Policy Title:	sodium phenylbutyrate
Policy Number:	RxA.354
Drug(s) Applied:	Buphenyl®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Sodium phenylbutyrate (Buphenyl®) is a nitrogen-binding agent. It is indicated as adjunctive therapy in the chronic management of patients with urea cycle disorders (UCDs) involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (ASS).

Limitation(s) of use: Buphenyl® should not be used to manage acute hyperammonemia, which is a medical emergency.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
sodium phenylbutyrate (Buphenyl®)	UCD	Weight < 20 kg: 450-600 mg/kg/day orally in equally divided doses with each meal or feeding Weight ⩾ 20 kg: 9.9-13 gm/m^2/day orally in equally divided doses with each meal or feeding	20 gm/day

Dosage Forms

- Tablet: 500 mg
- Powder: 250 gm bottle

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Urea Cycle Disorder: CPS, OTC, ASS (must meet all)**:**

1. Diagnosis of a UCD caused by one or more of the following, confirmed by enzymatic, biochemical or genetic analysis:
   a. CPS deficiency;
   b. OTC deficiency;
   c. ASS deficiency;
2. Prescribed by or in consultation with a physician experienced in treating metabolic disorders;
3. Dose does not exceed 20 g per day.

Approval duration:
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Urea Cycle Disorder: CPS, OTC, ASS (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 20 g per day.

Approval duration:
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

ASL: Argininosuccinate lyase
ASS: Argininosuccinate synthetase
CPSI: Carbamyl phosphate synthetase I
CTLN1: Type I citrullinemia
FDA: Food and Drug Administration
NAGS: N-acetyl glutamate synthetase
OTC: Ornithine transcarbamylase
UCD: Urea cycle disorder

APPENDIX B: Therapeutic Alternatives

- Not applicable.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Should not be used to manage acute hyperammonemia.

- Boxed warning(s):
  - None reported.

APPENDIX D: General Information

UCDs are caused by a deficiency in any of the below enzymes in the pathway that transforms nitrogen to urea:

- Carbamyl phosphate synthetase I (CPSI) deficiency
- Ornithine transcarbamylase (OTC) deficiency

- Argininosuccinate synthetase (ASS) deficiency (also known as classic citrullinemia or type I citrullinemia, CTLN1)
- Argininosuccinate lyase (ASL) deficiency (also known as argininosuccinic aciduria)
- N-acetyl glutamate synthetase (NAGS) deficiency
- Arginase deficiency

References

1. Buphenyl Prescribing Information. Lake Forest, IL: Horizon Pharma USA, Inc.; February 2020. Available at https://www.hzndocs.com/Buphenyl-Prescribing-Information.pdf. Accessed May 31, 2021.
2. Haberle J, Burlina A, Chakrapani A, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders: first revision. J Inherit Metab Dis. 2019;42(6):1192- 1230. doi:10.1002/jimd.12100. Accessed May 31, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Clinical Policy Title was updated 2. Drug(s) Applied was updated 3. Line of Business Policy Applies to was updated 4. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 5. Commercial approval duration and Medicaid approval duration updated. 6. References were updated	06/22/2020	09/14/2020
Policy was reviewed: 1. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 2. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 3. References were reviewed and updated.	5/31/2021	09/14/2021