Premier Health Plan

POLICY AND PROCEDURE

POLICY TITLE: ***Buphenyl (sodium phenylbutyrate) and Ravicti (glycerol phenylbutyrate)***
DEPARTMENT: **Clinical Pharmacy Services- Utilization Management**
ORIGINAL DATE: ***July 2010 (as adopted from UPMC Health Plan)***

Last P & T Committee Approval Date: *February 2018*

Product Applicability: *mark all applicable products below:*

COMMERCIAL	[ ] HMO [ ] PPO *Products*: [ ] Small [ ] Indiv. [ ] Large *Exchange*: [ ] Shop [ ] Indiv. [x] All
OTHER	[x] Self-funded/ASO

PURPOSE

The purpose of this policy is to define the prior authorization process for Buphenyl (sodium phenylbutyrate) and Ravicti (glycerol phenylbutyrate).

Sodium phenylbutyrate (Buphenyl) is indicated as adjunctive therapy in the chronic management of patients with urea cycle disorders involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS). It is indicated in all patients with neonatal-onset deficiency (complete enzymatic deficiency, presenting within the first 28 days of life). It is also indicated in patients with late-onset disease (partial enzymatic deficiency, presenting after the first month of life) who have a history of hyperammonemic encephalopathy.

Glycerol phenylbutyrate (Ravicti) is indicated for use as a nitrogen-binding agent for chronic management of adult and pediatric patients ≥ 2 years of age with urea cycle

disorders (UCDs) that cannot be managed by dietary protein restriction and/or amino acid supplementation alone. Glycerol phenylbutyrate must be used with dietary protein restriction and, in some cases, dietary supplements (e.g. essential amino acids, arginine, citrulline, protein-free calorie supplements).

- Limitations of Use
  - Glycerol phenylbutyrate is not indicated for the treatment of acute hyperammonemia in patients with UCDs
  - Safety and efficacy for the treatment of N-acetyglutamate synthase (NAGS) deficiency has not been established
  - The use of glycerol phenylbutyrate in patients < 2 months of age is contraindicated

DEFINITIONS

N/A

POLICY

It is the policy of the Health Plan to maintain a prior authorization process that promotes appropriate utilization of specific drugs with potential for misuse or limited indications. This process involves a review using Food and Drug Administration (FDA) criteria to make a determination of Medical Necessity, and approval by the Pharmacy & Therapeutics Committee of the criteria for prior authorization, as described in RX.002 Pharmacy and Therapeutics Committee and RX.003-Prior Authorization Process.

The drugs, Buphenyl (sodium phenylbutyrate) and Ravicti (glycerol phenylbutyrate), are subject to the prior authorization process.

PROCEDURE

Initial Authorization Criteria:

Must meet all of the criteria listed below:

- Must be prescribed by a physician who specializes in the treatment of inherited metabolic disorders or in consultation with this specialist.
- Must have a diagnosis of a urea cycle disorder. Chart documentation describing how diagnosis was confirmed (e.g. genetic testing results, enzyme assays, ammonia levels, progress notes, etc.) is required.
- For glycerol phenylbutyrate (Ravicti):

- Must have an adequate trial of sodium phenylbutyrate (Buphenyl) with either an inadequate response despite dose titration, significant side effects/toxicity, or have a contraindication to this therapy. Chart documentation of trial is required.

Reauthorization Criteria:

All prior authorization renewals are reviewed on an annual basis to determine the Medical Necessity for continuation of therapy. Authorization may be extended at 1-year intervals based upon chart documentation from the prescriber that the member's condition has improved based upon the prescriber's assessment while on therapy.

Limitations:

Length of Authorization (if above criteria met)	
Initial Authorization	Up to 3 months
Reauthorization	Up to 1 year

If the established criteria are not met, the request is referred to a Medical Director for review.

REFERENCES

1. Buphenyl [package insert]. Scottsdale, AZ: Ucyclyd Pharma Inc.; April 2009
2. Ravicti [package insert]. South San Francisco, CA: Hyperion Theraputics Inc.; January 2013
3. Licter-Konecki U, Diaz GA, Merritt JL, et al. Ammonia control in children with ureacycle disorders (UCDs): Phase 2 comparison of sodium phenylbutyrate and glycerol phenylbutyrate. *Molecular Genetics Metabolism* 2011:103;323-329
4. Diaz GA, Krivitzky LS, Mokhtarani M, et al. Ammonia control and neurocognitive outcome among urea cycle disorder patients treated with glycerol phenylbutyrate. *Hepatology* 2012. DOI 10.1002/hep.26058
5. Smith W, Diaz GA, Lichter-Konecki U, et al. Ammonia control in children ages 2 months through 5 years with urea cycle disorders: comparison of sodium phenylbutyrate and glycerol phenylbutyrate. *J Pediatr* 2013. http://dx.doi.org/10.1016/j.peds.2012.11.084
6. Lee B, Rhead W, Diaz GA, et al. Phase 2 comparison of novel ammonia scavenging agent with sodium phenylbutyrate in patients with urea cycle disorders: safety, pharmacokinetics, and ammonia control. *Molecular Genetics Metabolism* 2010;100:221-228
7. Haberle J, Boddaert N, Burlina A, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders. *Orphanet Journal of Rare Diseases* 2012;7:32. http://www.ojrd.com/content/7/2/32. Accessed February 20, 2013
8. The Urea Cycle Disorders Conference Group. Consensus statement for the management of patients with urea cycle disorders. *J Pediatr* 2001;138:S1-S5
9. Summar M, Tuchman M. Proceeding of a consensus conference for the management of patients with urea cycle disorders. *J Pediatr* 2001;138:S6-S10
10. Wilcken B. Problems in the management of urea cycle disorders. *Molecular Genetics Metabolism* 2004;81:S86-S91

RECORD RETENTION

Records Retention for Evolent Health documents, regardless of medium, are provided within the Evolent Health records retention policy and as indicated in CORP.028.E Records Retention Policy and Procedure.

REVIEW HISTORY

DESCRIPTION OF REVIEW / REVISION	DATE APPROVED
Annual review	*02/17, 02/18*