FOR HEALTHCARE PROVIDER OFFICE STAFF USE ONLY. DO NOT DISTRIBUTE.

Dear Healthcare Provider,

There are times when a prior authorization request may be denied by your patient's health plan. If that happens, an appeal can be submitted to the plan requesting the decision be reconsidered. Appeal requirements may vary according to the health plan.

To use the sample letter provided as a separate Word document, modify the content as needed based on your medical judgment and discretion when providing a diagnosis and characterization of your patient's medical condition. Additional information and a checklist are included below and on page 2.

Use of the information in this document does not guarantee the health plan will provide coverage for RAVICTI® (glycerol phenylbutyrate) Oral Liquid, and it is not intended to be a substitute for, or an influence on, your independent medical judgment.

Before sending the appeal letter to the health plan, please ensure all variable text (as indicated by brackets in pink and open text fields) is filled in or deleted as required.

APPEAL CHECKLIST

Documents for Filing a Response to Treatment Denial

Each appeal may require different information based on the plan's requirements. Below is a list of materials you may need to include in an appeal package. Review each denial and the insurer's requirements to determine what to include in a patient's appeal package.

Commonly Required Documents Include

- ☐ Letter of appeal
- ☐ Letter of medical necessity
- ☐ Patient authorization and notice of release of information
- ☐ Copy of the patient's health plan and/or prescription card (front and back)
- ☐ Denial information, including the patient's denial letter and/or explanation of benefits
- ☐ Supporting documentation:
  - ☐ RAVICTI Prescribing Information
  - ☐ RAVICTI clinical studies
  - ☐ Clinical documentation of:
    - ☐ Diagnosis (eg, genetic test results, etc)
    - ☐ Chronic hyperammonemia
    - ☐ Functional impairment
    - ☐ Dietary protein restriction or amino acid supplementation
    - ☐ Treatment history, including therapeutics, dosage, and duration
    - ☐ Use and reason for discontinuation of sodium phenylbutyrate
    - ☐ Any relevant clinical/chart notes

INDICATION

RAVICTI (glycerol phenylbutyrate) Oral Liquid is indicated for use as a nitrogen-binding agent for chronic management of patients with urea cycle disorders (UCDs) who cannot be managed by dietary protein restriction and/or supplementation alone. RAVICTI 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

- RAVICTI is not indicated for the treatment of acute hyperammonemia in patients with UCDs because more rapidly acting interventions are essential to reduce plasma ammonia levels.
- The safety and efficacy of RAVICTI for the treatment of *N*-acetylglutamate synthase (NAGS) deficiency has not been established.

Please see additional Important Safety Information on page 3 and accompanying Full Prescribing Information or visit RAVICTIhcp.com.

RAVICTI®
(glycerol phenylbutyrate) Oral Liquid

APPEAL TIPS

Tips for Filing an Appeal of Treatment Denial

This document provides information that may be useful when creating an appeal letter. Some plans have specific coverage authorization forms that must be used. It is important to determine the plan's requirements and follow them when requesting an appeal for RAVICTI to avoid further treatment delays. Horizon By Your Side is a patient support program that provides education to healthcare providers and appropriate office staff to answer non-medical logistical questions and to provide information about insurance processes and accessing treatment. Please contact health plans directly for specific information about their current coverage policies.

Identify the Reason for Denial

Find out, in writing, why the authorization request has been denied. The denial letter from the patient's health plan or the explanation of benefits should outline the reason(s) for denial. These can be obtained from the health plan if you did not receive them. The denial is also summarized in the health plan's online portal or should be available where you submitted the prior authorization.

Determine the Appeal Guidelines

Some health plans have short appeal periods, so it is important to contact the health plan to find out its deadline for submitting an appeal. Be sure to inquire about the number of appeals permitted (some plans allow only one) and the mailing address or fax number to which the appeal should be sent. You may also need to schedule a peer-to-peer consultation.

Contact the Review Department

The denial letter may include a telephone number for the review department. If so, the prescribing physician should call for further clarification about the denial. The reviewer may agree with the rationale and approve treatment during the call. If so, the appeal process is complete.

Compose the Appeal and Schedule a Consultation

The health plan will tell you what supporting documentation is needed. You may also need to schedule a peer-to-peer consultation.

Provide Additional Supporting Documentation

It is important to determine each health plan's appeal requirements, as they may vary according to payor. The appeal package should include all relevant medical documentation, including clinical notes and related test results, as well as any newly available information related to the patient's condition. The team at Horizon By Your Side works directly with patients to answer non-medical logistical questions and to provide information about insurance processes and accessing treatment.

Follow Up as Needed

Contact the health plan to learn about the appeal review timeline. Though some plans may respond within 7 days, most health plans respond within 30 to 60 days of receipt of the appeal package.

Maintain Complete Records

Retain a copy of all documentation submitted with the patient's appeal and record all subsequent communications with the patient's health plan, including the date and the name of the person contacted.

NOTE: As a reminder, do not send patient medical records to Horizon Therapeutics.

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- *Patients with known hypersensitivity to phenylbutyrate:* Reactions include wheezing, dyspnea, coughing, hypotension, flushing, nausea, and rash.

Please see additional Important Safety Information on page 3 and accompanying Full Prescribing Information or visit RAVICTIhcp.com.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid

INDICATION and IMPORTANT SAFETY INFORMATION

INDICATION

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LIMITATIONS OF USE

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IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- *Patients with known hypersensitivity to phenylbutyrate:* Reactions include wheezing, dyspnea, coughing, hypotension, flushing, nausea, and rash.

WARNINGS AND PRECAUTIONS

- *Neurotoxicity:* Phenylacetate (PAA), the major metabolite of RAVICTI, may be toxic at levels of 500 micrograms/mL or greater. If symptoms of vomiting, nausea, headache, somnolence, or confusion, are present in the absence of high ammonia or other intercurrent illness which explains these symptoms, consider the potential for PAA neurotoxicity which may need reduction in the RAVICTI dosage.
- *Pancreatic Insufficiency or Intestinal Malabsorption:* Low or absent pancreatic enzymes or intestinal disease resulting in fat malabsorption may result in reduced or absent digestion of RAVICTI and/or absorption of phenylbutyrate and reduced control of plasma ammonia. Monitor ammonia levels closely.

ADVERSE REACTIONS

The most common adverse reactions reported in clinical trials (at least 10% of patients) were:

- *Adult patients:* diarrhea, flatulence, and headache occurred during 4-week treatment (n=45) with RAVICTI; nausea, vomiting, diarrhea, decreased appetite, dizziness, headache, and fatigue occurred during 12-month treatment (n=51) with RAVICTI.
- *Pediatric patients ages 2 to 17 years:* upper abdominal pain, rash, nausea, vomiting, diarrhea, decreased appetite, and headache occurred during 12-month treatment (n=26) with RAVICTI.
- *Pediatric patients ages 2 months to less than 2 years:* neutropenia, vomiting, constipation, diarrhea, pyrexia, hypophagia, cough, nasal congestion, rhinorrhea, rash, and papule occurred during 12-month treatment (n=17) with RAVICTI.
- *Pediatric patients less than 2 months of age:* vomiting, rash, gastroesophageal reflux, increased hepatic enzymes, feeding disorder (decreased appetite, hypophagia), anemia, cough, dehydration, metabolic acidosis, thrombocytosis, thrombocytopenia, neutropenia, lymphocytosis, diarrhea, flatulence, constipation, pyrexia, lethargy, and irritability/agitation occurred during 24-month treatment (n=16) with RAVICTI.

DRUG INTERACTIONS

- Corticosteroids, valproic acid, or haloperidol may increase plasma ammonia level. Monitor ammonia levels closely.
- Probenecid may affect renal excretion of metabolites of RAVICTI, including phenylacetylglutamine (PAGN) and PAA.
- CYP3A4 substrates with narrow therapeutic index (eg, alfentanil, quinidine, cyclosporine): RAVICTI may decrease exposure to the concomitant drug.
- Midazolam: Use of RAVICTI decreased exposure of midazolam with concomitant use.

USE IN SPECIFIC POPULATIONS

- *Pregnancy:* RAVICTI should be used with caution in patients who are pregnant or planning to become pregnant. Based on animal data, RAVICTI may cause fetal harm. Report pregnancies to Horizon at 1-866-479-6742.
- *Lactation:* breastfeeding is not recommended during treatment with RAVICTI. There are no data on the presence of RAVICTI in human milk, the effects on the breastfed infant, nor the effects on milk production.

Please see accompanying Full Prescribing Information or visit RAVICTIhcp.com.