RAVICTI® (glycerol phenylbutyrate) Oral Liquid Access Journey

A resource to educate healthcare providers about patient access and coverage

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 pages 12-13 and see Full Prescribing Information.

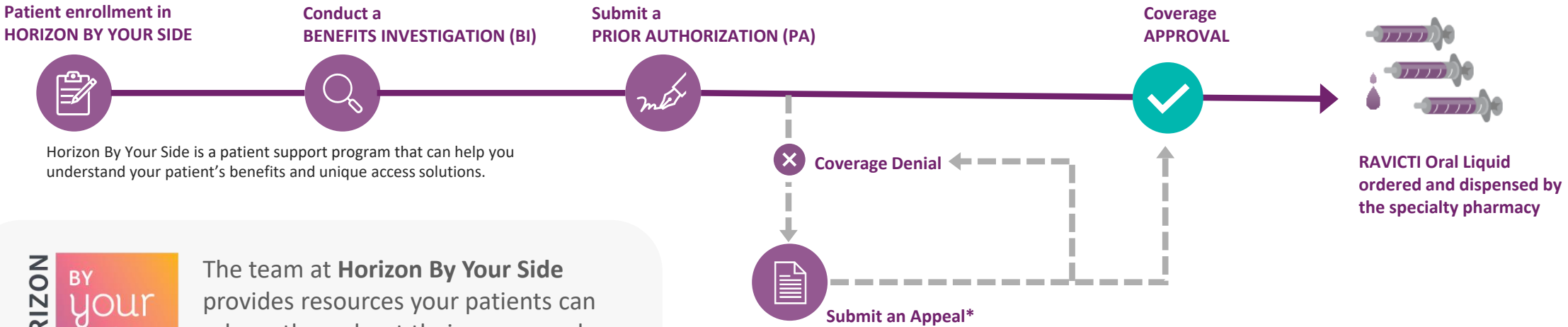
HORIZON® | RAVICTI® (glycerol phenylbutyrate) Oral Liquid

P-RVT-00578-3 08/23

RAVICTI Patient Access Road Map

This resource can help you identify the steps in the access process as well as available resources.

You can navigate through the road map by clicking on areas of the map or by using the navigation bar above. In each section, you will find more detailed information and resources available for that step of the process.



HORIZON BY your side

The team at **Horizon By Your Side** provides resources your patients can rely on throughout their access and treatment journey.

Call **1-844-4MY-HBYS (1-844-469-4297)**

Monday–Friday, 9 AM–8 PM ET

https://www.HorizonByYourSide.com

*Submitting an appeal does not guarantee approval, and this process may need to be repeated.

Please see Important Safety Information on pages 12-13 and see Full Prescribing Information.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid

Horizon Offers Patients a Range of Support Throughout Their Access and Treatment Journey

Coverage policies may vary, and the team at **Horizon By Your Side** can help identify policies early in the access process to help ensure maximum efficiency.

Horizon By Your Side

A partner your patients can rely on throughout their access and treatment journey that provides a wide array of patient-focused services. The team at Horizon By Your Side may provide nonmedical logistical treatment support and education about the insurance process.

Patient Access Liaison (PAL)

Provides dedicated, one-on-one support for your patient. The PAL works directly with individual patients to answer nonmedical logistical questions and provide support upon enrollment. Additionally, the PAL educates about navigating insurance processes and accessing treatment on your patient's behalf. The PAL has the expertise and tools to support the patient by educating on patient benefits, PA requirements, and payor policies.

Horizon Case Manager

Can help healthcare providers to understand their patients' benefits and unique access solutions. A Case Manager assigned to your patients may also be in touch with your office to make sure important insurance information is properly shared.

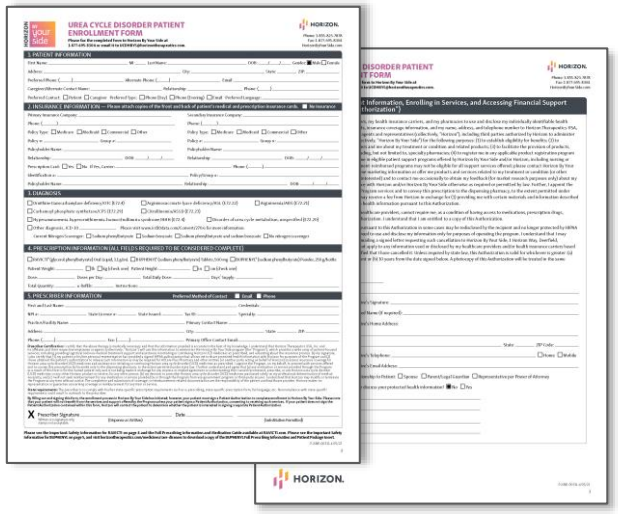
PA, prior authorization.

Please see Important Safety Information on pages 12-13 and see Full Prescribing Information.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid

Initiate Patient Enrollment

Many treatments require initial action from the healthcare provider and office staff for patients to get access to RAVICTI. The team at **Horizon By Your Side** provides a range of support tailored to meet the individual needs of your patients throughout their access and treatment journey with RAVICTI.



The Patient Enrollment Form (PEF) is the first step for your patients to receive support from the team at Horizon By Your Side, including:

- **BI** by researching insurance coverage, PA requirements, and appeal instructions if denied
- **Financial assistance** for eligible patients
- **Patient support** via a PAL who works directly with individual patients to answer nonmedical logistical questions and provide support throughout their journey
- **Insurance information** via a Case Manager who can help you understand your patients' benefits and unique access solutions

DOWNLOAD the PEF to initiate patient enrollment in Horizon By Your Side.

DOWNLOAD the Annotated PEF, a resource that provides details about the PEF.

BI, benefits investigation; PA, prior authorization; PAL, Patient Access Liaison.

Please see Important Safety Information on pages 12-13 and see Full Prescribing Information.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid

Conduct a Benefits Investigation (BI)

Coverage criteria will vary among medical plans and a BI will identify requirements specific to RAVICTI. A Case Manager can help educate you and your patient about the insurance process and accessing treatment.

A BI may help answer questions about:

RAVICTI coverage

- Is RAVICTI covered under the medical benefit or pharmacy benefit?

PA

- Will a PA be required for treatment with RAVICTI?
- If a PA is not required, is predetermination available?
- What is the process for obtaining a PA or predetermination?
- What information will be required and how long will the process take?
- How long will the PA remain valid?

Benefits coordination

- Does the patient have any other supplemental insurance benefits that would require coordination? Which benefit is primary? Which is secondary?

Patient financial responsibility and out-of-pocket (OOP) costs

- What is the annual deductible amount the patient must meet?
  - Has this amount been met?
  - How much is left?
- What is the patient's co-payment or co-insurance for RAVICTI?
- Is there a maximum OOP amount that the patient must meet?
  - Has this amount been met?
  - How much is left?

Prescription information

- Is RAVICTI medically appropriate?
- Is RAVICTI being prescribed in accordance with generally accepted standards of medical practice?

DOWNLOAD the RAVICTI PA Checklist to help your office organize the information that may be needed for a PA.

PA, prior authorization.

Please see Important Safety Information on pages 12-13 and see Full Prescribing Information.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid

Conduct a Benefits Investigation (BI) (cont'd)

Coding and claims submission

A BI can help answer questions such as:

- What are the specific coding and claims submission requirements for prescribing RAVICTI in this patient's plan?
- What type of documentation is required?

Reminder: Requirements for coverage will vary among health plans and a BI will identify requirements specific to RAVICTI, as well as what insurance your patient has.

RAVICTI ICD-10-CM Code*	
Code	Description
E72.20	Disorder of urea cycle metabolism, unspecified
E72.4	OTCD
E72.22	ASLD
E72.21	ARGD
E72.29	CPS1D
E72.23	ASSD
E72.4	HHH

RAVICTI NDC Codes	
Code	Description
75987-050-06	One 25-mL bottle per carton
75987-050-07	Four 25-mL bottles per carton

Once the team at Horizon By Your Side completes the BI, you will receive a Summary of Benefits notification generally within 1 to 2 business days of insurance verification.

*This may not be the only applicable code for reimbursement, nor does using this code guarantee coverage.
ARGD, arginase deficiency; ASLD, argininosuccinate lyase deficiency; ASSD, argininosuccinate synthetase deficiency; CPS1D, carbamoyl phosphate synthetase 1 deficiency; HHH, hyperornithinemia-hyperammonemia-homocitrullinuria; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; NDC, National Drug Code; OTCD, ornithine transcarbamylase deficiency.

Please see Important Safety Information on pages 12-13 and see Full Prescribing Information.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid

Submit a Prior Authorization (PA)

The PA process allows the health plan to review the reason for treatment with RAVICTI and to determine if it is medically necessary. Clinical documentation requirements will vary among health plans.

Common criteria a health plan policy may require for a PA:

Diagnosis information

- Diagnosis/ICD-10-CM codes
- Diagnosis confirmed through enzymatic, biochemical, or genetic testing
- Chronic hyperammonemia
- Ammonia levels
- Documentation of functional impairment

Treatment history

- Provide documentation showing that the patient is following a protein-restricted diet or amino acid supplementation
- Note if the patient has experienced inadequate response to treatment or intolerance to use of other nitrogen scavenger medicines; include dosage and duration
- For patients already on RAVICTI, provide documentation showing clinical improvement
- Note any consultations with a specialist (eg, metabolic geneticist, metabolic dietitian, genetics counselor)

Including a letter of medical necessity with a PA is important and may help avoid delays.

Your office may need to connect with the referring physician to gather the clinical documentation required to complete the PA. The dedicated Case Manager has the local expertise to provide education about PA, medical exception, or appeal processes.

ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification.

Please see Important Safety Information on pages 12-13 and see Full Prescribing Information.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid

Submit a Prior Authorization (PA) (cont'd)

The PA process allows the health plan to review the reason for the requested therapy and to determine medical appropriateness. Clinical documentation requirements will vary among health plans. When submitting a PA for RAVICTI, be sure to:

- **Submit the PA directly to the health plan or by using an electronic PA system such as CoverMyMeds®**
- **Thoroughly complete every section of the PA form and review the medical policy carefully, as each health plan may have unique requirements**
- **Provide supporting documentation, including but not limited to:**
  - Medical records
  - Diagnosis confirmed by one of the following methods: enzymatic, biochemical, or genetic testing
  - Chart notes
  - Publications and references
  - A letter of medical necessity
- **Inquire about how long the process will take once necessary documents have been submitted**

DOWNLOAD the PA Checklist for reminders and recommendations for submitting a PA.

DOWNLOAD the Letter of Medical Necessity Template and print it out on your office letterhead.

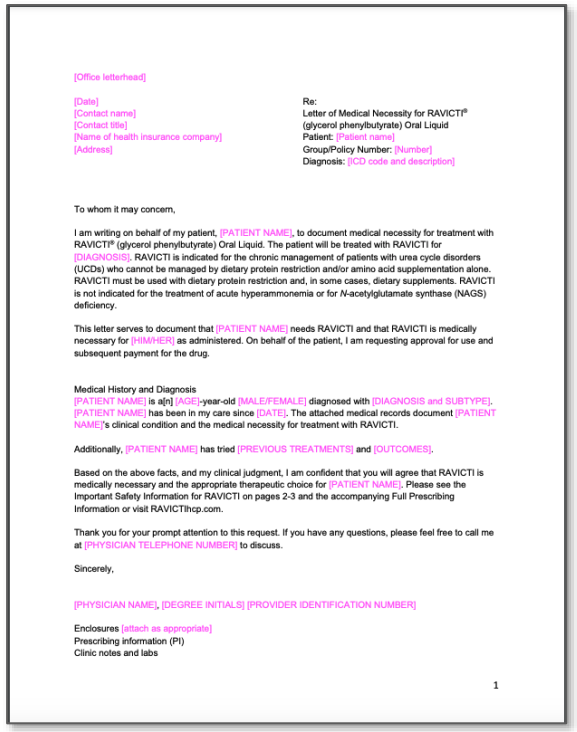
Please see Important Safety Information on pages 12-13 and see Full Prescribing Information.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid

Submit a Prior Authorization (PA) (cont'd)

Writing a letter of medical necessity

A patient-specific letter of medical necessity explains the physician's rationale and clinical decision-making in choosing RAVICTI.



[Office letterhead]

[Date]
[Contact name]
[Contact title]
[Name of health insurance company]
[Address]

Re:
Letter of Medical Necessity for RAVICTI®
(glycerol phenylbutyrate) Oral Liquid
Patient: [Patient name]
Group/Policy Number: [Number]
Diagnosis: [ICD code and description]

To whom it may concern,

I am writing on behalf of my patient, [PATIENT NAME], to document medical necessity for treatment with RAVICTI® (glycerol phenylbutyrate) Oral Liquid. The patient will be treated with RAVICTI for [DIAGNOSIS]. RAVICTI is indicated for the chronic management of patients with urea cycle disorders (UCDs) who cannot be managed by dietary protein restriction and/or amino acid supplementation alone. RAVICTI must be used with dietary protein restriction and, in some cases, dietary supplements. RAVICTI is not indicated for the treatment of acute hyperammonemia or for *N*-acetylglutamate synthase (NAGS) deficiency.

This letter serves to document that [PATIENT NAME] needs RAVICTI and that RAVICTI is medically necessary for [HIM/HER] as administered. On behalf of the patient, I am requesting approval for use and subsequent payment for the drug.

Medical History and Diagnosis
[PATIENT NAME] is a[n] [AGE]-year-old [MALE/FEMALE] diagnosed with [DIAGNOSIS and SUBTYPE]. [PATIENT NAME] has been in my care since [DATE]. The attached medical records document [PATIENT NAME]'s clinical condition and the medical necessity for treatment with RAVICTI.

Additionally, [PATIENT NAME] has tried [PREVIOUS TREATMENTS] and [OUTCOMES].

Based on the above facts, and my clinical judgment, I am confident that you will agree that RAVICTI is medically necessary and the appropriate therapeutic choice for [PATIENT NAME]. Please see the Important Safety Information for RAVICTI on pages 2-3 and the accompanying Full Prescribing Information or visit RAVICTIhcp.com.

Thank you for your prompt attention to this request. If you have any questions, please feel free to call me at [PHYSICIAN TELEPHONE NUMBER] to discuss.

Sincerely,

[PHYSICIAN NAME], [DEGREE INITIALS] [PROVIDER IDENTIFICATION NUMBER]

Enclosures [attach as appropriate]
Prescribing information (PI)
Clinic notes and labs

1

The following is a template letter of medical necessity for RAVICTI that can be customized based on your patient's medical history and demographic information. The template can help your office craft the letter and highlight the medical necessity for your patient.

NOTE: Some health plans may have specific forms that must be completed in order to document medical necessity.

- **Check with the health plan to identify specific documentation that needs to be submitted with a letter of medical necessity**
- **Provide relevant medical information and attach the patient's medical records and/or supporting documents for the health plan to review**
- **Include a copy of the Full Prescribing Information**

DOWNLOAD the Letter of Medical Necessity Template and print it out on your office letterhead.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid

Submit an Appeal

An appeal letter may be needed if a PA for RAVICTI is denied. When writing an appeal letter, ensure that you address the specific details of the denial reason(s), refer to the letter of denial for specific language regarding the reason for denial, and address any concerns that are patient-specific.

Supplemental documentation may include:

- Relevant clinical notes for your patient
- Recent test results
- Supporting scientific publications/journal articles
- A summary of your recommendation at the end of the letter
- A letter of medical necessity

Make sure you match the exact language from the denial letter.
It is imperative to address the specifics of the denial in the appeal letter.
Before you submit your appeal, make sure to:

- Check for any incomplete or missing information, as this is a common reason for denial
- Schedule a peer-to-peer meeting with the health plan
- Contact a Case Manager to learn about additional resources and next steps in the process

If a letter of medical necessity was not submitted with the PA, consider including it with the appeal letter.

Contact the health plan to learn about the appeal review timeline. Once you have submitted the letter, along with any supporting documentation, most health plans will review and decide on coverage within approximately:

72 HOURS
for urgent care

30 DAYS
for nonurgent care

60 DAYS
for services already provided

To initiate an expedited appeal, contact your patient's health plan to confirm its instructions for expedited requests.

DOWNLOAD the Appeal Letter Template to help your office draft an appeal letter.

DOWNLOAD the Payor Appeal Letter Checklist and Tips to help you through the appeal process.

PA, prior authorization.

Please see Important Safety Information on pages 12-13 and see Full Prescribing Information.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid

Best Practices to Maintain Throughout the Access Journey

DOCUMENT
Keep a record of policy requirements, which may vary considerably among health plans.

IDENTIFY
Ensuring smooth transactions among the provider, health plan, and patient starts with identifying each health plan's policy early on.

KNOW
Health plan policies provide clarity for patients on their coverage and OOP expenses.

CONTACT
Our Case Managers are ready to assist you with your questions.

HORIZON BY your side

The team at **Horizon By Your Side** provides resources your patients can rely on throughout their access and treatment journey.

Call **1-844-4MY-HBYS (1-844-469-4297)**
Monday–Friday, 9 AM–8 PM ET
https://www.HorizonByYourSide.com

OOP, out-of-pocket.

Please see Important Safety Information on pages 12-13 and see Full Prescribing Information.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid

INDICATION and IMPORTANT SAFETY INFORMATION

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.

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.

Please see additional Important Safety Information on page 13 and see Full Prescribing Information.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid

IMPORTANT SAFETY INFORMATION (cont'd)

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 Full Prescribing Information.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid