RAVICTI®
(glycerol phenylbutyrate) Oral Liquid

With RAVICTI, your patients with urea cycle disorders (UCDs) can

LIVE CONFIDENTLY[1]

A single moment could change everything.

Give them RAVICTI. Their future is in your hands.

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 review the RAVICTI Important Safety Information on page 22, the BUPHENYL® (sodium phenylbutyrate) Important Safety Information on page 23, the Full Prescribing Information for RAVICTI here, and the Full Prescribing Information for BUPHENYL here.

RAVICTI®
(glycerol phenylbutyrate) Oral Liquid
Rethink potential.

The lifelong, chronic nature of UCDs means patients are constantly

LIVING ON THE EDGE[2,3]

Ammonia elevations: it's not a matter of if, but when

The inherited risk of UCDs can result in elevated ammonia levels (greater than or equal to 35 µmol/L) for a prolonged period of time, leading to serious medical consequences.[4,5]

Metabolic stressors can occur anytime, anywhere

Everyday risks include excessive protein intake, stress, major life milestones, and illness.[6,7]

Despite UCD treatment, adherence may affect ammonia control

67% of physicians reported poor adherence to treatment to be a barrier or unmet need in the care of patients with UCDs.[4]

"With a UCD, so much is out of your control, but with RAVICTI you have control."

Caregiver of a patient taking RAVICTI

With RAVICTI, your patients with UCDs[a] can

LIVE CONFIDENTLY[1]

Unique mechanism of action designed for slow release of phenylbutyrate (PBA)[1,8]

Absorption of PBA is slower when administered as RAVICTI vs sodium phenylbutyrate, resulting in more sustained levels of active downstream metabolites.[1,8]

RAVICTI is the most-prescribed nitrogen-scavenging treatment for patients with UCDs in the United States today[9,b]

Long-term data exist for patients with RAVICTI, including a 2019 analysis of a continued-access safety study evaluating adverse events, ammonia control, and hyperammonemic crisis (HAC) rates.[5]

Established long-term ammonia control for patients of all ages[1]

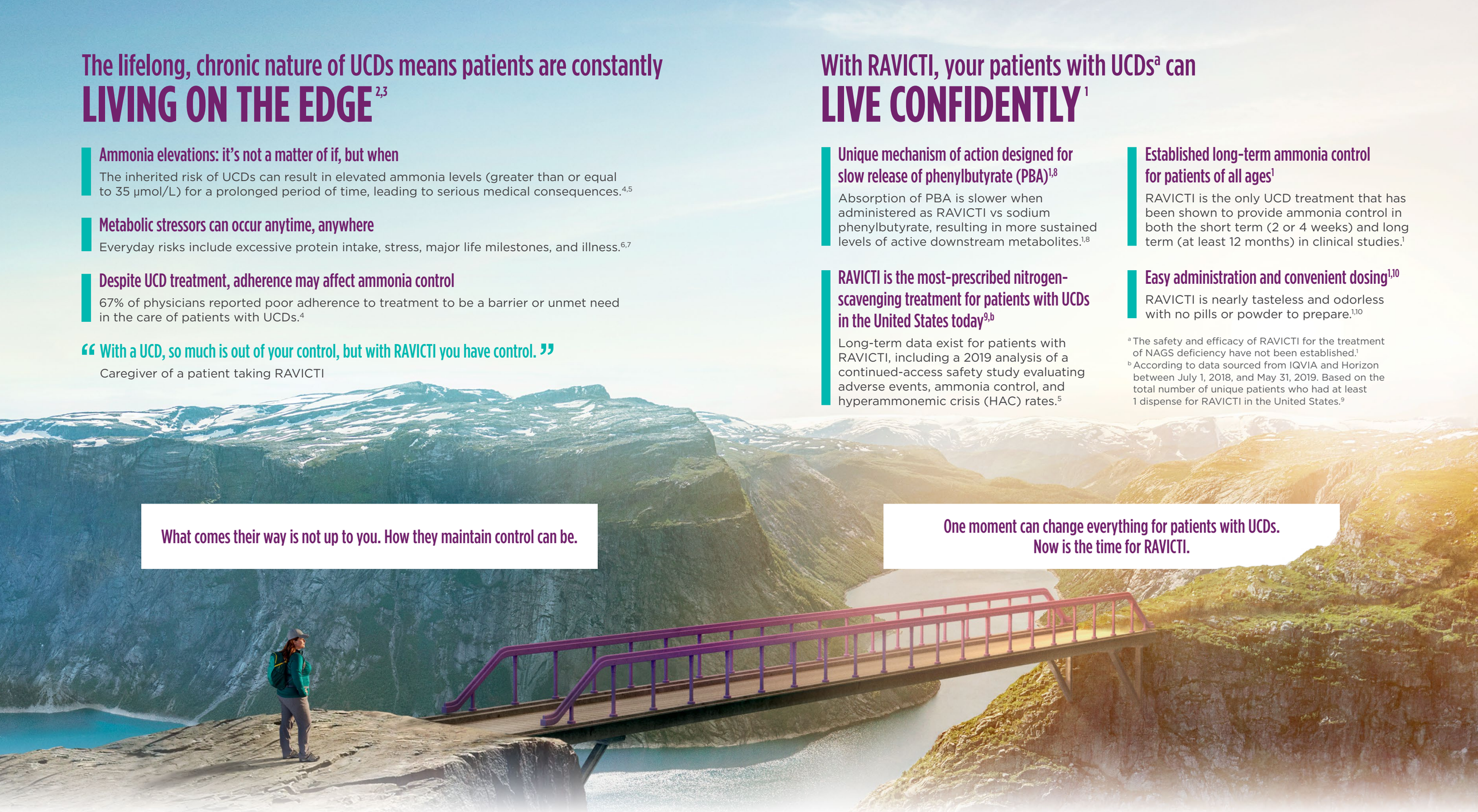
RAVICTI is the only UCD treatment that has been shown to provide ammonia control in both the short term (2 or 4 weeks) and long term (at least 12 months) in clinical studies.[1]

Easy administration and convenient dosing[1,10]

RAVICTI is nearly tasteless and odorless with no pills or powder to prepare.[1,10]

[a] The safety and efficacy of RAVICTI for the treatment of NAGS deficiency have not been established.[1]

[b] According to data sourced from IQVIA and Horizon between July 1, 2018, and May 31, 2019. Based on the total number of unique patients who had at least 1 dispense for RAVICTI in the United States.[9]



SELECTED IMPORTANT SAFETY INFORMATION—CONTRAINDICATIONS

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

Please review the RAVICTI Important Safety Information on page 22, the BUPHENYL® (sodium phenylbutyrate) Important Safety Information on page 23, the Full Prescribing Information for RAVICTI here, and the Full Prescribing Information for BUPHENYL here.

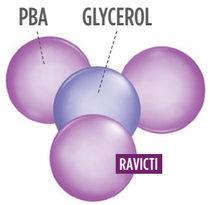
SELECTED IMPORTANT SAFETY INFORMATION—WARNINGS AND PRECAUTIONS

- *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.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid
Rethink potential.

RAVICTI has a unique mechanism of action designed for slow release of phenylbutyrate (PBA)[1,8]

An alternate vehicle for waste nitrogen removal can help control ammonia, which can fluctuate daily above the upper limit of normal in patients with UCDs[1,2,11]



RAVICTI is a triglyceride containing 3 molecules of PBA. RAVICTI uses glycerol rather than sodium as the primary vehicle of PBA.[1]

COMPONENTS OF PBA METABOLISM

- PBA
- PAA
- NITROGEN
- GLUTAMINE
- PAGN

A RELEASE OF PHENYLBUTYRATE (PBA)

Upon oral administration, release of PBA from RAVICTI is gradual due to pancreatic lipase digestion—occurring mostly in the small intestine rather than in the stomach.[1,8]

B CONVERSION TO PHENYLACETATE (PAA)

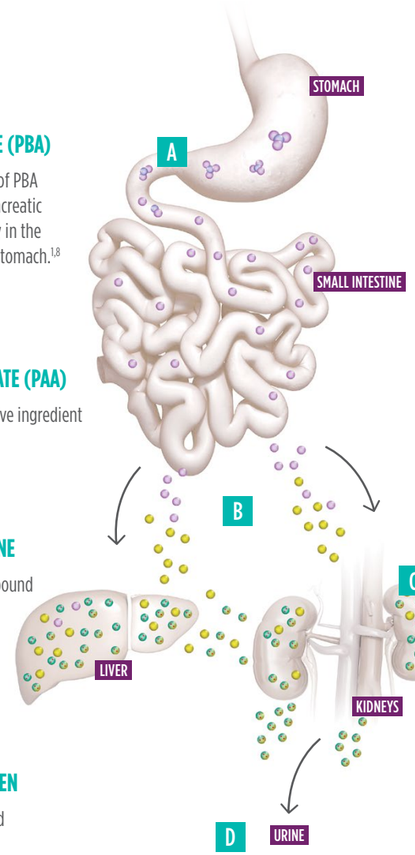
PBA is converted into PAA, the active ingredient of RAVICTI.[1]

C CONJUGATION WITH GLUTAMINE

PAA is a metabolically active compound that combines with glutamine in the liver and kidneys to form phenylacetylglutamine (PAGN).[1]

D EXCRETION OF WASTE NITROGEN

PAGN is excreted by the kidney and eliminated as urinary PAGN.[1]



Absorption of PBA is approximately 70% to 75% slower when administered as RAVICTI vs sodium phenylbutyrate.[1,8]

SELECTED IMPORTANT SAFETY INFORMATION—WARNINGS AND PRECAUTIONS

- *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.

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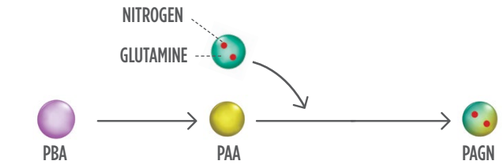
Using key biomarkers of PBA metabolism may help guide RAVICTI dosing for targeted ammonia control[1,12,13]

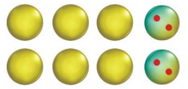
The plasma PAA:PAGN ratio and urinary PAGN may be used along with plasma ammonia and glutamine levels to help guide dosing decisions[1,12,13]

PBA METABOLISM AND ITS BIOMARKERS[1]

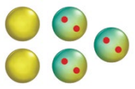


Elevated levels of PAA (>500 µg/mL) are associated with neurotoxicity.[1]

PLASMA PAA:PAGN RATIOS[1,12]



A high plasma PAA:PAGN ratio may indicate a slow or inefficient conjugation reaction to form PAGN, which may lead to increases in PAA without further conversion to PAGN.[1,12]



The plasma PAA:PAGN ratio has generally been **less than 1** in patients with UCDs who did not have significant plasma PAA accumulation.[1]

URINARY PAGN[1,13]

~70% of an administered PBA dose will be converted to urinary PAGN[1]

Urinary PAGN is an indicator of the effectiveness of PBA-based therapies and may be used to **assess patient compliance issues**.[13]

Phenylbutyrate metabolite analysis testing is available through Baylor Genetics and sponsored by Horizon. Order your test kits free of charge at bmgl.com/testing/order-kits

SELECTED IMPORTANT SAFETY INFORMATION—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.

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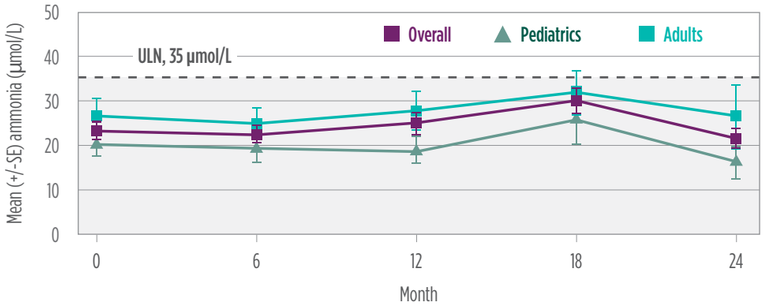
Rethink potential.

RAVICTI provided ammonia control and lower glutamine levels over 24 months, with no new safety concerns, in patients with UCDs[5]

Results from a continued-access, open-label, long-term safety study (primary end point: adverse events; secondary end points: ammonia levels, HAC rates and causes, and neuropsychological testing scores)[5]

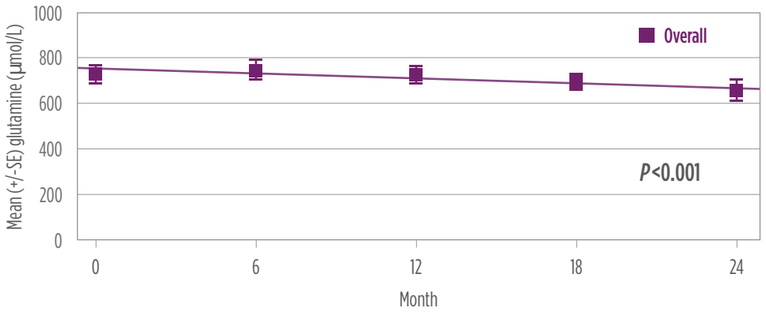
24-MONTH MEAN VENOUS AMMONIA LEVELS[5]



Overall (N)	87	63	61	62	24
Pediatrics (n)	44	25	23	23	11
Adults (n)	43	38	38	39	13

- Mean ammonia levels were below the upper limit of normal (ULN) (greater than 35 µmol/L) through month 36.[5]
- The overall incidence of treatment-emergent adverse events was 93.0% in adults vs 75.6% in pediatric patients, with most events reported as mild to moderate in severity.[5]

24-MONTH MEAN GLUTAMINE LEVELS[5]



Overall (N)	86	62	63	63	24

- Glutamine levels decreased over time with long-term RAVICTI administration in the overall population and this trend is seen in both the adult and pediatric populations.[5]

Please see the full clinical trial study design on pages 8 and 9.

The long-term, sustained control of ammonia and glutamine levels achieved with RAVICTI may help reduce life-threatening HACs in patients with UCDs.[5]

SELECTED IMPORTANT SAFETY INFORMATION—ADVERSE REACTIONS

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

- 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.

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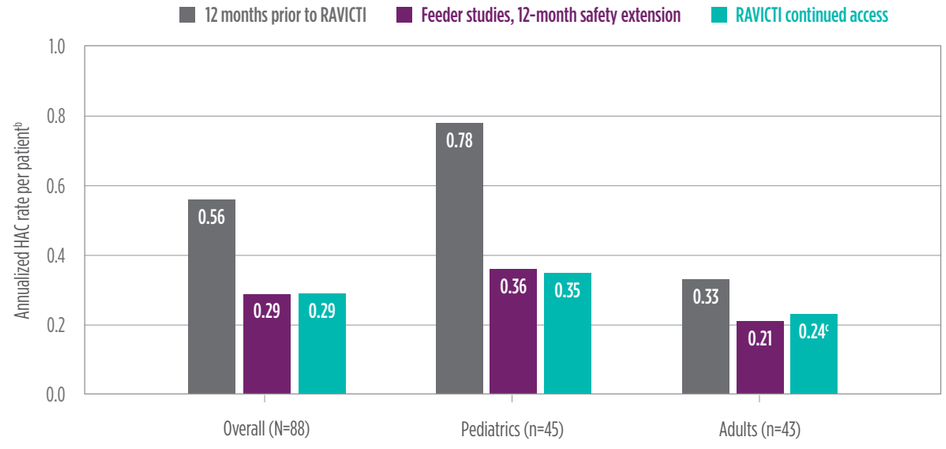
RAVICTI treatment resulted in lower HAC rates in patients with UCDs after 12 months[5]

The annualized HAC rate in the overall population decreased from 0.56 prior to RAVICTI treatment to 0.29 in the 12-month safety extension study[5]

ANNUALIZED HAC RATE AT BASELINE WITH PRE-ENROLLMENT TREATMENT[a] AND AFTER RAVICTI TREATMENT[5]



- The most commonly reported precipitating factors for HACs included intercurrent illness (22.7%), infection (13.6%), and noncompliance with study drug (13.6%).[5]

Please see the full clinical trial study design on pages 8 and 9.

[a]Pre-enrollment treatment: sodium phenylbutyrate.[5]
[b]Annualized HAC rate is calculated by the number of HACs divided by the person-years of dosing.[5]
[c]The adult HAC rate is higher during RAVICTI continued access due to 1 patient who experienced 2 crises during 45 days of participation in the study.[5]

The maintained decrease in annualized HAC rate in the continued-access study demonstrates the durability of response to RAVICTI.[5]

SELECTED IMPORTANT SAFETY INFORMATION—ADVERSE REACTIONS

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

- 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.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid
Rethink potential.

All ages. Multiple clinical trials. One established UCD treatment.[5]

The efficacy and safety of RAVICTI have been evaluated extensively in several clinical trials[5]

90 patients completed 12 months of treatment in the safety extension studies[5]

RAVICTI® (glycerol phenylbutyrate) Oral Liquid

0-2 years

- Uncontrolled open-label study consisting of a transition period to RAVICTI followed by a safety extension period of at least 6 months and up to 24 months of treatment with RAVICTI[14]
- Designed to capture information important for evaluating safety, pharmacokinetics, and efficacy in pediatric patients[14]
- Pooled analysis of 17 patients from different studies on RAVICTI for a range of 6 days to 18.4 months[14]

HPN-100-009
Study length: 6 months in 2 months to less than 2 years age group (n=10); study length: 18 months in 2 months to less than 2 years age group (n=16)[14]

Integrated safety and efficacy population
6 days to 18.4 months (mean 8.85 months)
(N=17)[14]

- Open-label study to assess safety, pharmacokinetics, and ammonia control in pediatric patients with UCDs during treatment with RAVICTI[3,15]
- Consisted of a 10-day switchover period, followed by long-term treatment for up to 12 months[3,15]

2-17 years

- Fixed-sequence, open-label, sodium phenylbutyrate to RAVICTI crossover studies[2,16]
- Compared ammonia levels of patients on RAVICTI with ammonia levels of patients on sodium phenylbutyrate[2,16]

Adults

- 4-week, randomized, double-blind, active-controlled, crossover, noninferiority study comparing RAVICTI with sodium phenylbutyrate[10]
- Evaluated ammonia levels in patients with UCDs who had been on sodium phenylbutyrate prior to enrollment[10]

HPN-100-012
10-day switchover period followed by long-term treatment for up to 12 months
(N=7)[3,15]

HPN-100-005
1-week study
(N=11)[2,15]

HPN-100-012
10-day study
(N=11)[16]

HPN-100-006
4-week study
(N=44)[10]

HPN-100-007
12-month, uncontrolled, open-label study evaluating monthly ammonia control and HACs
(N=51)[5,9,10]

HPN-100-011
Study to assess long-term safety during continued use of RAVICTI for the treatment of patients with UCDs who completed 12 months of treatment in studies HPN-100-005, HPN-100-007, or HPN-100-012
(N=88)[5]

SELECTED IMPORTANT SAFETY INFORMATION—ADVERSE REACTIONS

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

- 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.

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SELECTED IMPORTANT SAFETY INFORMATION—DRUG INTERACTIONS

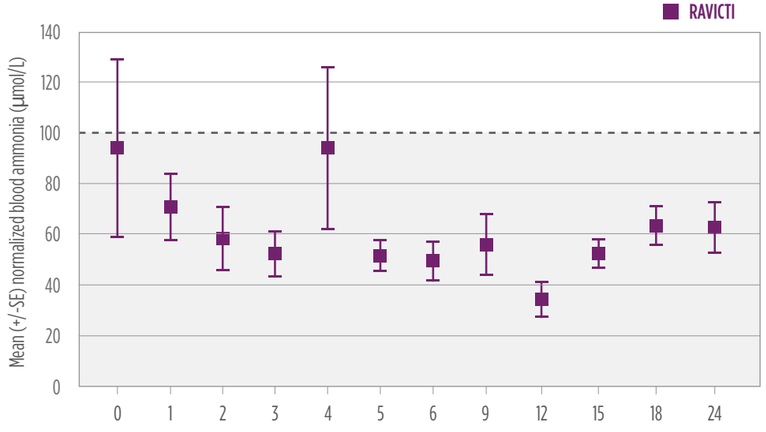
- Corticosteroids, valproic acid, or haloperidol may increase plasma ammonia level. Monitor ammonia levels closely.
- Probenecid may affect renal excretion of metabolites of RAVICTI, including phenylacetylglutamine (PAGN) and PAA.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid
Rethink potential.

RAVICTI provides ammonia control for pediatric patients less than 2 months of age[1]

In an uncontrolled, open-label clinical trial, mean ammonia levels were well controlled over 24 months[1,9]

24-MONTH MEAN VENOUS AMMONIA LEVELS[1,9] | **PEDIATRIC PATIENTS LESS THAN 2 MONTHS OF AGE**



Ammonia levels across different laboratories were normalized to a common normal pediatric range of 28 to 57 µmol/L. Normalized ammonia (µmol/L) = ammonia (µmol/L) × (57/ULN of a laboratory reference range specified for each assay).[1]

Please see the full clinical trial study design on pages 8 and 9.

- Mean venous ammonia levels in patients starting treatment at less than 2 months of age (n=16)[a] were less than 100 µmol/L during treatment with RAVICTI for up to 24 months (range, 35-94 µmol/L).[1]
- In this study, 16 of 16 (100%) patients less than 2 months of age successfully transitioned to RAVICTI within 7 days (4 days of transition followed by 3 days of observation).[1,b]
- Of 16 patients starting treatment at less than 2 months of age in this 24-month study, 5 patients (31%) reported a total of 7 HACs, all of which occurred in patients less than 1 month of age.[1]

[a]Sixteen, 14, 12, 6, and 3 pediatric patients completed 1, 3, 6, 12, and 18 months of treatment, respectively (median exposure of 10 months [range, 2 to 20 months]).[1]
[b]Successful transition was defined as no signs and symptoms of hyperammonemia and a venous ammonia value less than 100 µmol/L.[1]

Now you have the choice to start patients of all ages on RAVICTI—the only oral liquid nitrogen scavenger available.[1]

SELECTED IMPORTANT SAFETY INFORMATION—DRUG INTERACTIONS

- 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.

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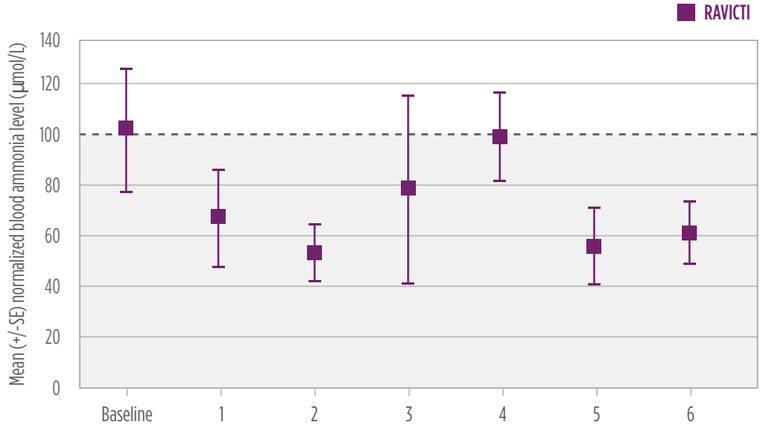
RAVICTI provides ammonia control for pediatric patients 2 months to less than 2 years of age[1]

In uncontrolled, open-label clinical trials, mean ammonia levels were well controlled over 6 months[1,9]

6-MONTH MEAN VENOUS AMMONIA LEVELS[1,9] | **PEDIATRIC PATIENTS 2 MONTHS TO LESS THAN 2 YEARS**



Ammonia levels across different laboratories were normalized to a common normal pediatric range of 28 to 57 µmol/L. Normalized ammonia (µmol/L) = ammonia (µmol/L) × (57/ULN of a laboratory reference range specified for each assay).[1]

Please see the full clinical trial study design on pages 8 and 9.

- In study HPN-100-009 (depicted in graph above), mean venous ammonia levels in patients 2 months to less than 2 years of age (n=10)[c] were less than 100 µmol/L during treatment with RAVICTI for up to 6 months (range, 53-99 µmol/L).[1]
- In study HPN-100-009, 9 of 10 (90%) patients 2 months to less than 2 years of age successfully transitioned to RAVICTI within 7 days.[1,d]
- In another set of studies (HPN-100-012 and HPN-100-011), mean venous ammonia levels in patients 2 months to less than 2 years of age (n=7)[e] were less than 100 µmol/L during treatment with RAVICTI for up to 12 months (range, 31-65 µmol/L).[1]
- Of the 17 pediatric patients 2 months to less than 2 years of age in 3 open-label studies, 7 patients (41%) reported a total of 11 HACs.[1]

RAVICTI is nearly tasteless and odorless; it can be taken orally, even in patients with a nasogastric or gastrostomy tube (g-tube).[1,10]

[c]Nine, 7, and 3 patients completed 1, 3, and 6 months of treatment, respectively (mean and median exposure of 4 and 5 months, respectively).[1]
[d]Successful transition was defined as no signs and symptoms of hyperammonemia and a venous ammonia value less than 100 µmol/L.[1]
[e]Seven, 6, 6, 6, and 3 patients completed 1, 6, 9, 12, and 18 months of treatment, respectively (mean and median exposure of 15 and 17 months, respectively); ammonia values were collected at 1, 3, 6, 9, and 12 months.[1]

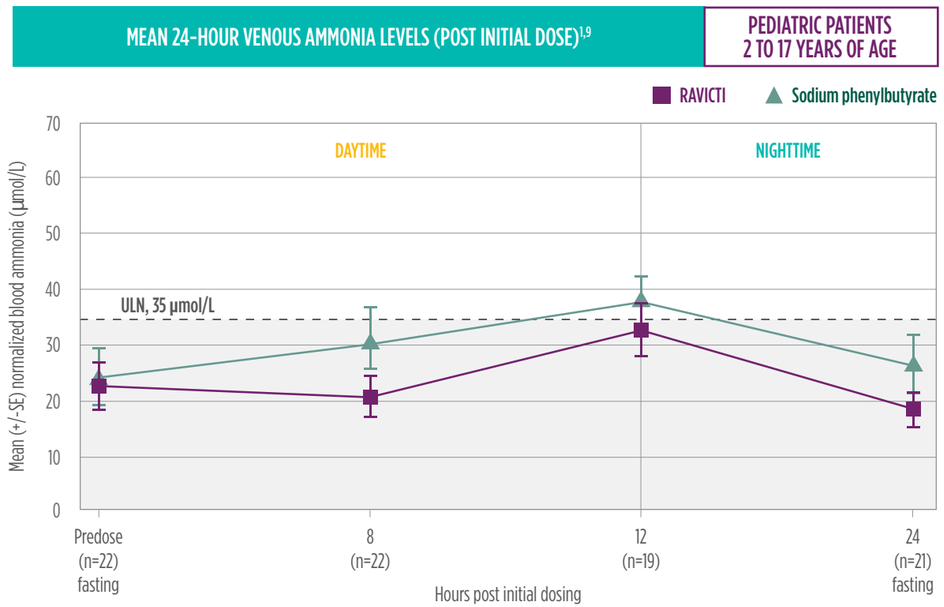
SELECTED IMPORTANT SAFETY INFORMATION—USE IN SPECIFIC POPULATIONS

- *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. A voluntary patient registry monitors pregnancy outcomes in women exposed to RAVICTI. For more information regarding the registry program, visit www.ucdregistry.com or call 1-855-823-2595.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid
Rethink potential.

RAVICTI provides 24-hour ammonia control in pediatric patients with UCDs[1]

In 2 fixed-sequence, open-label, crossover trials, RAVICTI was noninferior to sodium phenylbutyrate and was proven to control ammonia levels over a 24-hour period[1,9]



Ammonia levels across different laboratories were normalized to a common normal range of 9 to 35 µmol/L.
Normalized ammonia (µmol/L) = ammonia (µmol/L) × (35/ULN of a laboratory reference range specified for each assay).[1]

- In patients with UCDs 2 to 5 years of age (n=11), the ammonia $AUC_{0\text{-}24h}$ was 632 µmol•h/L vs 720 µmol•h/L for those on RAVICTI and sodium phenylbutyrate, respectively.[1]
- In patients with UCDs 6 to 17 years of age (n=11), the ammonia $AUC_{0\text{-}24h}$ was 604 µmol•h/L vs 815 µmol•h/L for those on RAVICTI and sodium phenylbutyrate, respectively.[1]

Please see the full clinical trial study design on pages 8 and 9.

11 of 11 pediatric patients from a short-term (2-week) study—or their caregivers—chose to continue with a long-term (12-month) RAVICTI extension study.[1,9,17]

SELECTED IMPORTANT SAFETY INFORMATION—USE IN SPECIFIC POPULATIONS

- *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

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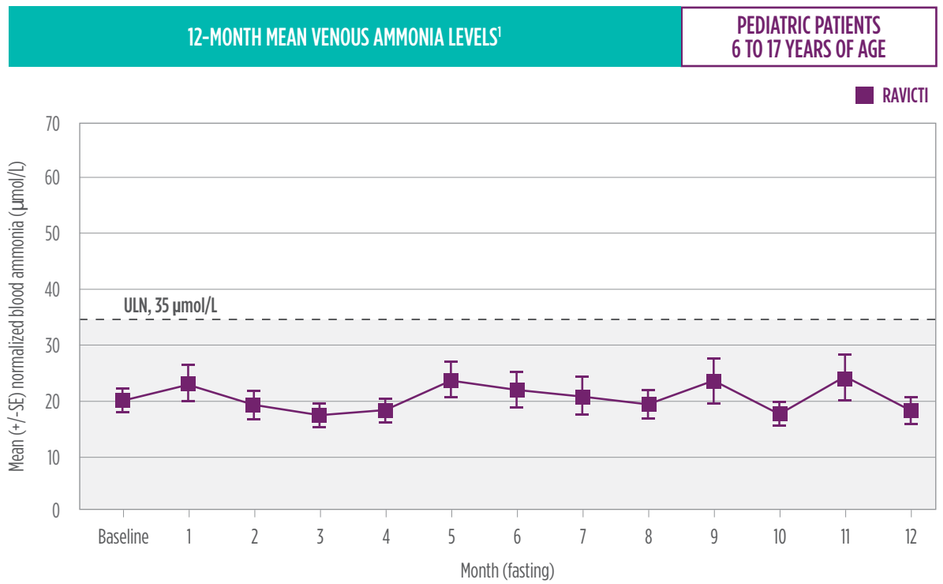
RAVICTI provides effective ammonia control sustained over 12 months in pediatric patients with UCDs[1]

In an uncontrolled, open-label, extension clinical trial, mean blood ammonia levels were well controlled over 12 months[1]



Ammonia levels across different laboratories were normalized to a common normal range of 9 to 35 µmol/L.
Normalized ammonia (µmol/L) = ammonia (µmol/L) × (35/ULN of a laboratory reference range specified for each assay).[1]

- Mean fasting venous ammonia values in pediatric patients (n=26) 6 to 17 years of age were within normal limits (≤35 µmol/L) during long-term treatment with RAVICTI (range, 17-23 µmol/L).[1]
- Of the 26 pediatric patients 6 to 17 years of age participating in these 2 trials, 5 patients (19%) reported a total of 5 hyperammonemic crises.[1]

Please see the full clinical trial study design on pages 8 and 9.

RAVICTI is the only UCD treatment that has been clinically studied over the long term (at least 12 months) in all age groups for control of ammonia.[1]

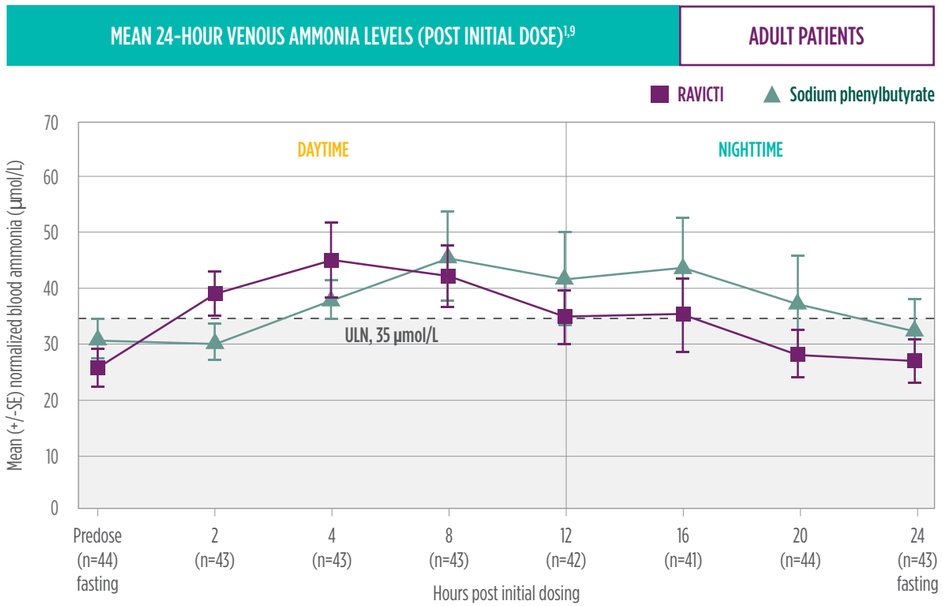
SELECTED IMPORTANT SAFETY INFORMATION—LIMITATIONS OF USE

- 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.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid
Rethink potential.

RAVICTI provides 24-hour ammonia control in adult patients with UCDs[1]

In a randomized, double-blind, active-controlled, crossover clinical trial, RAVICTI was noninferior to sodium phenylbutyrate and was proven to control ammonia levels over a 24-hour period[1,9]



Ammonia levels across different laboratories were normalized to a common normal range of 9 to 35 µmol/L.
Normalized ammonia (µmol/L) = ammonia (µmol/L) × (35/ULN of a laboratory reference range specified for each assay).[1]

- Mean $AUC_{0\text{-}24h}$ levels for venous ammonia (n=44) during steady-state dosing were 866 µmol•h/L and 977 µmol•h/L with RAVICTI and sodium phenylbutyrate, respectively.[1]

Please see the full clinical trial study design on pages 8 and 9.

Of those who completed the short-term trial, 40 of 44 (91%) adult patients previously treated with sodium phenylbutyrate chose to continue with RAVICTI for the long-term study.[1,9,10]

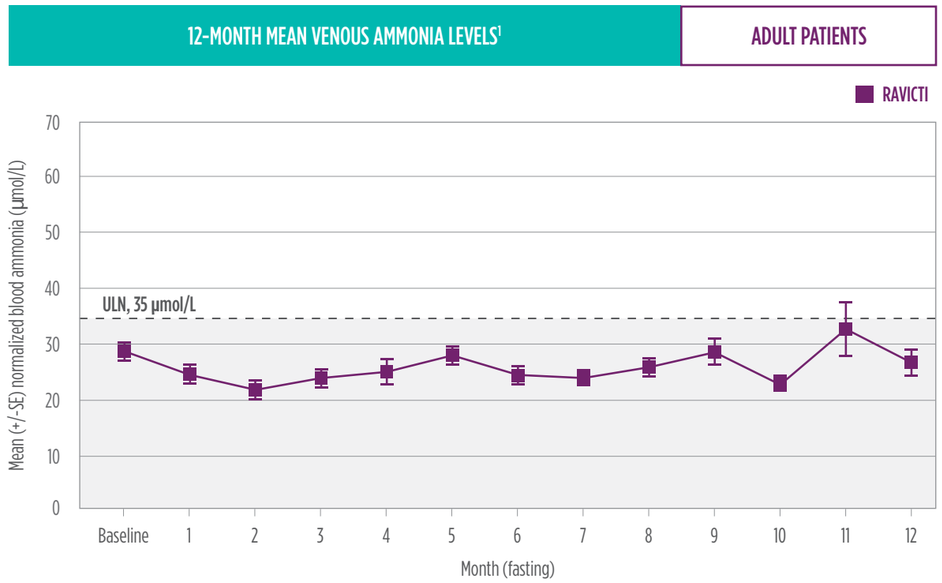
SELECTED IMPORTANT SAFETY INFORMATION—CONTRAINDICATIONS

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

Please review the RAVICTI Important Safety Information on page 22, the BUPHENYL® (sodium phenylbutyrate) Important Safety Information on page 23, the Full Prescribing Information for RAVICTI here, and the Full Prescribing Information for BUPHENYL here.

RAVICTI provides effective ammonia control sustained over 12 months in adult patients with UCDs[1]

In an uncontrolled, open-label, extension clinical trial, mean blood ammonia levels were well controlled over 12 months[1]



Ammonia levels across different laboratories were normalized to a common normal range of 9 to 35 µmol/L.
Normalized ammonia (µmol/L) = ammonia (µmol/L) × (35/ULN of a laboratory reference range specified for each assay).[1]

- Mean fasting venous ammonia values in adults (n=51) were within normal limits (≤35 µmol/L) during long-term treatment with RAVICTI (range, 6-30 µmol/L).[1]
- Of 51 adult patients participating in the 12-month, open-label treatment with RAVICTI, 7 patients (14%) reported a total of 10 hyperammonemic crises.[1]

Please see the full clinical trial study design on pages 8 and 9.

Your patients manage more than just their UCDs. Consider how the convenient dosing and administration of RAVICTI can help your patients.[1,10]

SELECTED IMPORTANT SAFETY INFORMATION—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.

RAVICTI®
(glycerol phenylbutyrate) Oral Liquid
Rethink potential.

Safety of RAVICTI

Adverse reactions reported in 2 or more adult patients with UCDs in a short-term clinical trial[1,a]

SYSTEM ORGAN CLASS PREFERRED TERM	NUMBER (%) OF PATIENTS[1]	
	Sodium phenylbutyrate (n=45)	RAVICTI (n=44)
Gastrointestinal disorders		
Abdominal discomfort	3 (7)	0 (0)
Abdominal pain	2 (4)	3 (7)
Diarrhea	3 (7)	7 (16)
Dyspepsia	3 (7)	2 (5)
Flatulence	1 (2)	6 (14)
Nausea	3 (7)	1 (2)
Vomiting	2 (4)	3 (7)
General disorders and administration-site conditions		
Fatigue	1 (2)	3 (7)
Metabolism and nutrition disorders		
Decreased appetite	2 (4)	3 (7)
Nervous system disorders		
Dizziness	4 (9)	0 (0)
Headache	4 (9)	6 (14)

Adverse reactions reported in pediatric patients with UCDs during long-term clinical trials

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

- 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.[1,b]
- 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.[1,c]
- 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.[1,d]

Please see the full clinical trial study design on pages 8 and 9.

[a]Assessment of adverse reactions in a randomized, double-blind, active-controlled, crossover study of 45 patients with UCDs at least 18 years of age being treated with either RAVICTI or sodium phenylbutyrate for 2 weeks.[1]
[b]Assessment of adverse reactions in 2 open-label studies of 26 patients with UCDs 2 to 17 years of age being treated with RAVICTI for 12 months.[1]
[c]Assessment of adverse reactions in 3 open-label studies of 17 patients with UCDs 2 months to less than 2 years of age (median exposure, 6 months [range, 0.2-18 months]).[1]
[d]Assessment of adverse reactions in 1 open-label study of 16 patients with UCDs who began treatment at less than 2 months of age (median exposure, 10 months [range, 2-20 months]).[1]

Please review the RAVICTI Important Safety Information on page 22, the BUPHENYL® (sodium phenylbutyrate) Important Safety Information on page 23, the Full Prescribing Information for RAVICTI here, and the Full Prescribing Information for BUPHENYL here.

HORIZON Patient Services™ | RAVICTI® (glycerol phenylbutyrate) Oral Liquid
Rethink potential.

Horizon Patient Services offers ongoing support for people taking RAVICTI

Horizon Patient Services is dedicated to improving the lives of people living with UCDs. The Horizon Patient Services program provides ongoing individualized support and education for your patients and their families.

A **patient access manager (PAM)** provides dedicated, one-on-one support for your patients during your patient's treatment journey. They work directly with individual patients to answer non-medical, logistical questions and provide support from treatment initiation.

A **case manager** assigned to your patient may also be in touch with your office to make sure important insurance information is properly shared.

These comprehensive services are free of charge and built around 3 components: **coordinate**, **connect**, and **champion**.

The Horizon Patient Services team will:

COORDINATE

- Help patients address financial barriers by providing education about their insurance benefits.
- Assist in connecting patients with their specialty pharmacy to schedule the shipment of their medicine so they avoid running out of supply.

CONNECT

- Connect your patients to others living with UCDs through live events, peer mentor programs, and online resources.
- Provide tools and resources to help your patients manage the day-to-day challenges of living with UCDs.
- Introduce patients and their families to UCD advocacy groups for more support and inform them of UCD-related events in their area.

CHAMPION

- Serve as a dedicated personal resource and the main point of contact for your patients' ongoing RAVICTI logistical needs.
- Provide your patients with RAVICTI education and answer their nonclinical questions.
- Help patients through changes that may impact their treatment.
- Respond to patient questions and concerns, and connect them with the right resources to get answers.

Visit Ravicti.com to explore all the resources and tools Horizon provides through the Horizon Patient Services program.

SELECTED IMPORTANT SAFETY INFORMATION—WARNINGS AND PRECAUTIONS

- *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.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid
Rethink potential.

RAVICTI resources, tools, and information to support healthcare professionals

At your fingertips, at your convenience, all accessible online

ravictiHCP.com

Prescribing

When prescribing RAVICTI to patients

Download **patient enrollment** and **HIPAA forms** to enroll patients into Horizon Patient Services. A case manager will be in touch with your office to ensure insurance information is properly shared.

Starting

When starting patients on RAVICTI

Use the **RAVICTI dosage guide** to identify starting dose for phenylbutyrate-naïve patients and for patients switching from sodium phenylbutyrate.

Managing

When managing patients taking RAVICTI

Optimize your patients' RAVICTI dosage for ammonia control by ordering a **Phenylbutyrate Metabolite Testing kit** through Baylor Genetics at no cost to you or your patients. Use the RAVICTI dosage guide when optimizing dosage of RAVICTI. A **patient assessment follow-up** can also be downloaded to assess how your patients are doing on RAVICTI.

Contact your Clinical Science Associate for UCD resources, immediate assistance, and additional support.

SELECTED IMPORTANT SAFETY INFORMATION—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.

Please review the RAVICTI Important Safety Information on page 22, the BUPHENYL® (sodium phenylbutyrate) Important Safety Information on page 23, the Full Prescribing Information for RAVICTI here, and the Full Prescribing Information for BUPHENYL here.

Horizon offers resources and support for patients who have been prescribed RAVICTI

If you determine that RAVICTI is right for your patients, Horizon Patient Services can help them get started and stay on therapy

Horizon Patient Services: helps patients manage financial barriers to RAVICTI and provides ongoing support

- Immediately download patient enrollment forms and HIPAA forms, available in English and Spanish at ravictiHCP.com.
- PAMs are available in person or by email, text, or phone with information and guidance. Patients can contact a PAM by calling 1-855-823-7878.
- These comprehensive services are free of charge and built around 3 components: coordinate, connect, and champion.

UCD Mentors: real patients and caregivers who understand what it means to live with a UCD

- UCD Mentors are patients and caregivers living with UCDs who know what patients with UCDs are going through because they also live every day with a UCD.
- Mentors are ready to connect with patients, share their experiences, and answer questions.
- Patients can get an introduction to each UCD Mentor by watching their videos at ravicti.com.

With Horizon, patients on RAVICTI are supported every step of the way.

SELECTED IMPORTANT SAFETY INFORMATION—ADVERSE REACTIONS

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

- 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.

RAVICTI®
(glycerol phenylbutyrate) Oral Liquid
Rethink potential.

Your patients with UCDs may not have time for complicated dosing

RAVICTI offers convenient dosing and easy administration, and requires minimal preparation[1,10]

RAVICTI is nearly tasteless and odorless and has no pills or powder to prepare[1,10]

- RAVICTI is the only FDA-approved oral liquid for the treatment of patients with UCDs.[1]
- RAVICTI can be taken orally, even in patients with a nasogastric or g-tube.[1]

The dosing schedule of RAVICTI works with the timing of your patients' meals or feedings[1]

- Administer RAVICTI orally with food or formula; for infants who are breastfed, administer just prior to breastfeeding.[1]
- For patients 2 years of age and older, the total daily dosage is given in 3 equally divided doses, **each rounded up to the nearest 0.5 mL**.[1]
- For patients less than 2 years of age, the total daily dosage is given in 3 or more equally divided doses, **each rounded up to the nearest 0.1 mL**.[1]
- The maximum daily dosage of RAVICTI (17.5 mL daily) is equivalent to 40 tablets of sodium phenylbutyrate.[1,10]

When prescribing RAVICTI to patients new to treatment with phenylbutyrate and on concurrent dietary protein restriction and/or dietary supplements, consider the patient's residual urea synthetic capacity, dietary protein requirements, and diet adherence.[1]

SELECTED IMPORTANT SAFETY INFORMATION—ADVERSE REACTIONS

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

- 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.

Please review the RAVICTI Important Safety Information on page 22, the BUPHENYL® (sodium phenylbutyrate) Important Safety Information on page 23, the Full Prescribing Information for RAVICTI here, and the Full Prescribing Information for BUPHENYL here.

A nasogastric or g-tube may be used to administer RAVICTI for patients who cannot swallow[1]

Steps for administering RAVICTI by using a nasogastric or g-tube

1

1. Use an oral syringe to withdraw the prescribed dose of RAVICTI from the bottle.[1]

2

2. Place the tip of the syringe into the tip of the nasogastric or g-tube.[1]

3

3. Using the plunger of the syringe, administer RAVICTI into the tube.[1]

4–5

4. Using a large-capacity syringe, **flush once** with 10 mL of water or formula and allow the flush to drain.[1]
5. **If necessary, flush a second time** with an additional 10 mL of water or formula to clear the tube.[1]

- Because RAVICTI is a liquid that is glycerol based, flushing the nasogastric or g-tube is required to ensure that the complete dose is administered.[1]
- For patients who require a volume of less than 1 mL per dose via nasogastric or g-tube, the delivered dose may be less than anticipated; closely monitor the ammonia levels of these patients.[1]

SELECTED IMPORTANT SAFETY INFORMATION—ADVERSE REACTIONS

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

- 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.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid
Rethink potential.

INDICATION and IMPORTANT SAFETY INFORMATION for RAVICTI® (glycerol phenylbutyrate) Oral Liquid

INDICATION

RAVICTI 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.

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. A voluntary patient registry monitors pregnancy outcomes in women exposed to RAVICTI. For more information regarding the registry program, visit www.ucdregistry.com or call 1-855-823-2595.
- *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.

Indication and Important Safety Information for BUPHENYL® (sodium phenylbutyrate) Tablets and Powder

INDICATIONS AND USAGE

BUPHENYL (sodium phenylbutyrate) Tablets for oral administration and BUPHENYL (sodium phenylbutyrate) Powder for oral, nasogastric, or gastrostomy tube administration are 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 (AS).

BUPHENYL 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.

BUPHENYL must be combined with dietary protein restriction and, in some cases, essential amino acid supplementation.

Any episode of acute hyperammonemia should be treated as a life threatening emergency.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- *Acute hyperammonemia:* BUPHENYL should not be used to manage acute hyperammonemia, which is a medical emergency.

WARNINGS AND PRECAUTIONS

- BUPHENYL should not be administered to patients with known hypersensitivity to sodium phenylbutyrate or any component of this preparation.
- Use caution with administering BUPHENYL to patients with:
  - Congestive heart failure or severe renal insufficiency, and in clinical states in which there is sodium retention with edema.
  - Hepatic or renal insufficiency or inborn errors of beta oxidation.
- Probenecid may affect renal excretion of the conjugated product of BUPHENYL as well as its metabolite.
- Use of corticosteroids may cause the breakdown of body protein and increase plasma ammonia levels.
- There have been published reports of hyperammonemia being induced by haloperidol and by valproic acid.

ADVERSE REACTIONS

- The most common adverse reactions (≥3%) reported in BUPHENYL clinical trials were decreased appetite, body odor, bad taste or taste aversion.
- In female patients, amenorrhea/menstrual dysfunction (irregular menstrual cycles) occurred in 23% of the menstruating patients.
- Neurotoxicity was reported in cancer patients receiving intravenous phenylacetate. Manifestations were predominately somnolence, fatigue, and lightheadedness; with less frequent headache, dysgeusia, hypoacusis, disorientation, impaired memory, and exacerbation of a pre-existing neuropathy.
- Laboratory adverse events occurring in >2% of UCD patients by body system were:
  - *Metabolic:* acidosis, alkalosis, hyperchloremia, and hypophosphatemia
  - *Nutritional:* hypoalbuminemia and decreased total protein
  - *Hepatic:* increased alkaline phosphatase and increased liver transaminases
  - *Hematologic:* anemia, leukopenia, leukocytosis, and thrombocytopenia

USE IN SPECIFIC POPULATIONS

- *Pregnancy:* BUPHENYL should be used with caution in patients who are pregnant or planning to become pregnant. Animal reproduction studies have not been conducted with BUPHENYL. It is not known whether BUPHENYL can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity.
- *Lactation:* breastfeeding is not recommended during treatment with BUPHENYL. There are no data on the presence of BUPHENYL in human milk.

Please see Full Prescribing Information.

RAVICTI® (glycerol phenylbutyrate) Oral Liquid
Rethink potential.

With RAVICTI, your patients with UCDs[a] can LIVE CONFIDENTLY[1]

Unique mechanism of action designed for slow release of PBA[1,8]

Absorption of PBA is approximately 70% to 75% slower when administered as RAVICTI vs sodium phenylbutyrate.[1,8]

Established long-term ammonia control for patients of all ages[1]

RAVICTI is the only UCD treatment that has been shown to provide ammonia control in both the short term (2 or 4 weeks) and long term (at least 12 months) in clinical studies.[1]

RAVICTI is the most-prescribed nitrogen scavenger for the treatment of UCDs[9,b]

RAVICTI allows patients to easily switch from sodium phenylbutyrate without any gap in treatment.[1]

Easy administration and convenient dosing[1,10]

RAVICTI is nearly tasteless and odorless with no pills or powder to prepare.[1,10]
RAVICTI can be taken with meals via oral dosing syringe and requires minimal dosing steps.[1,10]

RAVICTI. For what's next.

Call 1-855-UCD-SUPT (1-855-823-7878)

HORIZON Patient Services™

[a]The safety and efficacy of RAVICTI for the treatment of NAGS deficiency have not been established.[1]
[b]According to data sourced from IQVIA and Horizon between July 1, 2018, and May 31, 2019. Based on the total number of unique patients who had at least 1 dispense for RAVICTI in the United States.[9]

SELECTED IMPORTANT SAFETY INFORMATION—CONTRAINDICATIONS

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

References: 1. RAVICTI (glycerol phenylbutyrate) Oral Liquid [prescribing information] Horizon. **2.** Lichter-Konecki U, Diaz GA, Merritt JL II, et al. Ammonia control in children with urea cycle disorders (UCDs); phase 2 comparison of sodium phenylbutyrate and glycerol phenylbutyrate. *Mol Genet Metab.* 2011;103(4):323-329. doi:10.1016/j.ymgme.2011.04.013. **3.** Lee B, Diaz GA, Rhead W, et al. Blood ammonia and glutamine as predictors of hyperammonemic crises in patients with urea cycle disorder. *Genet Med.* 2015;17(7):561-568. doi:10.1038/gim.2014.148. **4.** Enns GM, Porter MH, Francis-Sedlak M, Burdett A, Vockley J. Perspectives on urea cycle disorder management: results of a clinician survey. *Mol Genet Metab.* 2019;128(1-2):102-108. doi:10.1016/j.ymgme.2019.07.009. **5.** Diaz GA, Schulze A, Longo N, et al. Long-term safety and efficacy of glycerol phenylbutyrate for the management of urea cycle disorder patients. *Mol Genet Metab.* 2019;127(4):336-345. doi:10.1016/j.ymgme.2019.07.004. **6.** Summar ML, Dobbelaere D, Brusilow S, Lee B. Diagnosis, symptoms, frequency and mortality of 260 patients with urea cycle disorders from a 21-year, multicentre study of acute hyperammonaemic episodes. *Acta Paediatr.* 2008;97(10):1420-1425. doi:10.1111/j.1651-2227.2008.00952.x. **7.** Häberle J, Boddaert N, Burlina A, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders. *Orphanet J Rare Dis.* 2012;7:32. doi:10.1186/1750-1172-7-32. **8.** Monteleone JPR, Mokhtarani M, Diaz GA, et al. Population pharmacokinetic modeling and dosing simulations of nitrogen-scavenging compounds: disposition of glycerol phenylbutyrate and sodium phenylbutyrate in adult and pediatric patients with urea cycle disorders. *J Clin Pharmacol.* 2013;53(7):699-710. doi:10.1002/jcph.92. **9.** Data on file. Horizon; 2017. **10.** Diaz GA, Krivitzky LS, Mokhtarani M, et al. Ammonia control and neurocognitive outcome among urea cycle disorder patients treated with glycerol phenylbutyrate. *Hepatology.* 2013;57(6):2171-2179. doi:10.1002/hep.26058. **11.** Lee B, Rhead W, Diaz GA, et al. Phase 2 comparison of a novel ammonia scavenging agent with sodium phenylbutyrate in patients with urea cycle disorders: safety, pharmacokinetics and ammonia control. *Mol Genet Metab.* 2010;100(3):221-228. doi:10.1016/j.ymgme.2010.03.014. **12.** Mokhtarani M, Diaz GA, Rhead W, et al. Elevated phenylacetic acid levels do not correlate with adverse events in patients with urea cycle disorders or hepatic encephalopathy and can be predicted based on the plasma PAA to PAGN ratio. *Mol Genet Metab.* 2013;110(4):446-453. doi:10.1016/j.ymgme.2013.09.017. **13.** Mokhtarani M, Diaz GA, Rhead W, et al. Urinary phenylacetylglutamine as dosing biomarker for patients with urea cycle disorders. *Mol Genet Metab.* 2012;107(3):308-314. doi:10.1016/j.ymgme.2012.08.006. **14.** Berry SA, Longo N, Diaz GA, et al. Safety and efficacy of glycerol phenylbutyrate for management of urea cycle disorders in patients aged 2 months to 2 years. *Mol Genet Metab.* 2017;122(3):46-53. doi: 10.1016/j.ymgme.2017.09.002. **15.** Longo N, Holt RJ. Glycerol phenylbutyrate for the maintenance treatment of patients with deficiencies in enzymes of the urea cycle. *Exp Opin Orphan Drugs.* 2017;5(12):999-1010. doi:10.1080/21678707.2017.1405807. **16.** 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;162(6):1228-1234.e1. doi:10.1016/j.jpeds.2012.11.084. **17.** Berry SA, Lichter-Konecki U, Diaz GA, et al. Glycerol phenylbutyrate treatment in children with urea cycle disorders: pooled analysis of short and long-term ammonia control and outcomes. *Mol Genet Metab.* 2014;112(1):17-24. doi:10.1016/j.ymgme.2014.02.007.

Please review the RAVICTI Important Safety Information on page 22, the BUPHENYL® (sodium phenylbutyrate) Important Safety Information on page 23, the Full Prescribing Information for RAVICTI here, and the Full Prescribing Information for BUPHENYL here.

HORIZON

RAVICTI® (glycerol phenylbutyrate) Oral Liquid
Rethink potential.