# Mallinckrodt Presents Data on TERLIVAZ® (terlipressin) for Injection in Patients with Hepatorenal Syndrome-Acute Kidney Injury (HRS-AKI) at the American College of Gastroenterology (ACG) Annual Meeting

October 29, 2024

*– Evaluation of real-world trends and outcomes in hospitalized U.S. HRS-AKI patients treated with TERLIVAZ –*

DUBLIN, Oct. 29, 2024 /PRNewswire/ -- Mallinckrodt plc, a global specialty pharmaceutical company, today announced a poster presentation on TERLIVAZ® (terlipressin) for injection in patients with hepatorenal syndrome (HRS) with rapid reduction in kidney function[1] at the annual meeting of the American College of Gastroenterology (ACG), taking place in Philadelphia from October 25-30, 2024.

TERLIVAZ is the first and only FDA-approved product indicated to improve kidney function in adults with HRS with rapid reduction in kidney function,[1] an acute and life-threatening condition requiring hospitalization.[2] HRS involving rapid reduction in kidney function[1] is estimated to affect more than 42,000 Americans annually, approximately 0.01% of the U.S. population,[3] making it a very rare condition; and rates of hospitalizations are increasing.[4]

**Please see Limitation of Use and Important Safety Information, including Boxed Warning, below.**

The analysis, using a large U.S. administrative claims database, showed real-world socio-demographics, hospital and clinical characteristics, treatment patterns, and clinical outcomes from a retrospective cohort of 125 patients hospitalized with HRS-AKI and treated with TERLIVAZ for two days or more.[5]

In this analysis[5]:

- The majority of HRS-AKI patients (74.4%) had underlying alcoholic liver disease (ALD)
- 97.6% of patients had emergent/urgent admissions, with 84.8% treated at teaching hospitals, and 64.8% at large hospitals with 500+ beds
- The in-hospital mortality rate among patients with HRS-AKI was 17.6%
- TERLIVAZ was used as the first-line treatment in one-fifth of cases (20.8%)
- Among patients with available SCr (baseline and post treatment) data (n=21), HRS reversal, defined as the return of pre-treatment serum creatinine (SCr) to ≤1.5 mg/dL, was 47.6% (n=10)

"The data emphasize the treatment challenges for a subset of HRS-AKI patients at high risk of death," said **Peter Richardson, MRCP (UK), Executive Vice President & Chief Scientific Officer**. "The renal function observed in this real-world cohort aligns with the treatment guidelines for this life-threatening condition."

The limitations of this study include, but are not limited to, small sample sizes, variables in methodology and possible errors and omissions within the data sets.[5]

This study was sponsored by Mallinckrodt Pharmaceuticals. Presentation details can be found below:

**Poster #P4591: Trends in the Early Adoption of Terlipressin Among Hospitalized Adults with Hepatorenal Syndrome in the U.S.: A Real-World Analysis**[5]

- **Presenter:** Robert J. Wong
- **Session Type:** Poster Presentation
- **Session Title:** Trends in the Early Adoption of Terlipressin Among Hospitalized Adults with Hepatorenal Syndrome in the U.S.: A Real-World Analysis
- **Session Date and Time:** Tuesday, October 29, 2024; 10:30 a.m. – 4:00 p.m. ET

**INDICATION AND LIMITATION OF USE**

TERLIVAZ is indicated to improve kidney function in adults with hepatorenal syndrome with rapid reduction in kidney function.

- Patients with a serum creatinine >5 mg/dL are unlikely to experience benefit.

**IMPORTANT SAFETY INFORMATION**

**WARNING: SERIOUS OR FATAL RESPIRATORY FAILURE**

- **TERLIVAZ may cause serious or fatal respiratory failure. Patients with volume overload or with acute-on-chronic liver failure (ACLF) Grade 3 are at increased risk. Assess oxygenation saturation (e.g., $SpO_2$) before initiating TERLIVAZ.**

- **Do not initiate TERLIVAZ in patients experiencing hypoxia (e.g., $SpO_2$ <90%) until oxygenation levels improve. Monitor patients for hypoxia using continuous pulse oximetry during treatment and discontinue TERLIVAZ if $SpO_2$ decreases below 90%.**

**Contraindications**

TERLIVAZ is contraindicated:

- In patients experiencing hypoxia or worsening respiratory symptoms.
- In patients with ongoing coronary, peripheral, or mesenteric ischemia.

**Warnings and Precautions**

- **Serious or Fatal Respiratory Failure:** Obtain baseline oxygen saturation and do not initiate TERLIVAZ in hypoxic patients. Monitor patients for changes in respiratory status using continuous pulse oximetry and regular clinical assessments. Discontinue TERLIVAZ in patients experiencing hypoxia or increased respiratory symptoms.

  Manage intravascular volume overload by reducing or discontinuing the administration of albumin and/or other fluids and through judicious use of diuretics. Temporarily interrupt, reduce, or discontinue TERLIVAZ treatment until patient volume status improves. Avoid use in patients with ACLF Grade 3 because they are at significant risk for respiratory failure.

- **Ineligibility for Liver Transplant:** TERLIVAZ-related adverse reactions (respiratory failure, ischemia) may make a patient ineligible for liver transplantation, if listed. For patients with high prioritization for liver transplantation (e.g., MELD ≥35), the benefits of TERLIVAZ may not outweigh its risks.

- **Ischemic Events:** TERLIVAZ may cause cardiac, cerebrovascular, peripheral, or mesenteric ischemia. Avoid use of TERLIVAZ in patients with a history of severe cardiovascular conditions or cerebrovascular or ischemic disease. Discontinue TERLIVAZ in patients who experience signs or symptoms suggestive of ischemic adverse reactions.

- **Embryo-Fetal Toxicity:** TERLIVAZ may cause fetal harm when administered to a pregnant woman. If TERLIVAZ is used during pregnancy, the patient should be informed of the potential risk to the fetus.

**Adverse Reactions**

- The most common adverse reactions (≥10%) include abdominal pain, nausea, respiratory failure, diarrhea, and dyspnea.

**Please click here to see full Prescribing Information, including Boxed Warning.**

**ABOUT HEPATORENAL SYNDROME (HRS)**

Hepatorenal syndrome (HRS) involving rapid reduction in kidney function[1] is an acute and life-threatening condition that occurs in people with advanced liver disease.[2] HRS is classified into two distinct types – a rapidly progressive type that leads to acute renal failure where patients are typically hospitalized for their care and a more chronic type that progresses over weeks to months.[2] HRS involving rapid reduction in kidney function[1] is estimated to affect more than 42,000 Americans annually, approximately 0.01% of the U.S. population,[3] making it a very rare condition; and rates of hospitalizations are increasing.[4] If left untreated, HRS with rapid reduction in kidney function[1] has a median survival time of less than two weeks and greater than 80 percent mortality within three months.[6]

**ABOUT MALLINCKRODT**

Mallinckrodt is a global business consisting of multiple wholly owned subsidiaries that develop, manufacture, market and distribute specialty pharmaceutical products and therapies. The company's Specialty Brands reportable segment's areas of focus include autoimmune and rare diseases in specialty areas like neurology, rheumatology, hepatology, nephrology, pulmonology, ophthalmology, and oncology; immunotherapy and neonatal respiratory critical care therapies; analgesics; and gastrointestinal products. Its Specialty Generics reportable segment includes specialty generic drugs and active pharmaceutical ingredients. To learn more about Mallinckrodt, visit www.mallinckrodt.com.

**CAUTIONARY STATEMENTS RELATED TO FORWARD-LOOKING STATEMENTS**

This release contains forward-looking statements, including with regard to TERLIVAZ®, its potential to improve health and treatment outcomes, and its potential impact on patients. The statements are based on assumptions about many important factors, including the following, which could cause

actual results to differ materially from those in the forward-looking statements: the effects of Mallinckrodt's recent emergence from bankruptcy; satisfaction of, and compliance with, regulatory and other requirements; actions of regulatory bodies and other governmental authorities; changes in laws and regulations; issues with product quality, manufacturing or supply, or patient safety issues or adverse side effects or adverse reactions associated with TERLIVAZ; and other risks identified and described in more detail in the "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of Mallinckrodt's most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and other filings with the SEC, all of which are available on its website. The forward-looking statements made herein speak only as of the date hereof and Mallinckrodt does not assume any obligation to update or revise any forward-looking statement, whether as a result of new information, future events and developments or otherwise, except as required by law.

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**References**

[1] TERLIVAZ® (terlipressin) for Injection. Prescribing Information. Mallinckrodt Hospital Products Inc. 2023.

[2] National Organization for Rare Disorders. Hepatorenal Syndrome. Available at: https://rarediseases.org/rare-diseases/hepatorenal-syndrome/. Accessed October 2024.

[3] United States Census Bureau: Quick Facts. Available at: https://www.census.gov/quickfacts/fact/table/US/PST045218. Accessed October 2024.

[4] Singh J., Dahiya D.S., Kichloo A., et al. Hepatorenal Syndrome: A Nationwide Trend Analysis from 2008 to 2018. *Annals of Med*. 2021;53:1. 2018-2024 doi.org/10/1080/07853890.

[5] Wong, R.J., Alegretti, A.S., Huang, X., et. al. Trends in the Early Adoption of Terlipressin Among Hospitalized Adults with Hepatorenal Syndrome in the U.S.: A Real-World Analysis. *Abstract to be presented in a poster presentation at the American College of Gastroenterology 2024 Meeting.* October 2024.

[6] Flamm, S.L., Brown, K., Wadei, H.M., et al. The Current Management of Hepatorenal Syndrome–Acute Kidney Injury in the United States and the Potential of Terlipressin. *Liver Transpl*. 2021;27:1191-1202. https://doi.org/10.1002/lt.26072.

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