



Mallinckrodt to Present Data on TERLIVAZ® (terlipressin) for Injection at the 2024 American Association for the Study of Liver Diseases (AASLD) Annual Meeting

October 30, 2024

– Four posters highlight TERLIVAZ research on the potential impact of dosing and outcomes in key subpopulations of adults with HRS with rapid reduction in kidney function¹ –

DUBLIN, Oct. 30, 2024 /PRNewswire/ -- [Mallinckrodt plc](#), a global specialty pharmaceutical company, today announced the presentation of four posters on TERLIVAZ® (terlipressin) for injection in patients with hepatorenal syndrome (HRS) with rapid reduction in kidney function¹ at [The Liver Meeting](#), the annual meeting of the American Association for the Study of Liver Diseases (AASLD) taking place in San Diego from November 15-19, 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 function¹ 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.

Three posters include pooled data from Phase 3 placebo-controlled studies with TERLIVAZ, examining the potential impact of waiting until Day 4 and after 12 doses before assessing HRS reversal; the effect of obesity, as measured by body mass index (BMI), on HRS reversal; and HRS reversal in patients treated with the standard dose and high dose. The fourth poster is an analysis of the Phase 3 CONFIRM study, examining the potential impact of TERLIVAZ treatment on HRS reversal, liver transplant rates, and Model for End-Stage Liver Disease (MELD) scores.

"The data being presented at AASLD expand our knowledge for several subpopulations of HRS patients where there is a critical need and broaden our understanding of potential HRS reversal," said **Peter Richardson, MRCP (UK), Executive Vice President & Chief Scientific Officer**. "We are committed to continuing to evaluate all available clinical data and real-world experience to support the safe and efficacious use of TERLIVAZ for appropriate patients."

Poster #4094: Patience is a Virtue: Evidence for Waiting Until Day 4 and After 12 Doses of Terlipressin Before Evaluating Treatment Response in Patients with HRS-AKI⁵

- **Presenter:** Manhal J. Izzy
- **Session Type:** Poster Presentation
- **Session Title:** Portal Hypertension and Other Complications of Cirrhosis
- **Session Date and Time:** Monday, November 18, 2024; 8:00 a.m. – 5:00 p.m. PT

This pooled patient cohort analysis from three Phase 3 studies evaluated the potential impact waiting until Day 4 (and after 12 doses) on HRS reversal in patients treated with TERLIVAZ.⁵

Poster #4095: The Effect of Obesity on the Clinical Response to Terlipressin in Patients with Hepatorenal Syndrome: Retrospective Assessment from a Pooled Patient Cohort⁶

- **Presenter:** Kavish R. Patidar
- **Session Type:** Poster Presentation
- **Session Title:** Portal Hypertension and Other Complications of Cirrhosis
- **Session Date and Time:** Monday, November 18, 2024; 8:00 a.m. – 5:00 p.m. PT

This pooled analysis of data from two Phase 3 studies assessed the potential effect of BMI and corrected BMI (adjusted for the presence of ascites) on the incidence of HRS reversal in patients treated with TERLIVAZ.⁶

Poster #4096: Role of High Versus Standard Dose of Terlipressin in Reversing HRS-AKI: Pooled Analysis from Phase 3 Clinical Trials⁷

- **Presenter:** Pratima Sharma
- **Session Type:** Poster Presentation
- **Session Title:** Portal Hypertension and Other Complications of Cirrhosis
- **Session Date and Time:** Monday, November 18, 2024; 8:00 a.m. – 5:00 p.m. PT

This pooled analysis of data from three Phase 3 studies assessed the efficacy and safety of TERLIVAZ in patients who received a standard or high (escalated) dose.⁷

Poster #4092: The impact of terlipressin treatment on liver transplantation rates in patients with hepatorenal syndrome-acute kidney injury (HRS-AKI) in the context of the changing MELD score definitions⁸

- **Presenter:** Pierre M. Gholam
- **Session Type:** Poster Presentation
- **Session Title:** Portal Hypertension and Other Complications of Cirrhosis
- **Session Date and Time:** Monday, November 18, 2024; 8:00 a.m. – 5:00 p.m. PT

This analysis showed rates of HRS reversal and liver transplant among a subpopulation of patients treated with TERLIVAZ and reported on changes of MELD scores in patients who would be eligible for treatment per U.S. guidelines.⁸

These analyses were sponsored by Mallinckrodt Pharmaceuticals.

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., SpO₂) before initiating TERLIVAZ.**
- **Do not initiate TERLIVAZ in patients experiencing hypoxia (e.g., SpO₂ <90%) until oxygenation levels improve. Monitor patients for hypoxia using continuous pulse oximetry during treatment and discontinue TERLIVAZ if SpO₂ 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 function¹ 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 function¹ 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 HRS hospitalizations are increasing.⁴ If left untreated, HRS with rapid reduction in kidney function¹ has a median survival time of less than two weeks and greater than 80 percent mortality within three months.⁹

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 Izzy, M.J., Gonzalez, S.A., Jalal, P.K., and Cardoza, S. Patience is a Virtue: Evidence for Waiting Until Day 4 and After 12 Doses of Terlipressin Before Evaluating Treatment Response in Patients with HRS-AKI. *Abstract to be presented in a poster presentation*


at the American Association for the Study of Liver Diseases – The Liver Week Meeting. November 2024.

⁶ Patidar, K.R., Allegretti, A.S., Cullaro, G., et al. The Effect of Obesity on the Clinical Response to Terlipressin in Patients with Hepatorenal Syndrome: Retrospective Assessment from a Pooled Patient Cohort. *Abstract to be presented in a poster presentation at the American Association for the Study of Liver Diseases – The Liver Week Meeting.* November 2024.

⁷ Sharma, P., Lim, N., Kwong, A.J., et al. Role of High Versus Standard Dose of Terlipressin in Reversing HRS-AKI: Pooled Analysis from Phase 3 Clinical Trials. *Abstract to be presented in a poster presentation at the American Association for the Study of Liver Diseases – The Liver Week Meeting.* November 2024.

⁸ Gholam, P.M., Gordon, S.C., Jesudian, A.B., et al. The impact of terlipressin treatment on liver transplantation rates in patients with hepatorenal syndrome-acute kidney injury (HRS-AKI) in the context of the changing MELD score definitions. *Abstract to be presented in a poster presentation at the American Association for the Study of Liver Diseases – The Liver Week Meeting.* November 2024.

⁹ 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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