TERLIVAZ® (terlipressin) for Hepatorenal Syndrome: Drug Order Set Considerations

TERLIVAZ is the first and only FDA-approved treatment for adults with hepatorenal syndrome (HRS) with rapid reduction in kidney function.[1]

Terlipressin is recommended as the preferred treatment for HRS with rapid reduction in kidney function by AASLD guidance and ACG guidelines.[2,3*†‡]

*2021 American Association for the Study of Liver Diseases (AASLD) and 2022 American College of Gastroenterology (ACG).[2,3] Please see individual guidance for specific recommendations.

†Diagnosis, evaluation, and management of ascites, spontaneous bacterial peritonitis and hepatorenal syndrome: 2021 Practice Guidance by the American Association for the Study of Liver Diseases. Biggins SW, Angeli P, Garcia-Tsao G, Ginès P, Ling SC, Nadim MK, Wong F, Kim WR. Copyright © 2021 American Association for the Study of Liver Diseases. Reproduced with permission of John Wiley & Sons, Inc.

‡TERLIVAZ was not evaluated in comparison to other treatments in a head-to-head clinical study.

Disclaimer Statement: *The purpose of this document is to provide considerations for the development of a TERLIVAZ drug order set. This resource is for informational purposes only. Medical judgment should be used when making individual patient treatment decisions. Please refer to the Prescribing Information for full product information.*

MEDICATIONS

Inclusion Criteria (criteria must be met)[1]

- ☐ Hepatorenal syndrome with rapid reduction in kidney function
  - Rapid reduction in kidney function: Increase in SCr ≥0.3 mg/dL from baseline within 48 hours or ≥50% increase in SCr that is known or presumed to have occurred within the preceding 7 days

Exclusion Criteria (any of the following exclude use of terlipressin)[1,4,5]

- ☐ Acute-on-chronic liver failure (ACLF) Grade 3: Any 3 of bilirubin ≥12.0 mg/dL, SCr ≥2.0, encephalopathy Grade 3-4, INR ≥2.5 or platelets ≤20 x 10^9/L, use of vasopressor(s), PaO_2/FiO_2 ratio ≤200 or SpO_2/FiO_2 ratio ≤214
- ☐ Hypoxia (e.g., SpO_2 <90%) or worsening respiratory symptoms
- ☐ Ongoing coronary, peripheral, or mesenteric ischemia
- ☐ History of severe cardiovascular conditions, cerebrovascular and ischemic disease
- ☐ Shock, sepsis, and/or uncontrolled bacterial infection

FiO_2, fraction of inspired oxygen; INR, international normalized ratio; PaO_2, partial pressure of oxygen in the blood; SCr, serum creatinine; SpO_2, oxygen saturation.

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.

SELECT 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%.**

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed Warning.

Terlivaz® terlipressin for injection

TERLIVAZ (Terlipressin)[1]

Initiation (3-day duration)

☐ Terlipressin
0.85 mg (1 vial), IV push, q6 hours
Comments: Reconstitute with 5 mL 0.9% NaCl injection and administer as an IV push over 2 minutes. Administer through a peripheral or central line; a dedicated central line is not required.

Maintenance (maximum of 14 days total therapy)

Assess SCr on Day 4: If SCr has decreased by 30% or more from baseline, CONTINUE terlipressin at 0.85 mg q6 hours. If SCr has decreased by less than 30% from baseline, INCREASE terlipressin to 1.7 mg (2 vials) q6 hours. Continue terlipressin until 24 hours after patient achieves a second consecutive value of ≤1.5 mg/dL at least 2 hours apart or for a maximum of 14 days. If SCr is at or above baseline, discontinue terlipressin.

☐ Terlipressin
0.85 mg (1 vial), IV push, q6 hours
Comments: Terlipressin maintenance dose (maximum of 11 additional days for a max total of 14 days). Reconstitute with 5 mL 0.9% NaCl injection and administer as an IV push over 2 minutes. Administer through a peripheral or central line; a dedicated central line is not required.*
1.7 mg (2 vials), IV push, q6 hours
Comments: Terlipressin maintenance dose (maximum of 11 additional days for a max total of 14 days). Reconstitute with 5 mL 0.9% NaCl injection and administer as an IV push over 2 minutes. Administer through a peripheral or central line; a dedicated central line is not required.*

Concomitant Albumin[1,6]

Concomitant albumin should be considered with terlipressin, as tolerated.

Monitor intravascular volume status throughout terlipressin/albumin therapy. Reduce albumin dose or discontinue albumin if patient is becoming volume overloaded.

Albumin dosing: Albumin 1 g/kg (max 100 g) loading dose on Day 1 and 20 g/day to 40 g/day maintenance dose as clinically indicated.

☐ albumin human, 25%
[ ] mg, IV Piggyback, Injection, Once
Comments: Albumin loading dose 1 g/kg (max 100 g). Maximum infusion rate [ ] ml/hr.

☐ albumin human, 25%
[ ] mg, IV Piggyback, Injection, Daily
Comments: Albumin maintenance dose 20-40 g/day. Begin day following loading dose. Dose may be reduced or discontinued as clinically indicated by volume status. May be used for up to 14 days with terlipressin. Maximum infusion rate [ ] ml/hr.

MONITORING[1]

Laboratory Monitoring

☐ Comprehensive metabolic panel (CMP)
Blood, Drawn Collect

Patient Monitoring

☐ Pulse Oximetry (continuous)

☐ Vital Signs (q [ ] hours)

Safety Monitoring Considerations

☐ Discontinue terlipressin in patients with hypoxia (if SpO_2 decreases below 90%) or with worsening respiratory symptoms

☐ Discontinue terlipressin if patient condition worsens to meet ACLF-3 criteria

☐ Discontinue terlipressin in patients with coronary, peripheral, or mesenteric ischemia

IV, intravenous; NaCl, sodium chloride; q, every; SCr, serum creatinine.

*In the CONFIRM trial, the mean duration of exposure to TERLIVAZ was 6.2 days (range 1 to 15 days).

SELECT IMPORTANT SAFETY INFORMATION

Contraindications

TERLIVAZ is contraindicated:

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

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed Warning.

Terlivaz® terlipressin for injection

IMPORTANT SAFETY INFORMATION (cont'd)

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 see full Prescribing Information, including Boxed Warning.

References:

1. TERLIVAZ® (terlipressin). Prescribing Information. Bridgewater, NJ; 2023: Mallinckrodt Hospital Products Inc.
2. Biggins SW, Angeli P, Garcia-Tsao G, et al. Diagnosis, evaluation, and management of ascites, spontaneous bacterial peritonitis and hepatorenal syndrome: 2021 practice guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2021;74(2): 1014-1048. doi:10.1002/hep.31884.
3. Bajaj JS, O'Leary JG, Lai JC, et al. Acute-on-chronic liver failure clinical guidelines. *Am J Gastroenterol*. 2022;117(2):225-252.
4. Data on File. Ref-05035. Mallinckrodt Pharmaceuticals.
5. Moreau R, Jalan R, Gines P, et al. Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. *Gastroenterology*. 2013;144:1426-1437.
6. ALBUTEIN (albumin [human] U.S.P.) 25% solution. Prescribing Information. Grifols USA, LLC.

Mallinckrodt Pharmaceuticals

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