Terlivaz®
terlipressin for injection

DOSING AND ADMINISTRATION GUIDE

INDICATION

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

LIMITATION OF USE

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%.**

Please see additional Important Safety Information throughout and full Prescribing Information, including BOXED WARNING.

TERLIVAZ—a vasoconstrictor with twice the selectivity for V1 receptors

WHAT IT IS

Proposed mechanism of action[1]

- TERLIVAZ is a synthetic vasopressin analogue
- Has twice the selectivity for vasopressin V1 receptors, targeting the splanchnic circulation,[2] vs V2 receptors[1]
- Acts as both a prodrug for lysine-vasopressin as well as having pharmacological activity on its own

HOW IT WORKS

TERLIVAZ is thought to increase renal blood flow by[1]:

- Reducing portal hypertension
- Reducing blood circulation in portal vessels
- Increasing effective arterial volume and mean arterial pressure (MAP)

TERLIVAZ activity was observed within 5 minutes after administration and maintained for at least 6 hours[a]

Pharmacodynamics[1]:

- **After a single 0.85-mg dose in patients with HRS-AKI, the following was seen within 5 minutes after dose and maintained for at least 6 hours:**
  - **Increase in diastolic, systolic, and MAP**
    - Max change in blood pressure and heart rate: 1.2 to 2 hours post dose
    - MAP: estimated maximum effect = increase of 16.2 mmHg
  - **Decrease in heart rate**
    - Estimated maximum effect for heart rate = decrease of 10.6 beats/min

Pharmacokinetics[1]:

- **Terminal half-life**
  - TERLIVAZ: 0.9 hours
  - Lysine-vasopressin: 3 hours

[a]Other pharmacological therapies currently utilized for the treatment of HRS-AKI have half-lives ranging from ~2.4 minutes to 4 hours.[3-6]

Actor Portrayal

IMPORTANT SAFETY INFORMATION

Contraindications

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

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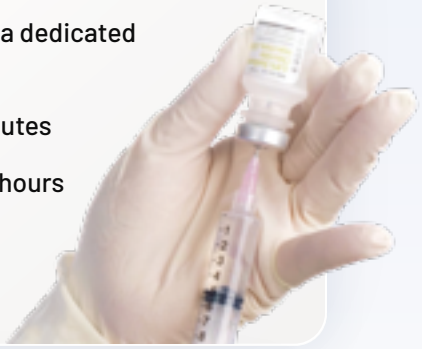
To enable treatment through day 4, consider stocking 20 vials of TERLIVAZ per patient[7]

RECONSTITUTION[1]

- Reconstitute with 5 mL 0.9% sodium chloride injection
- Reconstituted solution does not need to be protected from light

ADMINISTRATION[1]

- Administer through a peripheral or central line; a dedicated central line is not required
- Administer by slow IV bolus injection over 2 minutes
- Administer 0.85 mg (1 vial) of TERLIVAZ every 6 hours
- Flush line after administration



STORAGE[1]

- Store TERLIVAZ vials in the carton under refrigerated conditions at 2°C to 8°C (36°F to 46°F)
- Store in the original carton to protect from light prior to reconstitution
- If not administered immediately after reconstitution, store TERLIVAZ under refrigerated conditions at 2°C to 8°C (36°F to 46°F) for up to 48 hours. Do not freeze

IMPORTANT SAFETY INFORMATION

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.

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Dosing algorithm[1]

After diagnosis and prior treatment of HRS, assess for:

- Oxygen saturation[a]
- ACLF grade
- Volume status

Days 1-3

Record baseline SCr (last available SCr before initiating treatment)
Administer 0.85 mg (1 vial)[b] TERLIVAZ IV every 6 hours

Day 4

Assess SCr level vs basline to determine dose adjustment

If SCr has **decreased** by 30% or more from baseline	If SCr has **decreased** by less than 30% from baseline	If SCr is **at or above** baseline value
Continue 0.85 mg TERLIVAZ every 6 hours	TERLIVAZ may be increased to 1.7 mg (2 vials) every 6 hours	Discontinue TERLIVAZ

Continue TERLIVAZ until 24 hours after patient achieves a second consecutive SCr value of ≤1.5 mg/dL at least 2 hours apart or for a maximum of 14 days

After treatment[8]

Recurrence may occur after treatment discontinuation, and patient may be re-treated if appropriate

ACLF, acute-on-chronic liver failure; HRS, hepatorenal syndrome; IV, intravenous; SCr, serum creatinine; SpO_2, oxygen saturation.
[a]Do not use TERLIVAZ in patients experiencing hypoxia (eg, SpO_2 <90%) until hypoxia resolves.[1]
[b]One vial of TERLIVAZ is equivalent to 0.85 mg of terlipressin or 1 mg of terlipressin acetate.[1]

Please see a video about practical considerations for treating appropriate patients with TERLIVAZ

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (cont'd)

- **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.

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Considerations to manage the risk of respiratory failure

Monitor all patients for changes in respiratory status using continuous pulse oximetry and regular clinical assessments.[1]

Risk factors for respiratory failure[1]	If present prior to initiation[1]	During treatment[1]
Hypoxia (SpO_2 <90%)	Do not initiate until oxygenation levels improve	Discontinue TERLIVAZ
ACLF grade 3	Avoid use due to significant risk of respiratory failure	Avoid use due to significant risk of respiratory failure
Intravascular volume overload	Use caution. Reduce or discontinue the administration of albumin and/or other fluids, and judiciously use diuretics	Manage by reducing or discontinuing the administration of albumin and/or other fluids and judicious use of diuretics. Temporarily interrupt, reduce, or discontinue TERLIVAZ until patient's intravascular volume status improves

In the phase 3 pivotal trial, when respiratory failure occurred with TERLIVAZ, the median onset was 5 days, the mean onset was 7.5 days, and the range was 1 to 67 days.[7]

How to monitor intravascular volume status

Symptoms of volume overload can range in severity and include[9,10]

- Weight gain
- Edema
- Hypertension
- Dyspnea
- Jugular venous distention (indicative of heart failure)

Assessing fluid status consists of both invasive and noninvasive methods, including[9,10]

- Physical exam
- Vital signs
- Chest X-ray
- Central venous pressure
- Urine output
- Pulse pressure variation
- IVC diameter/compressibility

IVC, inferior vena cava.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions (cont'd)

- **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.

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Terlipressin is recommended as the preferred vasoconstrictor treatment for HRS with rapid reduction in kidney function[a]

AASLD GUIDANCE 2021[8,b]

"The treatment of choice for HRS-AKI[c] is vasoconstrictor drugs in combination with albumin. The preferred drug is terlipressin."

ACG GUIDELINES 2022[11]

"In hospitalized patients with cirrhosis and HRS-AKI[c] without high grade of ACLF or disease, we suggest terlipressin (moderate quality, conditional recommendation) or norepinephrine (low quality, conditional recommendation) to improve renal function.[d]"

Clinical experience of patients treated with TERLIVAZ in CONFIRM

84.4%
OF THE TIME WERE TREATED ON THE FLOOR[12,13]

6.2 DAYS
WAS THE MEAN DURATION OF TREATMENT[7]
8% of patients received treatment for >12 days[7]

20.3 DOSES
MEAN TOTAL OF DOSES RECIEVED[7]
28.6% of patients received a dose increase[7]

AASLD, American Association for the Study of Liver Diseases; ACG, American College of Gastroenterology; HRS-AKI; hepatorenal syndrome–acute kidney injury.

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

[b]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.

[c]Definition of kidney injury for HRS-AKI: increase in SCr of ≥0.3 mg/dL from baseline within 48 hours or percent increase in SCr that is ≥50% of what was known or presumed to have occurred within the prior 7 days.[8,11]

[d]In the ACG guidelines, a strength of recommendation is given as either strong (recommendations) or conditional (suggestions).[11]

IMPORTANT SAFETY INFORMATION

Adverse Reactions

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

References: 1. TERLIVAZ® (terlipressin). Prescribing Information. [Bridgewater, NJ: Mallinckrodt Hospital Products Inc.] **2.** Mattos AZ, Schacher FC, Mattos AA. Vasoconstrictors in hepatorenal syndrome: a critical review. *Ann Hepatol*. 2019;18(2):287-290. doi:10.1016/j.aohep.2018.12.002 **3.** LEVOPHED. Prescribing information. Hospira, Inc.; 2020. **4.** Midodrine hydrochloride. Prescribing information. Mylan Pharmaceuticals Inc.; 2022. **5.** Sandostatin. Prescribing information. Novartis Pharmaceuticals Corporation; 2023. **6.** Vasostrict. Prescribing information. Par Pharmaceuticals Companies, Inc.; 2023. **7.** Data on File – Ref-05035. Keenova Therapeutics. **8.** 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 **9.** Kalantari K, Chang JN, Ronco C, Rosner MH. Assessment of intravascular volume status and volume responsiveness in critically ill patients. *Kidney Int*. 2013;83(6):1017-1028. doi:10.1038/ki.2012.424 **10.** Castera MR, Borhade MB. Fluid management. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2025. Updated October 22, 2023. Accessed January 30, 2025. https://www.ncbi.nlm.nih.gov/books/NBK532305/ **11.** Bajaj JS, O'Leary JG, Lai JC, et al. Acute-on-chronic liver failure clinical guidelines. *Am J Gastroenterol*. 2022;117(2):225-252. doi:10.14309/ajg.0000000000001595 **12.** Karvellas CJ, Subramanian R, Olson JC, Jamil K. Role of terlipressin in patients with hepatorenal syndrome-acute kidney injury admitted to the ICU: a substudy of the CONFIRM trial. *Crit Care Explor*. 2023;5(4):e0890. doi:10.1097/CCE.0000000000000890 **13.** Huang X, Bindra J, Chopra I, Niewoehner J, Wan GJ. Treatment-related cost analysis of terlipressin for adults with hepatorenal syndrome with rapid reduction in kidney function. *Adv Ther*. 2023;40(12):5432-5446. doi:10.1007/s12325-023-02674-z

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US-2600314 / June 2026 www.Terlivaz.com

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