TERLIVAZ® is the first and only FDA-approved therapy to improve kidney function in adults with HRS with rapid reduction in kidney function[1]

Terlivaz®
terlipressin for injection

Key considerations when initiating TERLIVAZ

Actor Portrayal

Terlipressin is recommended as the preferred vasoconstrictor treatment for hepatorenal syndrome (HRS) with rapid reduction in kidney function by AASLD Guidance and ACG guidelines[2,3]

AASLD, American Association for the Study of Liver Diseases; ACG, American College of Gastroenterology.

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.

HRS diagnosis and treatment often involve coordinated and timely decisions from a multidisciplinary team[2,a]

- Hepatologist/transplant hepatologist
- Nephrologist/transplant nephrologist
- Transplant surgeon
- Gastroenterologist
- Intensivist
- Hospitalist
- Pharmacist
- Nurse practitioner
- Physician assistant

Early intervention is recommended to help achieve better outcomes.[5,6]

If left untreated, the kidney damage from HRS that is initially reversible can lead to permanent damage in the form of irreversible renal failure.[4]

[a]Multidisciplinary teams may include other healthcare professionals not listed.

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.

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Identifying the appropriate HRS patient is the critical first step

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AASLD criteria for HRS diagnosis[2]

- Cirrhosis with ascites
- 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
- Absence of shock
- No improvement after 48 hours of diuretic withdrawal and volume expansion with albumin (1 g/kg body weight per day)
- No current or recent treatment with nephrotoxic drugs
- Absence of parenchymal kidney disease

VA criteria for TERLIVAZ® (terlipressin) use[7,a]

Inclusion

- ✓ Hospitalized inpatient
- ✓ Documented initial nonresponse to volume expansion (eg, albumin)
- ✓ Documented diagnosis of HRS with acute kidney injury made by a VA expert in gastroenterology/hepatology, nephrology, intensive care, or liver transplant surgery

Exclusion

- ✗ ACLF grade 3[b]
- ✗ SCr >5 mg/dL
- ✗ Listed for liver transplant with MELD ≥35
- ✗ Hypoxia (eg, SpO_2 <90%) or worsening respiratory symptoms. May use TERLIVAZ once oxygenation improves
- ✗ Ongoing signs or symptoms of coronary, peripheral, or mesenteric ischemia
- ✗ History of severe cardiovascular conditions, cerebrovascular and ischemic disease

Review the TERLIVAZ Monograph and Criteria for Use documents published by the VA to aid in implementation of TERLIVAZ in your institution.[a]

[a]Full guidance available at https://www.va.gov/formularyadvisor/drugs/4041768-TERLIPRESSIN-INJ-PWDR.
[b]Based on Chronic Liver Failure Consortium (CLIF-C) Organ Failure Score.
ACLF, acute-on-chronic liver failure; MELD, model for end-stage liver disease; SCr, serum creatinine; SpO_2, oxygen saturation; VA, Veterans Affairs.

SELECT 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.

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

Initiating and dosing TERLIVAZ®

- **Consider stocking at least 20 vials** of TERLIVAZ per patient treatment initiation
- In the phase 3 pivotal trial, TERLIVAZ **was used ~85%**[a] **of the time on the floor**[8]
  - Mean duration of **treatment was 6.2 days**[8]
  - Mean number of doses exposed was 20.3[8,b]
- The full Prescribing Information **does not include a requirement for cardiac monitoring**[1,c]
- TERLIVAZ can be administered through a peripheral IV line; **a dedicated central line is not required**[1]

Dosing algorithm[1]

After diagnosis and prior to treatment of HRS, assess for:
• Oxygen saturation* • ACLF grade • Volume status

Days 1-3
Initial dose: 0.85 mg (1 vial) TERLIVAZ IV every 6 hours
Baseline SCr[d]: Record on Day 1

Day 4
Assess SCr level vs baseline

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 (1 vial) 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[2]
Recurrence may occur after treatment discontinuation, and patient may be retreated if appropriate

***Do not use TERLIVAZ in patients experiencing hypoxia (eg, SpO_2 <90%) until hypoxia resolves.**

IV, intravenous.
[a]Please note, this is an approximate value; the exact value was 84.4% on the floor.
[b]One dose is 0.85 mg of TERLIVAZ per vial.
[c]**You are advised to use your own medical judgment in making patient-specific treatment decisions.**
[d]Baseline SCr is the last available SCr before initiating treatment.

SELECT 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.

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

Considerations to reduce the risk of respiratory failure

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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	Reduce or discontinue the administration of albumin and/or other fluids and judiciously use diuretics. Temporarily interrupt, reduce, or discontinue TERLIVAZ until patient volume status improves

In the phase 3 pivotal trial, when respiratory failure occurred with TERLIVAZ, it generally did not occur immediately following drug initiation.[8]

The median onset was 5 days, the mean onset was 7.5 days, and the range was 1 to 67 days.[8]

SELECT IMPORTANT SAFETY INFORMATION

Warnings and Precautions (cont'd)

- **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.

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

Establishing a TERLIVAZ® (terlipressin) protocol that encourages early treatment of HRS may help to reverse rapid reduction in kidney function[6]

REVIEW ADDITIONAL RESOURCES AND SUPPORT FOR TERLIVAZ.

SELECT IMPORTANT SAFETY INFORMATION

Adverse Reactions

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

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References:

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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. doi:10.14309/ajg.0000000000001595. https://journals.lww.com/ajg/Fulltext/2022/02000/Acute_on_Chronic_Liver_Failure_Clinical_Guidelines.15.aspx
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5. Angeli P, Gines P, Wong F, et al. Diagnosis and management of acute kidney injury in patients with cirrhosis: revised consensus recommendations of the International Club of Ascites. *Gut*. 2015;64(4):531-537. doi:10.1136/gutjnl-2014-308874
6. Curry MP, Vargas HE, Befeler AS, Pyrsopoulos NT, Patwardhan VR, Jamil K. Early treatment with terlipressin in patients with hepatorenal syndrome yields improved clinical outcomes in North American studies. *Hepatol Commun*. 2023;7(1):e1307. doi:10.1097/01.HC9.0000897228.91307
7. Veterans Affairs. Terlipressin (TERLIVAZ) in hepatorenal syndrome with acute kidney injury criteria for use. https://www.va.gov/formularyadvisor/DOC_PDF/CFU_Terlipressin_TERLIVAZ_in_Hepatorenal_Syndrome_Criteria_Mar_2023.pdf.
8. Data on File. Ref-05035. Mallinckrodt Pharmaceuticals.

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