Algorithm for Diagnosis and Management of HRS-AKI/HRS-1*

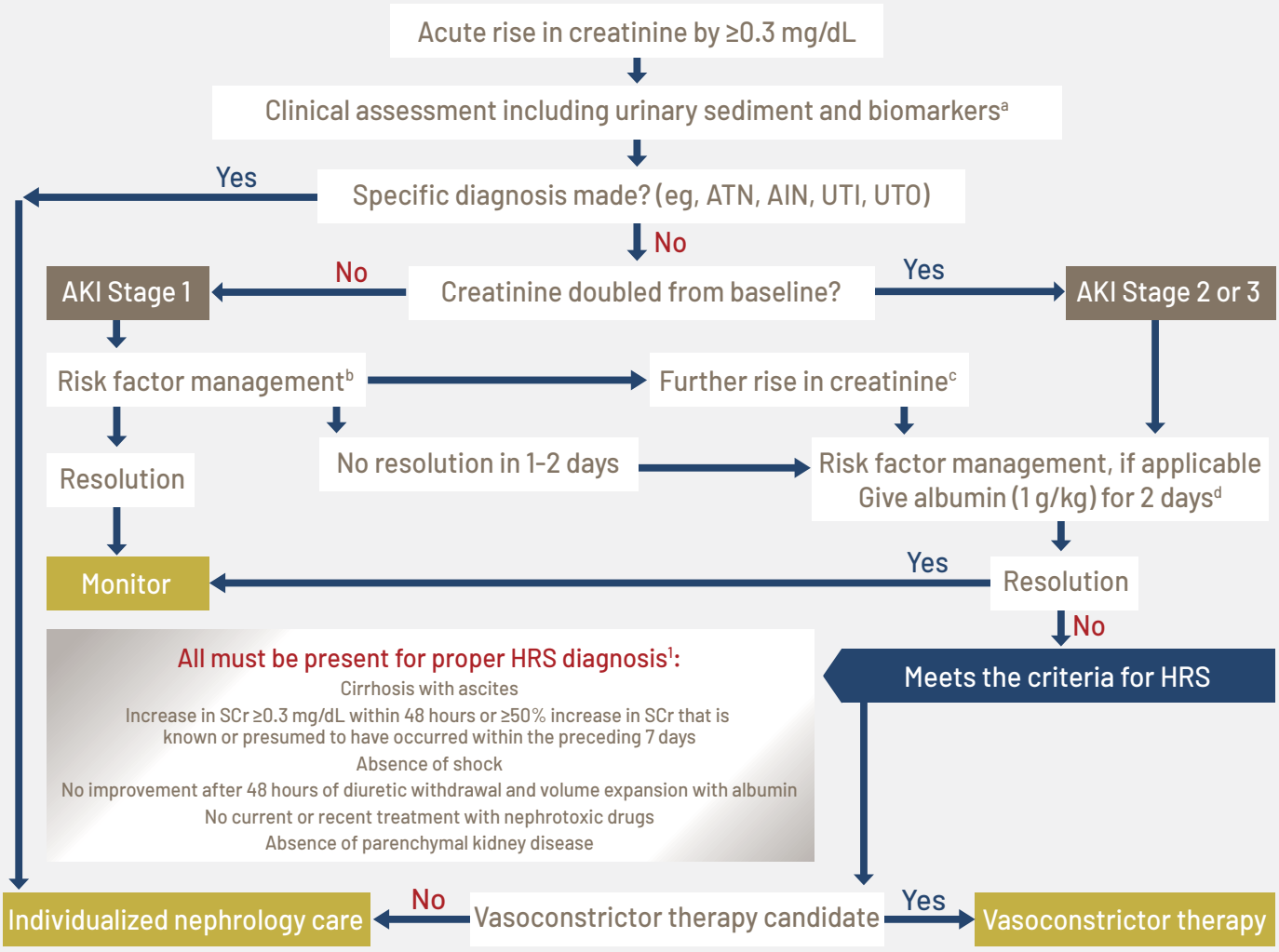
Based on the 2021 American Association for the Study of Liver Diseases (AASLD) Guidance[1]

This document is intended as an information reference only and is not intended to replace your independent judgment.
You are ultimately responsible for determining the appropriate diagnosis and treatment for each patient.

Confirm diagnosis of cirrhosis and ascites

Diagnose and manage AKI

- AKI is defined as an increase in SCr ≥0.3 mg/dL within 48 hours; OR a percentage increase in SCr ≥50% from baseline, known or presumed to have occurred within the prior 7 days.
- An SCr value from the previous 3 months can be used as a baseline SCr. In patients where more than one SCr value is available, the value closest to the hospital admission should be used.



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 on the next page of this document and full Prescribing Information, including BOXED WARNING.

AASLD, American Association for the Study of Liver Diseases; AIN, acute interstitial nephritis; AKI, acute kidney injury; ATN, acute tubular necrosis; HRS, hepatorenal syndrome; SCr, serum creatinine; UTI, urinary tract infection; UTO, urinary tract obstruction.

[a] Clinical assessment includes evaluation for prerenal (eg, overdiuresis, dehydration) or structural (eg, shock, nephrotoxins, obstructive uropathy) etiologies.

[b] Risk-factor management includes the withdrawal of nephrotoxic drugs, reduction or withdrawal of diuretics, detection, and treatment of infections, if present, and volume replacement (if severely volume-depleted) using 5% albumin or crystalloids, preferably balanced, initially.

[c] Patients experiencing a further rise in serum creatinine despite risk-factor management may immediately proceed to the next step, namely albumin challenge. Some members of the writing group advocate taking into account the absolute creatinine value in addition to the change in creatinine to expedite this step to allow earlier institution of vasoconstrictors in patients with a high (eg, >1.5 mg/dL) creatinine.

[d] These patients are expected to have ascites, commonly refractory, and almost always hyponatremia.

Terlivaz® terlipressin for injection

The AASLD Guidance[1] Lists Terlipressin as the Preferred Vasoconstrictor for the Treatment of HRS With Rapid Reduction in Kidney Function[a]

AASLD Guidance Treatment Recommendations[1*]

- Preferred drug: terlipressin (in combination with albumin)
- In settings where terlipressin is not available, norepinephrine should be given
- If neither can be administered, a trial of midodrine and octreotide may be considered
- When treating with vasoconstrictor therapy, albumin should be infused at 1 g/kg on Day 1 of therapy, followed by 40-50 g/day and continued for the duration of therapy

Other treatment options, such as RRT and transplant, could be considered for certain patients if vascoconstrictor therapy is not recommended.

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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 see full Prescribing Information, including BOXED WARNING.

RRT, renal replacement therapy.

[a]TERLIVAZ has not been studied in comparison to other treatment options in a head-to-head clinical trial.

*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.

1. Biggins SW, Angeli P, Garcia-Tsao G, et al. Erratum: Diagnosis, Evaluation, and Management of Ascites and Hepatorenal Syndrome: 2021 Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology*. 2024 Nov;80(5):89. doi:10.1097/HEP.0000000000000983. 2. Bajaj JS, O'Leary JG, Lai LC, et al. Acute-on-chronic liver failure clinical guidelines. *Am J Gastroenterol*. 2022;117(22):225-252.

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