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Decompensated Chronic Liver Failure: Focus on Pharmacotherapy

Updated March 2026

Hepatic decompensation is defined by the appearance of the clinical manifestations of portal hypertension:[1,2]

- Ascites (commonly the first evidence of decompensation): abdominal fluid accumulation caused by extravasation of lymph into the peritoneum and sodium retention due to portal hypertension and splanchnic vasodilation, respctively.[2.3]
  - Complications of ascites include electrolyte imbalances (e.g., hyponatremia), SBP, AKI, and HRS.[2]
- HE: brain dysfunction due to ammonia accumulation.[4]
- Variceal hemorrhage

Medications to Use with Caution or Avoid

- Medications that can trigger HRS:[2,26]
  - Drugs that reduce kidney perfusion (e.g., ACE inhibitors, ARBs, alpha blockers, NSAIDs [including celecoxib], dipyridamole)
  - Nephrotoxic drugs (e.g., aminoglycosides, amphotericin)
- Medications that can trigger HE:
  - medications that can alter mental status (e.g., antidepressants, benzodiazepines, opiates, sedating antipsychotics, antihistamines)[9,10]
  - medications that can cause GI bleeding (e.g., NSAIDs, anticoagulants)[10]
  - medications that can cause AKI (e.g., NSAIDs)[10]
  - medications that cause constipation[10]
  - medications that cause dehydration[10]
  - medications that cause electrolyte disturbances (e.g., diuretics)[10]

Dietary and Lifestyle Interventions

- Alcohol abstinence.[2] Acute alcohol consumption (e.g., binge drinking) can trigger HE.[9]
- Sodium restriction (e.g., 2,000 mg/day)[2]
- Fluid restriction (reserve for significant hyponatremia [e.g., serum sodium ≤125 mmol/L) or if sodium drops precipitously.[2]
- Plant and dairy proteins might be less likely to contribute to HE than animal protein, but ensure adequate protein intake if substitution is made.[14] Benefit is likely small.[14]

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DIURETICS for ASCITES

- Use the lowest effective dose; diuretics can precipitate HE or kidney injury, especially in patients without peripheral edema.[5,8]
- The most commonly used diuretic is **spironolactone**.[2]
  - Start with spironolactone 100 mg once daily.[2] Doses can be adjusted every three to four days to achieve weight loss of about 0.5 kg/day (no edema present) to ≤1 kg/day (edema present).[8]
  - **Amiloride** or **eplerenone** could be substituted in patients who cannot tolerate spironolactone, but they are not as effective.[8]
    - Recommend an initial amiloride dose of 10 mg/day. Amiloride can be titrated to a max of 30 mg/day.[2]
- Patients with long-standing ascites will need a combination of spironolactone and furosemide (initial 40 mg/day).[2]
  - Spironolactone and furosemide are commonly used in a 100 mg:40 mg ratio.[8]
  - In patients with concomitant chronic kidney disease, higher doses of loop diuretics relative to aldosterone antagonists may be needed.[2]
  - Torsemide or bumetanide could be tried in patients with poor response to furosemide.[2]
- Max recommended doses are spironolactone 400 mg/day and furosemide 160 mg/day.[8]
  - Monitor electrolytes and kidney function at least weekly during the first month of therapy.[7]
- In the hospital, loop diuretics can be given two to three times daily, or via continuous infusion.[8]

LACTULOSE for HE

- Lactulose reduces ammonia levels and is the cornerstone of treatment of HE. It is associated with reduced mortality in overt encephalopathy.[17] Lactulose is used to treat acute episodes and prevent future episodes of HE.[10,14]
- Dosing: oral lactulose 20 to 30 mL 2 to 3 times daily (every 4 hours for inpatients), titrating to 2 to 4 soft bowel movements/day.[10] Advise against evening dosing.[10]
- If oral administration is not possible, lactulose can be given rectally.[13] Dosing: Lactulose 300 mL (200 g) in 700 mL water or normal saline given as an enema and retained for 30 to 60 minutes.[13] May repeat every 4 to 6 hours.[13] Resume oral therapy as soon as able, giving the first dose before stopping rectal administration.[13]

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ANTIBIOTICS are used for

- **Treatment of HE**. Antibiotics are thought to work by reducing ammonia-producing GI bacteria.[4,12]
  - Rifaximin 550 mg BID is added to lactulose therapy in patients with continued HE episodes despite lactulose therapy, or for acute episodes that don't respond to lactulose within 24 hours.[4,10]
    - US: rifaximin may require prior authorization, so start the process before discharge to reduce risk of therapy interruption and readmission.[10]
  - Neomycin is a rifaximin alternative.[11]
    - Concerns with neomycin include ototoxicity and nephrotoxicity, especially with long-term use.[12] Monitor kidney function in patients taking it for >2 weeks.[12] It can also interfere with absorptions of macronutrients, medications (e.g., digoxin, penicillin), vitamins (e.g., B12, vitamin K), and iron.[12]
  - Neomycin dosing ranges from 500 to 1,000 mg every six hours for five to six days.[12,13]
- **Primary Prophylaxis of SBP** in at-risk patients.
  - At-risk patients: post-upper GI hemorrhage; OR patients with ascitic fluid protein levels <1.5 g/dL AND kidney insufficiency [SCr >1.2 mg/dL, BUN >25 mg/dL, or serum sodium <130 mEq (mmol)/L] OR patients with liver failure [Child-Pugh score >9 and bilirubin >3 mg/dL]).[2]
    - post-upper GI bleed: ceftriaxone 1 g daily, until bleeding and vasopressors are stopped, up to seven days.[2]
    - other patients (or step-down from ceftriaxone): ciprofloxacin 500 mg PO q 12 h or TMP/SMX 1 DS tablet q 12 h[2,15]
- **Treatment of SBP**
  - Treatment includes an antibiotic plus albumin (see albumin section).[16]
  - Start antibiotics in the emergency department; every hour delay increases mortality.[16]
  - Third generation cephalosporins are appropriate if multi-drug resistance is not of concern (i.e., community-acquired organism).[2,15]
    - Example: ceftriaxone 1 g every 24 hours.[15]
  - A carbapenem is recommended if multi-drug resistance is of concern (e.g., nosocomial infection, recent hospitalization, exposure to broad-spectrum antibiotics).[2] Also consider MRSA and VRE coverage, depending on institutional prevalence.[17]
    - Example: piperacillin/tazobactam 4.5 g IV q 6 h +/- vancomycin or daptomycin[15]
- **Secondary Prophylaxis of SBP**
  - Ciprofloxacin 500 mg once daily.[2,15] Alternatives: TMP/SMX 1 DS tablet once daily or rifaximin 400 mg TID or 550 mg BID[15]
- **Prophylaxis in Upper Gastrointestinal Bleeding**
  - Start intravenous antibiotics at presentation and continue for 2 to 5 days (until stability for discharge or 5 days, whichever is less).[19] Continue in the event of active infection.[19] Consider ceftriaxone 1 g q 24 h, but consider local resistance patterns.[19]
  - A meta-analysis suggests that prophylaxis reduces infection risk, but not mortality.[18] Level A-1 evidence to support prophylaxis is lacking.[18]

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ALBUMIN is used

- With **paracentesis**. Administer albumin to patients who have >5 L of fluid removed to prevent postparacentesis circulatory dysfunction and maintain blood flow to the kidneys.[2]
  - Recommend IV albumin 6 to 8 g for each L of fluid removed during paracentesis.[2]
- With pressors (norepinephrine or terlipressin) for **HRS**.[2]
  - Administer with albumin 1 g/kg IV on day 1 (max dose 100 g; max rate 1 to 2 mL/min), then 40 to 50 g/day as long as pressor is continued.[2.13,23,] Alternative: 25 g every 6 to 8 hours.[13]
  - Adjust dose and infusion rate based on volume status and signs/symptoms of cardiopulmonary dysfunction.[13] Assess before each dose.[13] In addition. consider a 48-hour stopping rule where the dose is held and the patient is assessed before resuming albumin.[13]
- With antibiotics in **SBP**.
  - Use with an antibiotic prevents one kidney injury and in-hospital death for every five patients treated [Evidence Level A-1]).[2,20] Patients most likely to benefit are those with SCr >1 mg/dL, BUN >30 mg/dL, or bilirubin ≥4 mg/dL.[2,20] Dosing: 1.5 mg/kg IV (day1), then 1 g/kg IV (day 3).[20]
- To treat **hypoalbuminemia**.
  - Daily albumin infusions to maintain albumin levels ≥3 g/dL is NOT better than standard of care at preventing the composite endpoint of new infection, kidney dysfunction, or death [Evidence Level B-1].[22] Albumin administration may lead to fluid overload and pulmonary edema.[22]

Generally use albumin 25%; its oncotic pressure draws fluid into the vascular space, and poses less risk of worsening edema or fluid overload compared to albumin 5%.[21]Limit infusion rate to 2 mL/min to limit fluid overload (e.g., pulmonary edema, worsening heart failure).[21] Sodium content is similar to normal saline; monitor for hypernatremia.[21] Remind nurses to administer albumin with vented tubing when supplied in a glass (noncollapsible) container.

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PRESSORS

For treatment of HRS

- Either terlipressin (a vasopressin analogue) **plus albumin** or norepinephrine **plus albumin** (second-line) is reecommended.[23] Meta-analysis of small studies with limitations suggests similar efficacy, but different side effect profiles.[23]
- Norepinephrine is given as a continuous infusion and requires dose titration.[24] Requires ICU and perhaps central line placement.[23]
  - Aim to increase MAP by ≥10 mm Hg or achieve urine output of >200 mL/4 hours.[2]
- Terlipressin (Terlivaz). Compared to albumin plus placebo, NNT = 7 for terlipressin plus albumin to reverse HRS-AKI [Evidence Level A=1].[25]
  - Off-label dosing: 2 mg/day continuous infusion. Increase every 24 to 48 hours up to 12 mg/day until SCr decreases.[2,23] Compared to labeled dosing, this regimen may reduce the risk of ischemia.[2,13]
- Response to norepinephrine or terlipressin is defined by SCr decrease to <1.5 mg/dL or to within 0.3 mg/dL of the baseline within 14 days.[13]
- If SCr does not improve within 4 days with the maximum tolerated dose, stop treatment.[13]
- Octreotide plus midodrine plus albumin has lower efficacy (third-line).[2,13]

For acute GI bleeding[19]

- Octreotide (IV): 50 mcg x 1, then 25 to 50 mcg/hr x 2 to 5 days
- Somatostatin (IV): 250 mcg x 1, then 250 to 500 mcg/hour x 2 to 5 days
- Terlipressin (IV): 2 mg every 4 to 6 hrs (first 24 to 48 hrs), then 1 mg IV every 4 to 6 hours x 2–5 days

Abbreviations

ACE = angiotensin converting enzyme; AKI = acute kidney injury; ARB = angiotensin receptor blocker; BID = twice daily; DS = double-strength; GI = gastrointestinal; HE = hepatic encephalopathy; HRS = hepatorenal syndrome; ICU = intensive care unit; IV = intravenous; MAP = mean arterial pressure; MRSA = methicillin-resistant *Staphylococcus aureus*; NSAID = nonsteroidal anti-inflammatory drug; SBP = spontaneous bacterial peritonitis; SCr = serum creatinine; TMP/SMX = trimethoprim/sulfamethoxazole; VRE = vancomycin-resistant enterococcus.

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Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the LEVEL OF EVIDENCE for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	1. High-quality randomized controlled trial (RCT) 2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).*
[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician 2004;69:548-56. https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html.]

References

1. de Franchis R, Bosch J, Garcia-Tsao G, et al. Baveno VII - Renewing consensus in portal hypertension. J Hepatol. 2022 Apr;76(4):959-974.
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 Aug;74(2):1014-1048.
3. Tapper EB, Parikh ND. Diagnosis and Management of Cirrhosis and Its Complications: A Review. JAMA. 2023 May 9;329(18):1589-1602.
4. Wijdicks EF. Hepatic Encephalopathy. N Engl J Med. 2016 Oct 27;375(17):1660-1670.

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References

5. Aithal GP, Palaniyappan N, China L, et al. Guidelines on the management of ascites in cirrhosis. Gut. 2021 Jan;70(1):9-29.
6. Asrani S. Management of Patients With Refractory Ascites. Gastroenterol Hepatol (N Y). 2025 Jul;21(7):431-433.
7. McPherson S, Lucey MR, Moriarty KJ. Decompensated alcohol related liver disease: acute management. BMJ. 2016 Jan 26;352:i124.
8. Orman ES, Fortune BE, John BV, Asrani SK. AGA Clinical Practice Update on the Management of Ascites, Volume Overload, and Hyponatremia in Cirrhosis: Expert Review. Gastroenterology. 2025 Dec;169(7):1547-1557.
9. American Liver Foundation. Diagnosing Hepatic Encephalopathy (HE). March 16, 2023. https://liverfoundation.org/liver-diseases/complications-of-liver-disease/hepatic-encephalopathy/diagnosing-hepatic-encephalopathy/. (Accessed February 4, 2026).
10. Reau N, Bernstein D, Kwo P, et al. A practical approach to the diagnosis and management of hepatic encephalopathy. Am J Med. 2026 Jan;139(1):14-23.e4.
11. Vilstrup H, Amodio P, Bajaj J, et al. Hepatic encephalopathy in chronic liver disease: 2014 Practice Guideline by the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver. Hepatology. 2014 Aug;60(2):715-35.
12. Tasnif YO, Hebert MF. Complications of end-stage liver disease. In: Zeind CS, Carvalho MG, Cheng JWM, et al., editors. Applied Therapeutics: the Clinical Use of Drugs. 12th ed. Philadelphia, PA: Wolters Kluwer Health, 2024:572-590.
13. Clinical Pharmacology powered by ClinicalKey. Tampa (FL): Elsevier. 2026. http://www.clinicalkey.com. (Accessed February 4, 2026).
14. European Association for the Study of the Liver. EASL Clinical Practice Guidelines on the management of hepatic encephalopathy. J Hepatol. 2022 Sep;77(3):807-824. Erratum in: J Hepatol. 2023 Nov;79(5):1340.
15. VASF Spontaneous Bacterial Peritonitis (SBP) Treatment Guidelines. November 29, 2023. https://idmp.ucsf.edu/content/vasf-spontaneous-bacterial-peritonitis-sbp-treatment-guidelines. (Accesseed February 4, 2026).
16. Karvellas CJ, Bajaj JS, Kamath PS, et al. AASLD Practice Guidance on Acute-on-chronic liver failure and the management of critically ill patients with cirrhosis. Hepatology. 2024 Jun 1;79(6):1463-1502.
17. Nanchal R, Subramanian R, Alhazzani W, et al. Guidelines for the Management of Adult Acute and Acute-on-Chronic Liver Failure in the ICU: Neurology, Peri-Transplant Medicine, Infectious Disease, and Gastroenterology Considerations. Crit Care Med. 2023 May 1;51(5):657-676.
18. Prosty C, Noutsios D, Dubé LR, et al. Prophylactic Antibiotics for Upper Gastrointestinal Bleeding in Patients With Cirrhosis: A Systematic Review and Bayesian Meta-Analysis. JAMA Intern Med. 2025 Oct 1;185(10):1194-1203.
19. Kaplan DE, Ripoll C, Thiele M, et al. AASLD Practice Guidance on risk stratification and management of portal hypertension and varices in cirrhosis. Hepatology. 2024 May 1;79(5):1180-1211.
20. Sort P, Navasa M, Arroyo V, et al. Effect of intravenous albumin on renal impairment and mortality in patients with cirrhosis and spontaneous bacterial peritonitis. N Engl J Med. 1999 Aug 5;341(6):403-9.
21. Kugelmas M, Loftus M, Owen EJ, et al. Expert perspectives for the pharmacist on facilitating and improving the use of albumin in cirrhosis. Am J Health Syst Pharm. 2023 Apr 4:zxad070.
22. China L, Freemantle N, Forrest E, et al. A Randomized Trial of Albumin Infusions in Hospitalized Patients with Cirrhosis. N Engl J Med. 2021 Mar 4;384(9):808-817.
23. Loftus M, Brown RS Jr, El-Farra NS, et al. Improving the Management of Hepatorenal Syndrome-Acute Kidney Injury Using an Updated Guidance and a New Treatment Paradigm. Gastroenterol Hepatol (N Y). 2023 Sep;19(9):527-536.
24. Olson JC, Subramanian RM. Comparative efficacy of terlipressin and norepinephrine for treatment of hepatorenal syndrome-acute kidney injury: A systematic review and meta-analysis. PLoS One. 2024 Jan 29;19(1):e0296690.
25. Wong F, Pappas SC, Curry MP, et al. Terlipressin plus Albumin for the Treatment of Type 1 Hepatorenal Syndrome. N Engl J Med. 2021 Mar 4;384(9):818-828.
26. Davenport A, Ahmad J, Al-Khafaji A, et al. Medical management of hepatorenal syndrome. Nephrol Dial Transplant. 2012 Jan;27(1):34-41.