TABLE 4. Relapse Prevention Medications in Alcoholic Liver Disease

Medication	Dosing	Metabolism (M) and Excretion (E)	Mechanism of Action	ALD Considerations
Naltrexone*	50 mg/d orally or 380 mg monthly sq	M: Hepatic E: Mostly renal, fecal 2%-3%	Opioid receptor antagonist	Not studied in patients with ALD Hepatotoxicity concerns
Acamprosate*	666 mg tid	M: None E: Renal	NMDA receptor antagonist	Not studied in patients with ALD No reported instances of hepatotoxicity
Gabapentin	600-1,800 mg/d	M: None E: Renal 75%, fecal 25%	Modulates GABA activity through action at presynaptic calcium channels	Not studied in patients with ALD Monitor closely for renal dysfunction and worsening mental status/sedation
Baclofen	30-60 mg/d	M: Hepatic, limited E: Renal	GABA-B receptor agonist	Single RCT in patients with ALD showed benefit
Topiramate	75-400 mg/d	M: Not extensively metabolized E: Renal	GABA action augmentation, glutamate antagonism	Not studied in patients with ALD

Note: Adapted from Winder et al.[237]
*FDA-approved for AUD treatment. Disulfiram is not included on this list because it is not recommended for use in patients with ALD.
Abbreviations: GABA, gamma-aminobutyric acid; NMDA, *N*-methyl-D-aspartate; sq, subcutaneous; and tid, 3 times per day.

to be approximately 12 for acamprosate and 20 for naltrexone. Disulfiram and naltrexone undergo hepatic metabolism and can cause liver damage, whereas acamprosate has no hepatic metabolism. Of note, none of these medications have been studied in patients with AH and AC. In addition, there are several medications with some benefit in relapse prevention that have not been FDA-approved for AUD treatment. These agents include gabapentin, baclofen, topiramate, ondansetron, and varenicline.[72-75] Baclofen, a gamma-aminobutyric acid–B (GABA-B) receptor agonist, is the only AUD pharmacotherapy that has been tested in an RCT in patients with AC with AUD as well as in two small, uncontrolled observational studies.[71,76,77] In a randomized trial consisting of patients with both compensated and decompensated AC, a 12-week course of baclofen (10 mg three times daily) resulted in improved rates of total alcohol abstinence and decreased relapse compared with the control during 1 year of observation while exhibiting an acceptable safety profile.[71,78] Notably, patients with hepatic encephalopathy were excluded from this trial, as baclofen may impair mentation, a side effect that may be exacerbated in more advanced liver disease. Based on limited data, and in the absence of an RCT demonstrating efficacy, acamprosate does not appear to be toxic to the liver and is probably safe.

Guidance Statements

- **Referral to AUD treatment professionals is recommended for patients with advanced ALD and/or AUD, to ensure access to the full range of AUD treatment options.**
- **Multidisciplinary, integrated management of ALD and AUD is recommended and improves rates of alcohol abstinence among patients with ALD.**
- **Based on limited data, the use of acamprosate or baclofen can be considered for the treatment of AUD in patients with ALD.**

Pathophysiology and Risk Factors for Alcohol-Associated Liver Disease

Given the widespread levels of heavy alcohol use worldwide, it is clear that a minority of heavy drinkers develop significant liver disease. The injurious effect of alcohol on the liver is not linearly dose-dependent, but there is a threshold beyond which the risk for serious liver disease increases with increasing levels of consumption.[79] According to the "Dietary Guidelines for Americans 2015-2020,"