Pocket Guide:

Antiseizure Medications (ASMs) and Liver Health

PURPOSE

This guide provides a brief overview of potential hepatotoxicity associated with ASMs to assist clinicians in monitoring and managing liver health in patients with epilepsy. For detailed information, please refer to the full version of the Antiseizure Medications and Liver Health resource, here

GENERAL PRECAUTIONS

- Some ASMs may cause drug-induced liver injury (DILI); regular liver function tests (LFTs) are recommended for high-risk medications.[1]
- Avoid combining hepatotoxic ASMs with other liver-damaging agents (e.g., alcohol, herbal supplements like enhanced-absorption turmeric preparations, or green tea extract).
- Many cases of liver injury occur in the context of hypersensitivity reactions such as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) and Stevens-Johnson Syndrome (SJS).
- Discontinue the suspect medication immediately if a drug reaction is suspected or significant liver dysfunction occurs. Follow up testing, supportive care and / or other interventions may also be indicated.

CATEGORIES OF ASM-INDUCED LIVER INJURY[2]

High Risk (Category A/B): Well-documented hepatotoxicity (e.g., valproic acid, phenytoin, carbamazepine, felbamate, phenobarbital).

Moderate Risk (Category C/D): Rare or less frequent hepatotoxicity (e.g., gabapentin, lacosamide, oxcarbazepine, topiramate).

Low (Category E, E*): Unlikely to cause liver injury, but some reports may exist (e.g., cannabidiol, brivaracetam, diazepam). In some cases, toxicity is suspected but unproven.

Unknown(Category X): Inadequate information available

RESOURCES

1. FDA. U.S. Food & Drug Administration. Drug Approvals and Databases. Last Accessed Jan 2, 2015.
2. NIDDK. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012. Last accessed Feb 21, 2025.

Drug	Hepato-toxicity Risk	Key Considerations
Adreno-corticotropic hormone (ACTH)	High	Risk of acute liver failure. Long-term use can cause steatosis and exacerbate chronic viral hepatitis; withdrawal can reactivate viral or autoimmune hepatitis.
Carbamazepine (CBZ)	High	Risk of DILI in hypersensitivity reactions (DRESS, SJS); monitor LFTs.
Felbamate (FBM)	High	Risk of transaminase elevation, acute liver failure and death. Written consent is required before use, monitor LFTs in addition to blood counts.
Phenobarbital (PB)	High	Risk of transaminase elevation; DILI often from SJS or DRESS. Possible cross-reactivity with PHT, CBZ, PRM, and LTG.
Phenytoin (PHT) and Fosphenytoin (FOS)	High	May cause hepatocellular injury, DRESS; contraindicated in prior hepatic reaction. Possible cross-reactivity with PHT, CBZ, PRM, LTG, ETX.
Valproic Acid (VPA)	High	Risk of acute liver failure, hyperammonemia, mitochondrial toxicity; avoid in POLG mutations. monitor LFTs. Risk of DILI may increase when combined with EIASMs (i.e. CBZ, PHT, etc.). Caution in young children.
Cenobamate (CNB)	Moderate	Slow up-titration to minimize risk of DRESS.
Clonazepam (CZP)	Moderate	Rare cases, monitor LFTs.

SPECIFIC ASM CONSIDERATIONS

Drug	Hepato-toxicity Risk	Key Considerations
Diazepam (DZP)	Moderate (oral route)	Rare cases of transaminase elevation or DILI. Buccal form not to be used in neonates or infants. IV formulation low risk.
Eslicarbazepine acetate (ESL)	Moderate	Rare hepatotoxicity; possible cross-reactivity with OXC, PHT, LTG and CBZ.
Gabapentin (GBP)	Moderate	Rare reports of hepatotoxicity or DRESS.
Lacosamide (LCM)	Moderate	Rare risk of transaminase elevation.
Lamotrigine (LTG)	Moderate	Associated with SJS and DRESS; slow up-titration to minimize risk. Higher risk with rapid titration or concurrent VPA use.
Levetiracetam (LEV)	Moderate	Rare risk of transaminase elevation, DILI, DRESS.
Lorazepam (LZP)	Moderate	Rare transaminase elevation or liver injury.
Oxcarbazepine (OXC)	Moderate	Rare hepatotoxicity, SJS, DRESS; cross-reactivity risk with CBZ.
Pregabalin (PGB)	Moderate	Rare severe acute hepatitis.
Topiramate (TPM)	Moderate	Risk of transaminase elevation, hyperammonemia, acute liver dysfunction and failure. Increased risk with VPA. Risk of SJS.
Vigabatrin (VGB)	Moderate	Risk of DILI and hepatitis. Can decrease AST/ALT making them unreliable markers for hepatic injury.
Zonisamide (ZNS)	Moderate	Risk of transaminase elevation, DRESS / SJS.
Brivaracetam (BRV)	Low	Risk of transaminase elevation, hypersensitivity.
Cannabidiol (CBD)	Low	Risk of transaminase elevation, especially with VPA; monitor LFTs.
Clobazam (CLB)	Low	Rare, associated with DRESS. Increased risk of transaminase elevations when used with CBD.
Ethosuximide (ESM)	Low	Risk of transaminase elevation and rare DRESS, monitor LFTs.
Everolimus (EVL)	Low	Asymptomatic mild transaminase elevation common; can reactivate chronic hepatitis (screen before use).
Gabapentin (GBP)	Low	Rare hepatotoxicity; well tolerated in liver disease.
Midazolam (MDZ)	Low	Rare transaminase elevation.
Primidone (PRM)	Low	Rare transaminase elevation; potential cross-reactivity with PHT and PB. Can worsen porphyria.
Rufinamide (RUF)	Low	Rare transaminase elevation or SJS.
Stiripentol (STP)	Low	Transaminase elevation and DILI reported. Consider monitoring LFTs.
Tiagabine (TGB)	Low	No reports of injury, but use has been limited.
Fenfluramine (FFA)	Unknown	Unknown
Ganaxolone (GNX)	Unknown	Unknown

ABBREVIATIONS

ALT: alanine transaminase;
AST: aspartate transaminase;
DRESS: drug reaction with eosinophilia and systemic symptoms;
EIASM: enzyme-inducing antiseizure medications;
LFT: liver function tests;
POLG: polymerase gamma;
SJS: Stevens-Johnson syndrome.

FURTHER INFORMATION

- This document is not intended to constitute treatment recommendations
- Updated product information should be referenced through the FDA database