

Liver Function Tests Recommendations For Commonly Used Hepatotoxic Agents

Over 600 drugs, chemicals, and herbal remedies can cause hepatotoxicity. The most commonly used indicators of liver injury are aspartate aminotransferase (AST, formerly SGOT) and alanine aminotransferase (ALT, formerly SGPT). At times, monitoring of other liver function tests may be necessary. The following list includes some of the more common drugs that require liver function monitoring. There may be situations where more frequent monitoring is required. Drug-induced hepatotoxicity can develop rapidly, often before abnormal lab tests are noticed.

Drug	Monitoring Recommendations	Comments
Amiodarone (<i>Cordarone</i>)	LFTs prior to initiation and at regular intervals (every 6 months), especially for patients receiving high maintenance doses.	If LFTs are >3 times the ULN, or doubles in a patient with an elevated baseline, decrease the dose or stop the drug.
Azathioprine (<i>Imuran</i>)	ALT, AST, alkaline phosphatase, and bilirubin every 2 weeks for the first 4 weeks and monthly thereafter.	Discontinue therapy if hepatic veno-occlusive disease is suspected.
Carbamazepine (<i>Tegretol</i>)	LFTs at baseline and periodically.	
Felbamate (<i>Felbatol</i>)	AST, ALT, and bilirubin at baseline and every 1 to 2 weeks while treatment continues.	If a patient develops abnormal LFTs, discontinue treatment immediately.
Fenofibrate and Gemfibrozil	LFTs periodically.	Discontinue therapy if LFTs >3 times ULN persist.
Imatinib (<i>Gleevec</i>)	LFTs (transaminases, bilirubin, and Alk.Phos.) at baseline, monthly, and as clinically indicated.	If elevations in bilirubin >3 times ULN or transaminases >5 times ULN, withhold until bilirubin <1.5 times ULN and transaminase <2.5 times ULN. Treatment may then be continued at a reduced dosage.
Isoniazid	LFTs and bilirubin at baseline. Repeat LFTs periodically (monthly or more, as needed) especially in high-risk patients (e.g., ≥35 yrs., daily alcohol use, chronic liver disease, etc.).	Discontinue use if LFTs are >3 to 5 times the ULN or if patients develop symptoms of hepatitis.
Isotretinoin (<i>Accutane</i>)	LFTs at baseline and at weekly or biweekly intervals until response to treatment is established.	
Itraconazole (<i>Sporanox</i>)	LFTs in patients with pre-existing hepatic function abnormalities or patients who have had prior drug-induced liver toxicity. LFTs should be considered in all patients, especially with therapy lasting 1 month or longer.	If LFTs are >3 times the ULN, or doubles in a patient with an elevated baseline, decrease the dose or stop the drug
Ketoconazole (<i>Nizoral</i>)	LFTs (GGT, Alk.Phos., ALT, AST, and bilirubin) at baseline and at frequent intervals during therapy. Canadian labeling suggests LFTs after 2 weeks and monthly or more frequently during treatment.	Discontinue treatment if transient minor elevations of liver enzymes persist , worsen, or symptoms develop.
Leflunomide (<i>Arava</i>)	ALT at baseline and at monthly intervals during the first six months then, if stable, every 6 to 8 weeks thereafter.	Reduce dose if ALT elevation is >2 to ≤3 times ULN. Discontinue if ALT >3 times ULN and start treatment with cholestyramine.
Methotrexate (<i>Rheumatrex</i>)	AST, ALT, Alk.Phos., and albumin at baseline, and every 1 to 2 months during therapy. Liver biopsy recommended in appropriate patients.	Further evaluation is needed for persistent LFT abnormalities and/or decreased serum albumin. More frequent monitoring may be needed during antineoplastic therapy, during initial or changing doses, or during periods of increased methotrexate levels.
Nefazodone (<i>Serzone</i>)	LFTs at baseline and periodically thereafter (e.g., at 3 to 6 month intervals).	Discontinue therapy if AST or ALT >3 times ULN.

Drug	Monitoring Recommendations	Comments
Nevirapine (<i>Viramune</i>)	LFTs at baseline. Intensive monitoring during the first 18 weeks of treatment. Continue frequent monitoring during therapy. Check immediately at any sign or symptom of hepatitis and for all patients who develop a rash in the first 18 weeks	If AST or ALT >2 times ULN, then liver tests should be monitored more frequently during regular clinic visits. If AST or ALT increase to >5 times ULN, stop therapy immediately.
Niacin (SR) (<i>Niaspan</i>)	AST and ALT at baseline, followed by every 6 to 12 weeks for the first year, then periodically thereafter (e.g., at 6-month intervals).	Discontinue therapy if LFTs increase to 3 times ULN, or if elevated LFTs are associated with symptoms.
NSAIDs	LFTs at baseline and periodically.(?)	Discontinue treatment if abnormal LFTs persist or worsen. ALT may be the most sensitive indicator of NSAID-induced liver dysfunction.
Pioglitazone & Rosiglitazone (<i>Actose & Avandia</i>)	ALT at baseline and periodically thereafter. Some experts are monitoring at 3 to 6 month intervals. Canadian labeling advises that liver enzymes be monitored every two months for the first twelve months, and periodically thereafter.	Discontinue therapy if ALT levels >3 times ULN persist or if the patient is jaundiced. Both rosiglitazone & pioglitazone-associated fatal liver failure have been reported.
Pyrazinamide	LFTs and bilirubin at baseline. Repeat LFTs periodically.	Discontinue therapy if signs of hepatotoxicity occur.
Rifampin (<i>Rifadin</i>)	LFTs including bilirubin at baseline. LFTs every 2 to 4 weeks especially if drug is used in patients with impaired hepatic function.	Discontinue therapy if signs of hepatotoxicity occur.
Statins	LFTs at baseline. Also, at 12 weeks following both the initiation of therapy and dose elevation. Check every 6 months thereafter. Canadian labeling recommends ALT or AST levels be repeated promptly and more frequently if found elevated.	Reduce the dose or stop the drug if an increase in ALT or AST of >3 times ULN occurs.
Tacrine (<i>Cognex</i>)	ALT every other week from at least week 4 to week 16 following initiation of treatment, then every 3 months thereafter. If therapy is interrupted for >4 weeks, resume initial LFT monitoring schedule when therapy restarted.	Modify the dose and monitoring regimen for ALT elevations >2 times ULN (refer to product information).
Valproic acid (<i>Depakote</i>)	LFTs at baseline and at frequent intervals thereafter, especially during the first 6 months.	
Voriconazole (<i>Vfend</i>)	LFTs (including bilirubin) at baseline and periodically.	Discontinue if clinical signs and symptoms consistent with liver disease develop.

Abbreviations: Alk.Phos.= Alkaline Phosphatase, GGT= Gamma-glutamyltransferase, LFT= Liver Function Test, ULN= Upper Limits of Normal, ALT= Alanine Aminotransferase (formerly serum glutamate-pyruvate transaminase or SGPT), and AST= Aspartate Aminotransferase (formerly serum glutamic-oxaloacetic transaminase or SGOT).