



## General Commissioning Statement

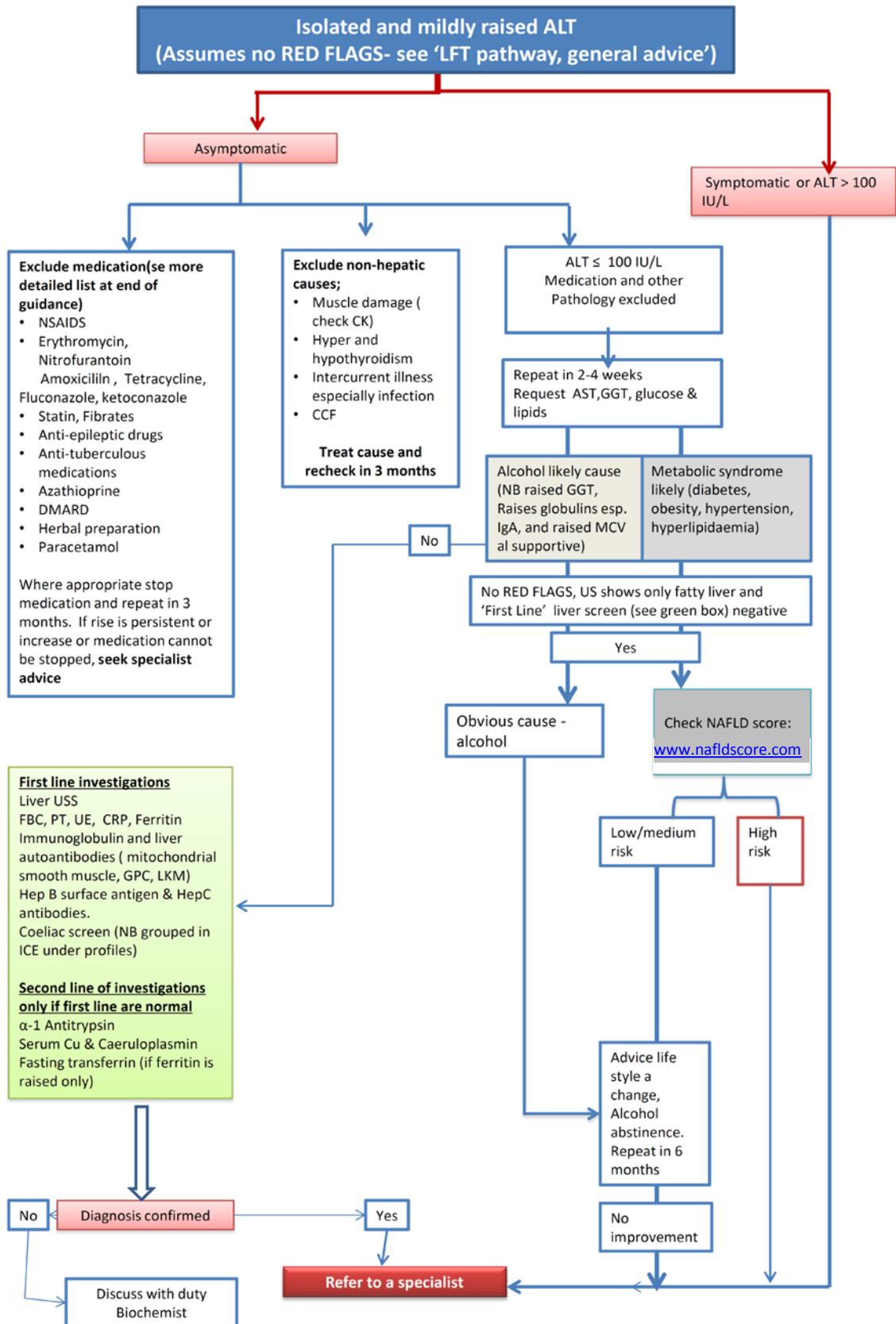
Condition or Treatment	Investigation of Patients With Abnormal Liver Biochemistry
<b>Background</b>	<ol style="list-style-type: none"> <li>1. Transient increases in liver biochemistry result are common, often triggered by <b>intercurrent illness</b> (typically infection) and <b>drugs</b></li> <li>2. In most patients it is appropriate to wait a few months and repeat, following guidance below.</li> <li>3. Patterns addressed are: <ul style="list-style-type: none"> <li>• An isolated rise in <b>transaminases</b> (ALT /AST) (see appendix 1)</li> <li>• An isolated rise in <b>alkaline phosphatase</b> (Alk Phos) (see appendix 2)</li> <li>• A raised <b>ALK Phos and bilirubin</b> (see appendix 3)</li> <li>• An isolated rise in <b>bilirubin</b> (see appendix 4)</li> <li>• <b>Appendix 5</b> gives more detail about drug-induced liver injury for specific drugs</li> </ul> <p>Where <b>transaminases and Alk Phos</b> are raised together you should usually follow guidance for the most proportionately raised enzyme: if in doubt about appropriateness of initial primary care investigation using these guidelines please discuss with gastroenterology via Advice and Guidance in Choose and Book.</p> </li> <li>4. Remember advanced liver disease may be accompanied by only minor, or no derangements of liver biochemistry. However, there are almost always other clues in such cases, so always consider the whole clinical picture:</li> </ol> <p><b>HIGH RISK FEATURES (lower threshold for referral)</b>            SYMPTOMS - fatigue, pruritus, oedema            BACKGROUND - drugs, alcohol, obesity/metabolic syndrome</p> <p><b>RED FLAG FEATURES (refer immediately)</b>            SYMPTOMS weight loss, abdominal pain            SIGNS –</p> <ul style="list-style-type: none"> <li>• of Chronic Liver Disease (eg spider nevi, clubbing, palmar erythema)</li> </ul>

Notes

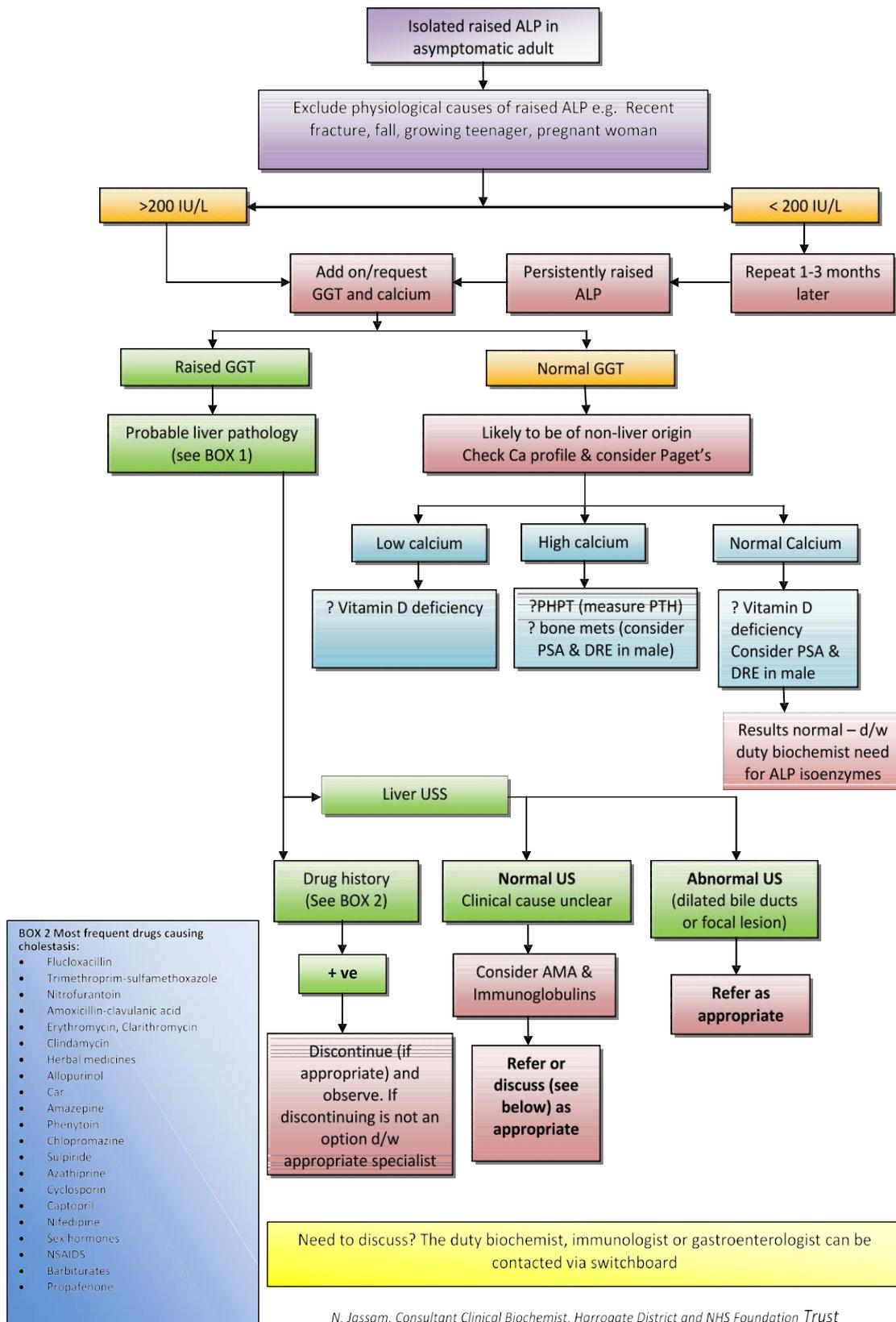
1.This Statement will be reviewed in the light of new evidence, or guidance from NICE

	<ul style="list-style-type: none"> <li>• of liver failure (eg ascites, splenomegaly, encephalopathy)</li> </ul> <p>LAB TESTS - raised PT, low platelets, high bilirubin, low albumin</p>
<b>Commissioning guidance</b>	See appendices below
<b>Referral guidance</b>	Referral guidance only
<b>Effective from</b>	20/11/17
<b>Summary of evidence / rationale</b>	Produced by HDFT gastroenterology and biochemistry teams
<b>Date</b>	10/10/17
<b>Review Date</b>	1/12/19
<b>Contact for this policy</b>	<a href="mailto:brucewilloughby@nhs.net">brucewilloughby@nhs.net</a>

# Appendix 1: isolated and mildly raised ALT



## Appendix 2: Isolated raised ALP in asymptomatic adult



### **Appendix 3: Approach To Patient With Raised Bilirubin *and* Alkaline Phosphatase, or features of obstructive jaundice**

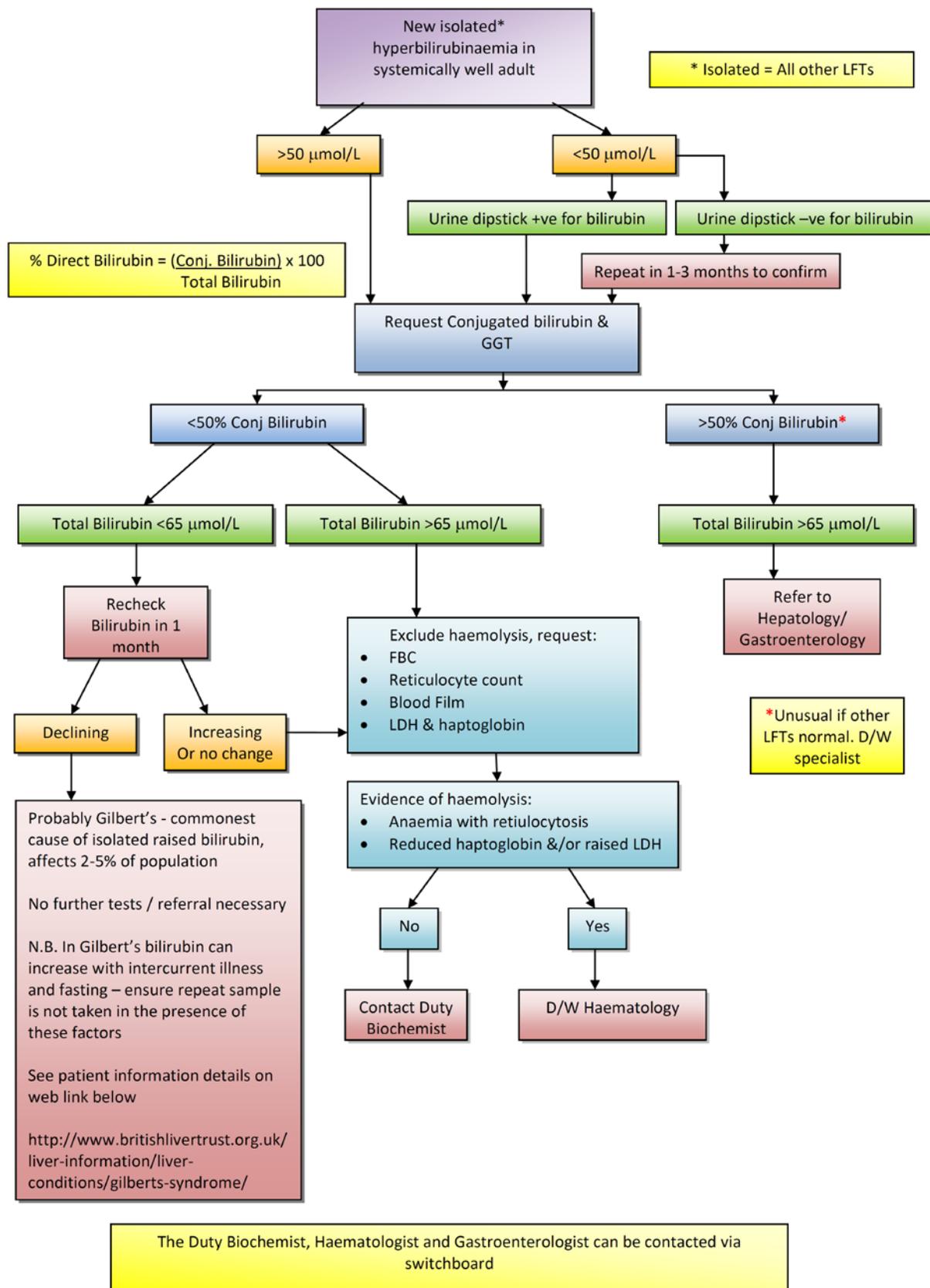
1. Classic obstructive jaundice is the (usually sudden) development of jaundice, with pale stools, dark urine and often pruritus, usually due to large bile duct obstruction by CBD stones or malignancy.

Patients with CBD stones may become septic very quickly – **if there is any suggestion of infection urgent admission** usually required.

**If patients are well and pain free organise urgent abdominal ultrasound followed by urgent referral.** The ultrasound may diagnose the cause (eg CBD stone or pancreatic cancer) or suggest the best referral pathway (dilated CBD- refer to general surgery, non-dilated ducts, refer to gastroenterology).

2. A combination of raised bilirubin and alk phos on laboratory testing without the classic obstructive picture may still be caused by large bile duct problems such as stones, but suggests the possibility of small to medium bile duct disease such as PBC or PSC. Request **urgent abdominal US along with liver auto-antibodies in first instance**, and refer to gastroenterology/hepatology.

## Appendix 4: New isolated raised bilirubin in systemically well adult



## Appendix 5: Drugs and abnormal Liver Biochemistry

### A) General comments

- Most drugs are eliminated by the liver, and transient asymptomatic serum enzyme elevations have been described for most drugs, typically during the first few months of therapy.
- Drug-induced liver injury may develop a long time (even years) after a drug is started.
- Remember to ask about **recreational drugs** and **self-purchased herbs, supplements etc.** (e.g. alternative / Chinese medicines; green tea, vitamin A, weight loss / body building supplements) which occasionally are the cause of liver toxicity. The spectrum of liver disease is wide.
  - Ecstasy may cause hepatitis and cirrhosis
  - Cocaine abuse has been associated with acute hepatic injury and enzyme elevation
  - 'Legal Highs' – have a high risk of causing liver injury
- Fatty liver change is associated with alcohol, corticosteroids, antidepressant and antipsychotic medications, aspirin, valproate, piroxicam, high doses of tetracycline and, most commonly, tamoxifen.

Amiodarone and methotrexate can cause fatty liver, though with these agents inflammation and fibrosis usually overshadows the fatty change.

- Cancer chemotherapeutic agents can cause severe liver toxicity including veno-occlusive disease (where typically abdominal pain, swelling and jaundice accompany enzyme elevations) – if suspected discuss urgently re admission.
- Cirrhosis/fibrosis may follow prolonged therapy with amiodarone, methotrexate, isoniazid, enalapril, and valproate.
- Paracetamol (acetaminophen) overdose: transaminase rise common, bilirubin rise accompanies, needs urgent admission.

### B) Comments on specific drugs

- Aspirin, commonest trigger for Reye syndrome (encephalopathy, hepatic steatosis and lactic acidosis) urgent admission required

- Amoxicillin: can cause a moderate rise in transaminases, sometimes cholestasis.
- Amiodarone: causes abnormal liver function test results in 15-50% of patients. The spectrum of liver injury is wide, ranging from isolated asymptomatic transaminase elevations, fatty liver disease and a hepatic injury that resembles alcoholic hepatitis / fulminant liver failure and cirrhosis/fibrosis.
- Androgenic steroids- can cause cholestasis
- Antabuse (disulfiram) rarely acute drug-induced hepatitis / liver failure reported- suggest monitor LFTs during use.
- Anticonvulsants: phenytoin, carbamazepine, lamotrigine may result in a mixed cholestasis/hepatitis picture. See also comments about Valproate below.
- Antiretroviral agents- mild changes in liver enzyme levels common- secondary care specialist will advise on any routine monitoring necessary. Be aware rarely severe liver injury (e.g. hepatic steatosis and lactic acidosis) may develop.
- Augmentin: hepatotoxicity is common, in particular cholestasis.
- Azathioprine (and closely related mercaptopurine) can cause a cholestatic reaction
- Chlorpromazine: features of cholestasis.
- Ciprofloxacin: cholestatic jaundice has been reported with repeated use of quinolones. Approximately 2% of patients taking ciprofloxacin show elevated transaminases.
- Diclofenac: Elderly females are more susceptible to diclofenac - induced liver injury. Transaminase rise is the usual laboratory finding
- Erythromycin/ Clarithromycin: cholestasis reaction is the most common adverse effect, and usually begins within 2-3 weeks of therapy. May cause increased liver enzyme levels.
- Fibrates: fenofibrate has been reported to cause acute and chronic hepatotoxicity/
- Fluconazole: The spectrum of hepatic reactions ranges from mild elevations in transaminase levels to hepatitis, cholestasis, and fulminant hepatic failure.
- Hydralazine may cause chronic hepatitis .

- Isoniazid. Mild hepatic transient elevation of transaminases occurs in 10-20% of patients. Occasionally, progressive liver damage can occur. If transaminase values exceed 3-5 times the upper limit of the reference range, discontinuation of the drug should be strongly considered.
- Mercaptopurine: see azathioprine.
- Methotrexate: wide spectrum of liver injury including fatty liver disease, hepatitis and fibrosis/cirrhosis.
- Methyldopa: LFTs should be performed during the first 6-12 weeks of therapy. In some patients, findings are consistent with those of cholestasis and hepatocellular injury. Rarely, fatal hepatic necrosis has been reported.
- Nitrofurantoin: can cause a chronic hepatitis pattern.
- NSAIDs: can cause a hepatitis type reaction or mixed picture
- Oral contraceptives: Oral contraceptives can lead to intrahepatic cholestasis with pruritus and jaundice in a small number of patients. Patients with recurrent idiopathic jaundice of pregnancy, severe pruritus of pregnancy, or a family history of these disorders are more susceptible to hepatic injury. Oral contraceptives are contraindicated in patients with a history of recurrent jaundice of pregnancy.
- Rifampicin: may cause mild hepatitis or isolated cholestasis.
- Statins:
  - Moderate rises in transaminases are common (< 3 times the upper limit of the reference range) and are often transient, and probably represent enzyme induction rather than liver injury.
  - Elevations are not accompanied by any symptoms **and do not usually require interruption of treatment.**
  - However, a chronic hepatitis can develop. Persistent increases in serum transaminase levels (>3 times the upper limit of the reference range) occur in approximately 1% of patients, and these patients should be monitored until liver function returns to normal after drug withdrawal
- Sulfonylureas: can cause cholestasis
- Tetracyclines: chronic hepatitis reported with minocycline. Acute severe liver injury can follow IV tetracycline.

- Valproate: typically causes microsteatosis. Caution in patients with a prior history of hepatic disease. Those at particular risk include those with seizure disorders treated with multiple anticonvulsants. Hepatic failure resulting in death have occurred, usually during the first 6 months of treatment and are preceded by nonspecific symptoms such as malaise, weakness, lethargy, oedema, anorexia, vomiting, and even loss of seizure control. Liver function tests should be performed prior to therapy and at frequent intervals, especially in the first 6 months.