

BETTER AVOID.

Risks: Amitriptyline undergoes extensive hepatic metabolism. CYP2D6 is the primary metabolic pathway, while CYP1A2, CYP2C19 and CYP3A4 are minor contributors. The drug may cause mild and transient increases in liver enzymes (occurring in 10–12% of patients) and is a rare cause of clinically apparent acute cholestatic liver injury. These aminotransferase abnormalities are usually mild, asymptomatic, and transient and are a rare cause of clinically apparent acute cholestatic liver injury. Reduced hepatic function can lead to increased drug exposure and heightened sensitivity to the anticholinergic and cardiovascular effects of amitriptyline.

Risk monitoring: Monitor ALT, AST, ALP, GGT, and bilirubin regularly, especially during the initial months of treatment or if hepatic function deteriorates. Watch for jaundice, abdominal pain, rash, fever, or other signs of hepatic injury. Monitor for signs of increased exposure, such as sedation, confusion, gait instability, falls, and hyponatraemia. Consider CYP2D6 genotyping.

Dose adjustment: Use with caution in patients with hepatic impairment, as clearance is reduced, and plasma concentrations are increased. For Child–Pugh A or B, administer approximately 50% of the usual indication-specific dose, with slow titration in small increments (e.g., 5–12.5 mg) every 1–2 weeks, not exceeding 100 mg/day or the maximum recommended dose, whichever is lower.

Recommendation:

Better to avoid amitriptyline in patients with severe hepatic impairment (Child–Pugh C). For mild to moderate hepatic impairment (Child–Pugh A or B), use reduced doses with close monitoring. Discontinue immediately if hepatic injury or significant enzyme elevation occurs.