

BETTER AVOID.

Risks: Duloxetine undergoes extensive hepatic metabolism via the major enzymes CYP2D6 and CYP1A2, which necessitates caution in patients with hepatic impairment. Genetic polymorphisms of CYP2D6 may contribute to interindividual variability in metabolism. At higher doses, duloxetine inhibits CYP2D6 and CYP2B6, potentially affecting the metabolism of other drugs that use these pathways. Liver enzyme elevations occur in less than 1% of patients and are usually mild and transient, rarely requiring dose modification or discontinuation. However, rare cases of clinically apparent liver injury with marked enzyme elevations, with or without jaundice, have been reported.

Risk monitoring: Monitor ALT, AST, ALP, GGT, and bilirubin regularly, especially during the first months of treatment or if hepatic function worsens. Watch for jaundice, abdominal pain, rash, fever, or other signs of hepatic injury. Monitor for signs of increased exposure, including cardiovascular toxicity, confusion, gait instability, falls, and hyponatraemia.

Dose adjustment: Duloxetine should be avoided in patients with hepatic impairment. If treatment is deemed necessary in mild impairment (Child–Pugh A), start at a dose of ≤ 30 mg once daily and titrate very slowly (no more frequently than every 2–4 weeks) with close monitoring for adverse effects. Do not exceed 30 mg/day.

Recommendation:

Avoid duloxetine in patients with hepatic impairment (Child–Pugh A to C). Discontinue treatment immediately if hepatic injury or significant liver enzyme elevation occurs.