

BETTER AVOID.

Risks: Amitriptyline is a tricyclic antidepressant (TCA) that is metabolised to the active metabolite nortriptyline, which also possesses anticholinergic and cardiotoxic effects. The potential for cardiotoxicity (QTc and QRS prolongation, arrhythmia, and orthostatic hypotension) increases in patients with pre-existing cardiac disease; therefore, it should be used with caution in patients with cardiac comorbidities. Reduced hepatic or renal function can lead to increased drug exposure and heightened sensitivity to the anticholinergic and cardiovascular effects of amitriptyline. CYP2D6 is the major hepatic metabolic pathway, while CYP1A2, CYP2C19 and CYP3A4 are minor pathways. Potent inhibitors of these enzymes may increase plasma concentrations and exacerbate cardiotoxicity. TCAs have also been rarely associated with the syndrome of inappropriate antidiuretic hormone secretion (SIADH) and/or hyponatraemia, particularly in the elderly, which may further compromise cardiovascular stability.

Risk monitoring: Monitor blood pressure, heart rate, ECG, and serum sodium levels at baseline and at regular intervals (the highest risk of SIADH occurs within 2–4 weeks after therapy initiation). Observe for dizziness, syncope, or peripheral oedema. Review concomitant treatments for potential pharmacokinetic interactions, especially via CYP2D6. Consider genotyping for CYP2D6.

Dose adjustment: No specific dose adjustment is required in patients with reduced ejection fraction (EF < 40%). The dosing regimen should be similar to that used in elderly patients. Start with the lowest possible dose (25 mg) and titrate slowly up to a maximum of 75 mg in elderly patients, considering renal and hepatic function as well as the cumulative CNS and anticholinergic load.

Recommendation:

Avoid use in patients with severe heart failure, conduction abnormalities, or unstable cardiovascular disease. If therapy is essential, initiate treatment at the lowest possible dose and closely monitor ECG, serum sodium, and concomitant cardiovascular medications.