**USE WITH CAUTION.**

**Risks:** Duloxetine can exacerbate or cause the syndrome of inappropriate antidiuretic hormone secretion (SIADH) or hyponatraemia, both of which may further compromise cardiovascular stability. SNRIs are cardiotoxic (QTc prolongation, arrhythmia, orthostatic hypotension) and may pose risks for patients with pre-existing cardiac disease. Carefully consider potential cardiovascular effects. The risk of duloxetine-induced hypertension in older adults appears low, but the risk of orthostatic hypotension and SIADH increases with age. Renal and hepatic impairment may decrease clearance and increase drug accumulation, enhancing cardiovascular adverse effects. CYP2D6 is the major hepatic pathway, while potent enzyme inhibitors and poor metabolisers may show higher plasma concentrations and increased cardiotoxicity.

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

**Dose adjustment:** No specific dose adjustment is required for patients with reduced ejection fraction (EF < 40%). Dosing should follow recommendations for elderly patients. Low initial doses (e.g., 20 mg/day) and lower maintenance doses (e.g., 30–60 mg/day) are recommended for frail or comorbid elderly patients. Titrate slowly and monitor for tolerability.

**Recommendation:**

Drugs that increase serum norepinephrine levels, such as SNRIs, may be harmful in individuals with unstable or advanced heart failure or significant cardiovascular disease. Duloxetine should be used with caution, particularly in older adults with cardiac comorbidities. If therapy is necessary, start at the lowest effective dose and closely monitor ECG, serum sodium, and interacting cardiovascular medications.