USE WITH CAUTION.

Risks: Duloxetine can exacerbate or induce the syndrome of inappropriate antidiuretic hormone secretion (SIADH) or hyponatraemia, leading to instability, falls, delirium, and cognitive decline in frail older adults. Newer evidence suggests that SNRIs may increase the risk of falls. Elderly women may have up to a 25% longer elimination half-life. Renal impairment can also alter the drug's disposition and increase exposure.

Risk monitoring: Monitor for sedation, confusion, gait instability, falls, and serum sodium, particularly during initiation or dose adjustments. Regularly check blood pressure and renal function. Review therapy frequently, considering potential cardiovascular effects and CYP2D6-mediated pharmacokinetic interactions.

Dose adjustment: No specific dose recommendation exists for frailty. The usual starting dose is 60 mg once daily; however, lower initial doses (e.g., 30 mg/day) may be appropriate in frail or sensitive patients to improve tolerability. The maximum dose is 120 mg/day as tolerated, although higher doses have not shown additional benefit. For patients with reduced renal function (CrCl < 30 mL/min), duloxetine should be avoided. In elderly or comorbid patients, starting doses of 20–30 mg/day and maintenance doses of 30–60 mg/day are recommended. Titrate slowly and monitor for adverse effects.

Recommendation:

Duloxetine is listed in BEERS 2023 as a potentially inappropriate medication due to the risk of SIADH and falls and in STOPPFall 2021 for increased fall risk. Although EU(7)-PIM does not list duloxetine, it should be used with caution in patients with a history of falls, postural hypotension, or those at risk of hyponatraemia. Duloxetine may be considered a START medication for older adults with moderate to severe neuropathic pain when other first-line treatments (e.g., topical agents, gabapentinoids) are ineffective or not tolerated.