APPENDIX E: Interactions for first-line and second-line antidepressants

Interactions [*19, 44, 77-98]	First-Line: Bupropion	Citalopram	Desvenlafaxine	Duloxetine	Escitalopram	Fluoxetine	Fluvoxamine	Mirtazapine	Paroxetine, Immediate-Release and Controlled-Release	Sertraline	Venlafaxine	Vortioxetine	Second-Line: Levomilnacipran	Moclobemide	Quetiapine	Trazodone	Tricyclic antidepressants	Vilazodone
QTc prolongation: QTc prolongation and torsades de pointes have occurred in patients at risk of QTc prolongation, patients taking concomitant medications that prolong QTc, or in cases of drug overdose. Avoid combined use with drugs associated with prolonged QTc interval/ torsades de pointes (e.g. amiodarone, azithromycin, clarithromycin, domperidone, erythromycin, haloperidol, methadone, pimozide, quinine, sotalol, ziprasidone). Caution: combined use and/or higher doses increases risk of QT prolongation. Avoid, especially in patients at high risk of QT prolongation/torsades		▲			▲	▲	▲	▲	▲	▲	▲				▲	▲	▲	
Serotonin syndrome: Use caution if co-administering with drugs that affect serotonergic neurotransmitter systems (e.g. dextromethorphan, fentanyl, lithium, meperidine, methadone, pentazocine, selegiline, SSRIs, St. John's wort, tapentadol, tramadol, triptans, tryptophan).		▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲
MAOIs: Use with MAOIs, linezolid or methylene blue may lead to a potentially fatal reaction with tremor, agitation, hypomania, hyperthermia, hypertension, convulsions and death. For antidepressants that interact with MAOIs, follow the manufacturer's recommendations on the proper time period to wait between administration of MAOI and the other antidepressant.	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲		▲	▲	▲
Additive sedation: Sedative effects may be potentiated by alcohol, benzodiazepines and other CNS depressants.		▲		▲	▲		▲	▲	▲	▲	▲				▲	▲	▲	▲
Hypotension: May potentiate antihypertensive drug effects.				▲				▲				▲			▲	▲	▲	
Bleeding risk: Potential additive bleeding risk (particularly GI bleeding) with drugs such as warfarin, NSAIDs, and antiplatelet agents.		▲	▲	▲	▲	▲	▲		▲	▲	▲	▲	▲			▲		▲
Additive anticholinergic effects: May cause anticholinergic effects that could be additive with other anticholinergic medications, leading to blurred vision, confusion, constipation, dry mouth and urinary retention; use with caution in patients with conditions such as benign prostatic hyperplasia, angle-closure glau-coma, or increased intraocular pressure. Also, extra caution in older adults who are at higher risk.								▲	▲					▲	▲		▲	
CYP3A4 substrate**: Toxicity may be increased by inhibitors of CYP3A4 (e.g. clarithromycin, erythromycin, grapefruit juice, ketoconazole). Effectiveness may be reduced by inducers of CYP3A4 such as carbamazepine, phenytoin, rifampin and St John's Wort		▲	▲		▲			▲			▲	▲	▲		▲	▲		▲
CYP2D6 substrate**: Toxicity may be increased by inhibitors of CYP2D6 (e.g. bupropion, fluoxetine, paroxetine, quinidine, duloxetine).				▲	▲	▲			▲			▲					▲	
CYP2D6 inhibitor**: May increase the concentrations and toxicity of drugs metabolized by CYP2D6 (e.g. amitriptyline, clomipramine, desipramine, duloxetine, fluoxetine, imipramine, paroxetine).	▲			▲		▲			▲								▲	
CYP1A2 substrate**: Do not use with potent inhibitors of CYP1A2 such as ciprofloxacin, fluvoxamine, and ketoconazole. Effectiveness may be reduced by inducers of CYP1A2 (e.g. barbiturates and carbamazepine).				▲			▲										▲	

*Caution: This table provides an overview of common drug interactions but is NOT an exhaustive list. For a full list, please refer to the product monograph or a drug information reference such as Lexi-Comp. Interactions are subject to change; check with a pharmacist if you have any questions.

** For CYP450 interactions, only major substrates and moderate or strong inhibitors are listed.