



ADHD—attention deficit hyperactivity disorder, ADR—adverse drug reaction, CBT—cognitive behavioural therapy, CKD—chronic kidney disease, ESRD—end-stage renal disease, GI—gastrointestinal, HAM-A—Hamilton Anxiety Rating Scale, HAM-D—Hamilton Depression Rating Scale, MACE—major adverse cardiovascular events, MI—myocardial infarction, NNH—number needed to harm, NNT—number needed to treat, OR—odds ratio, PN—peripheral neuropathy, QIDS-C—Quick Inventory of Depressive Symptomatology—Clinician Rating, RCT—randomized controlled trial, SMD—standardized mean difference, SNRI—serotonin-norepinephrine reuptake inhibitor, SSRI—selective serotonin reuptake inhibitor, TCA—tricyclic antidepressant.

*The full list of references for Figures 1A and 1B is available in **Appendix 1** from <https://www.cfp.ca>. Go to the full text of the article online and click on the **CFPlus** tab.

Considerations in Antidepressant Decision Making

Adverse Effects^{13,52}

Headache ⁶⁰	<ul style="list-style-type: none"> • Most likely: bupropion, escitalopram • Likely: SSRIs, SNRIs, vortioxetine • Least likely: mirtazapine
Dysrhythmia ⁴⁸ and blood pressure ¹²	<ul style="list-style-type: none"> • QTc prolongation: citalopram, escitalopram, mirtazapine (caution if baseline QTc >450 ms) • BP/HR changes: bupropion, SNRIs ➢ BP/HR neutral: SSRI, vortioxetine, mirtazapine
Sedation ⁴⁶	<ul style="list-style-type: none"> • Most sedating: mirtazapine (esp. at low doses) • Possibly sedating: SSRI, SNRI, vortioxetine • Activating: bupropion
GI disturbances ⁴¹	<ul style="list-style-type: none"> • Nausea/vomiting: duloxetine, vortioxetine > SNRIs > SSRIs > mirtazapine • Constipation: SNRIs, paroxetine, sertraline > bupropion, vortioxetine > SSRIs • Anorexia: SNRIs > SSRIs, vortioxetine
Sexual dysfunction ^{3,15,32,47,57}	<ul style="list-style-type: none"> • Most likely: SSRI/SNRIs (30-70%; all aspects) • Likely: mirtazapine, vortioxetine • Least likely: bupropion (may improve SSRI-induced dysfunction; SMD 1.60 vs placebo)³
Seizure risk ¹	<ul style="list-style-type: none"> • Most likely: bupropion (1/1000; dose-related)⁵⁵ • Unlikely: SNRI, SSRI, mirtazapine, vortioxetine at therapeutic doses
Weight gain ^{21,63}	<ul style="list-style-type: none"> • Most likely: mirtazapine (+0.4 to +2.4 kg) citalopram (+0.1 to +7.1 kg) • Less likely to likely: SSRI, SNRI, vortioxetine • Least likely: bupropion (-2.4 to -0.4 kg)
Withdrawal symptoms ^{16,30}	<ul style="list-style-type: none"> • Most likely: paroxetine, venlafaxine, desvenlafaxine • Likely: SNRI and SSRI • Least likely: fluoxetine/vortioxetine(?) • Potentially none: mirtazapine, bupropion

Drug Interactions^{31,33}

CYP inhibitors

- CYP 2D6: **strong:** fluoxetine, paroxetine
- **moderate:** bupropion, duloxetine, sertraline (>100mg)
- CYP3A4: **moderate:** fluvoxamine, fluoxetine
- CYP1A2: **strong:** fluvoxamine
- CYP2C19: **strong:** fluvoxamine
- **moderate:** fluoxetine

CYP substrates

- 2D6: vortioxetine, venlafaxine, fluvoxamine, fluoxetine, mirtazapine, paroxetine
- 2C19: citalopram, escitalopram
- 1A2: duloxetine, fluvoxamine
- 3A4: mirtazapine

Serotonin syndrome:

Monitor: combining antidepressants with opioids, dextromethorphan, lithium, etc

Administration

- **CRUSH-able:** escitalopram,⁶⁴ sertraline (open capsule),⁶⁴ paroxetine IR,⁶⁴ fluvoxamine,⁶⁴ citalopram,⁶⁴ mirtazapine⁶⁴
- **DO NOT CRUSH:** desvenlafaxine SR²⁸, bupropion ER/SR^{28,45}, paroxetine CR,²⁸ duloxetine beads,^{28,61} venlafaxine beads*²⁸
- **Enteral tube considerations:** duloxetine beads^{9,61} and venlafaxine beads^{11,17} clog enteral tubes, dilute fluoxetine liquid with water(1:1)⁸
- **Orally disintegrating table available:** escitalopram,²⁸ mirtazapine²⁸
- **Commercial liquid available:** fluoxetine²⁸

*venlafaxine liquid compound= daily dose divided twice daily or 3 times daily and can be used in enteral tubes⁴⁹

Cost

Please check provincial formulary for list of antidepressants that are covered by provincial plans.

Other

- Patient's preference
- Previous antidepressant trials

Pharmacokinetics

Absorption^{27,36}

- Structural GI changes (gastric bypass/short gut/ostomy)
- Absorption erratic with ER medications (bupropion ER, duloxetine, desvenlafaxine, venlafaxine)
- Initiation: Avoid → choose non-ER antidepressants
- Stabilized: Monitor and change if necessary

Renal dosing⁴:

eGFR	Max starting dose
<60	<ul style="list-style-type: none"> • Bupropion 150 mg/day (max daily dose) • Desvenlafaxine 50 mg every 2 days (eGFR<30 max daily: 50 mg every 2 days) • Paroxetine 10 mg/day
<30	<ul style="list-style-type: none"> • Escitalopram 10 mg/day • Sertraline 50 mg/day (eGFR<15: 25 mg/day) • Duloxetine 30 mg/day • Venlafaxine 112.5 mg/day (max daily dose) • Mirtazapine 15 mg/day (max daily dose)

Hepatic dosing²³:

- Caution in dosing and reductions may be necessary (longer half-life of many medications)
- Avoid: duloxetine, sertraline(?) in hepatic impairment

BP—blood pressure, CR—controlled-release, CYP—cytochrome P450 enzyme, eGFR—estimated glomerular filtration rate, ER—extended-release, GI—gastrointestinal, HR—heart rate, IR—immediate-release, QTc—corrected QT interval, SMD—standardized mean difference, SNRI—serotonin-norepinephrine reuptake inhibitor, SR—sustained-release, SSRI—selective serotonin reuptake inhibitor.

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