







First-line medications for depression and anxiety disorders^{1,3-5,7,9,11-30}




The following medications are considered first-line in the CANMAT 2016 MDD Guidelines and 2014 Anxiety Guidelines.¹⁷ Some international guidelines recommend all SSRIs and SNRIs broadly (+/- agents) as first-line for MDD, anxiety or both.^{6,8,28} CANMAT classifies the SNRI levomilnacipran (Fetzima®) as second-line for MDD due to lack of comparative and relapse-prevention data.¹ Other options (e.g., amitriptyline, trazodone) are not first-line in any of the reviewed guidelines due to side effects.



Available evidence for drug selection has many limitations, including limited head-to-head trials between drugs and potential for bias. If you have questions about drug selection, consult a pharmacist or specialist through [eConsult](#).

Selective Serotonin Reuptake Inhibitors (SSRI)											
Side effects of all SSRIs:						Warnings for all SSRIs:					
CNS: headache, sleep disturbance, drowsiness, nervousness, dizziness, somnolence, fatigue GI: nausea, vomiting, diarrhea Anticholinergic: dry mouth, constipation, blurred vision, hyperhidrosis CV: orthostatic hypotension, tachycardia Urogenital: sexual dysfunction						Anxiety/agitation may worsen initially (first 1-2 weeks) GI bleeding (consider gastroprotective agent if high risk) Hyponatremia (especially in elderly) Fractures (especially in first 6 weeks) Suicidal thinking & self-harm (patients 30 years and under)					
Medication	First-line for				Features (Consider in addition to other patient and medication factors)	Side effects, warnings and contraindication (In addition to those listed above)	Overall tolerability*	Activating or sedating?	Interaction risk	Dosing**	Coverage and cost for usual dose (\$/100 days)
	MDD	GAD	SAD	Panic							
Citalopram (Celexa)[Ⓒ] 10 mg, 20 mg, 40 mg tablet	X			X	A preferred pharmacological option in pregnancy	QTc prolongation risk Contraindicated in patients with known QT prolongation or congenital long QT syndrome		Activating/ sedating	+ (CYP) Caution: combined QT-prolongation risk	Initial: 10-20 mg daily (am/pm) Usual: 20-40 mg daily Max: 40 mg daily (20 mg in older adults, liver disease, concurrent CYP 2C19 inhibitor)	ODB: ✓ NIHB: ✓ \$24 - 60
Escitalopram (Cipralex)[Ⓒ] 10 mg, 20 mg tablet	X	X	X	X	A preferred pharmacological option in pregnancy	QTc prolongation risk Contraindicated in patients with known QT prolongation or congenital long QT syndrome		Activating/ sedating	+ (CYP) Caution: combined QT-prolongation risk	Initial: 5-10 mg daily (am/pm) Usual: 10-20 mg daily Max: 20 mg daily (10 mg in older adults, liver disease, concurrent CYP 2C19 inhibitor)	ODB: ✓ NIHB: ✓ \$26 - 45
Fluoxetine (Prozac)[Ⓒ] 10 mg, 20 mg, 40 mg, 60 mg capsule 4 mg/mL oral solution	X			X	Easy to discontinue (self-taper)	Side effects: insomnia, agitation, anorexia Higher rates of confusion QTc prolongation risk		Activating	+++	Initial: 10-20 mg daily (am) Usual: 20 mg daily Max: 80 mg daily (lower dose recommended for older adults)	ODB: ✓ (excludes 10mg tab) NIHB: ✓ \$45 - 152
Fluvoxamine (Luvox)[Ⓒ] 50 mg, 100 mg tablet	X		X	X		Side effects: severe GI upset, anorexia, anticholinergic potential Caution when using in older adults		Sedating	+++	Initial: 25-50 mg daily (hs) Usual: 100-200 mg daily Max: 300 mg daily Divide doses above 150 mg (max 150 mg at bedtime) Hepatic/renal disease: increase dose slowly & monitor carefully	ODB: ✓ NIHB: ✓ \$55 - 132

Paroxetine (Paxil®) ^G 10 mg, 20 mg, 30 mg tablet CR: 12.5 mg, 25 mg tablets	X	X	X	X	A preferred pharmacological option for breastfeeding	Side effects: anticholinergic potential, withdrawal effects, weight gain Avoid in older adults and pregnancy		Sedating	+++	Initial: 10-20 mg daily (hs) Usual: 20 mg daily (40 mg for GAD) Max: 50 mg daily (40 mg for older adults/debilitated patients) CR formulation Initial: 12.5-25 mg daily (hs) Usual: 25 mg daily (50 mg for GAD) Max: 62.5 mg daily (50 mg for older adults/debilitated patients)	ODB: ✓ (excludes 10mg and CR tablets) NIHB: ✓ (excludes CR tablets) \$27 - 125 CR: \$252 - 790
Sertraline (Zoloft®) ^G 25 mg, 50 mg, 100 mg capsule	X	X	X	X	A preferred pharmacological option for older adults, pregnancy and breastfeeding May be a preferred option in CV disease			Activating	++	Initial: 25-50 mg daily (am/pm) Usual: <i>MDD: 50-100 mg daily</i> <i>GAD: 50-150 mg daily</i> <i>SAD & Panic: 50-200 mg daily</i> Max: 200 mg daily	ODB: Y NIHB: Y \$26 - 81

Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)

Medication	First-line for				Features (Consider in addition to other patient and medication factors)	Side effects, warnings and contraindication (In addition to those listed above)	Overall tolerability*	Activating or sedating?	Interaction risk	Dosing**	Coverage and cost for usual dose (\$/100 days)
	MDD	GAD	SAD	Panic							
Desvenlafaxine (Pristiq®) ^G 50 mg, 100 mg tablets	X					Side effects of all SNRIs: CNS: headache, sleep disturbance, drowsiness, nervousness, dizziness, somnolence, fatigue		Activating > sedating	+	Initial: 50 mg daily Usual: 50 mg daily Max: 100 mg daily	ODB: x NIHB: x \$268
Duloxetine (Cymbalta®) ^G 30 mg, 60 mg capsule	X	X			A preferred option for older adults Helpful for some types of pain	GI: nausea, vomiting, diarrhea, decreased appetite Anticholinergic: dry mouth, constipation, blurred vision, hyperhidrosis		Activating > sedating	++	Initial: 30 mg daily (may be considered for tolerability) Usual: 60 mg daily Max: 60 mg daily (120 mg daily for GAD)	ODB: ✓ NIHB: ✓ \$48 - 167
Venlafaxine (Effexor®) ^G 37.5 mg, 75 mg, 150 mg capsule	X	X	X	X	Helpful for some types of pain	CV: increased blood pressure, orthostatic hypotension Urogenital: sexual dysfunction Warnings for all SSRIs: Anxiety/agitation may worsen initially (first 1-2 weeks) Increased risk of bone fracture		Activating > sedating	+		ODB: ✓ NIHB: ✓ \$19 - 69

<p>Pregabalin (Lyrica®)^G Calcium Modulator, GABA Anxiolytic</p> <p>25 mg, 50 mg, 75 mg, 150 mg, 300 mg capsule</p>		X	X		<p>Helpful for some types of pain</p>	<p>CNS: headache, sleep disturbance, memory impairment, ataxia, diplopia, dizziness, somnolence, sedation, fatigue</p> <p>GI: nausea, vomiting, diarrhea</p> <p>Anticholinergic: dry mouth, blurred vision</p> <p>Other: skin rash, peripheral edema, weight gain</p> <p>Angioedema Hypersensitivity reactions Caution in renal impairment New-onset congestive heart failure in CV-compromised adults Reduced GI mobility (caution with concurrent opioid use)</p>		Sedating	0/+	<p>Initial: 150 mg daily (75 mg BID or 50 mg TID)</p> <p>Some experts recommend 50 mg daily</p> <p>Titration: Increase weekly</p> <p>Usual: <i>GAD:</i> 300 mg daily (150 mg BID) <i>SAD:</i> 600 mg daily (300 mg BID)</p> <p>Max: 600 mg daily (300 mg BID)</p>	<p>ODB: ✓ NIHB: ✓ \$25 - 99</p>
<p>Vortioxetine (Trintellix®) Serotonin Receptor Antagonist and Serotonin Reuptake Inhibitor (SARI)</p> <p>5 mg, 10 mg, 20 mg tablet</p>	X					<p>CNS: headache, sleep disturbance, nervousness, dizziness, fatigue</p> <p>GI: nausea, vomiting, diarrhea, abdominal pain, bloating, decreased appetite</p> <p>Anticholinergic: dry mouth, constipation, hyperhidrosis</p> <p>CV: orthostatic hypotension</p> <p>Other: cough, flu-like symptoms, pruritus, joint and muscle pain</p> <p>Anxiety/agitation may worsen initially (first 1-2 weeks) Increased risk of bone fracture Caution in narrow-angle glaucoma</p>		Activating/ sedating	++	<p>Initial: 10 mg daily (5 mg daily in older adults >65; consider decreasing to 5 mg if higher dose is not tolerated)</p> <p>Usual: 10–20 mg daily</p> <p>Max: 20 mg daily</p>	<p>ODB: ✓ NIHB: ✓ \$320 - 363</p>

Legend: MDD = major depressive disorder, GAD = generalized anxiety disorder, SAD = social anxiety disorder, Panic = panic disorder +/- agoraphobia, G = generic available

*Overall tolerability is based on availability of evidence that primarily evaluates drop-out rates from trials. Specific drug side effects and patient factors may influence overall tolerability in practice.

**Titration information:

Depression: For most agents, increase dose no more than once a week.

Anxiety OR if sensitive to side effects, or has kidney disease, liver disease, advanced age, or other factors warranting caution: Start with the lowest dose and increase every 1-2 weeks.