Appendix C: First-Line Antidepressants

"First-line" antidepressant treatment represents a balance of efficacy, tolerability and expert consideration per the Canadian Network for Mood and Anxiety Treatments (CANMAT) recommendations. Other pharmacotherapies are reserved for situations where first-line antidepressants are not indicated or cannot be used, or when first-line treatments have not worked.

Generic Name (Trade Name), Dosage Forms and Strengths	Usual Adult Daily Dose*	Adverse Reactions	Cost per 30 Days †	Therapeutic Considerations	Elimination Half-Life (h)
Selective Serotonin Reuptake Inhibitors (SSRIs) Note: SSRIs can be associated with prolonged corrected QT interval. This can lead to Torsades de Pointes (a rare cardiac arrhythmia), especially at higher doses and if taking multiple QT interval prolonging medications. Risk factors for QT prolongation syndrome include: low ventricular ejections fraction (<40%), left ventricular hypertrophy, dilated cardiomyopathy; myocardial ischemia, myocarditis; congenital long QT syndrome; bradycardia, AV and SA blocks; electrolyte abnormalities (hypokalemia, hypomagnesemia, hypocalcemia); use of multiple QT interval prolonging medications, older age (> 65 years); and female sex. For those at significant risk, baseline and follow up ECGs may be warranted using clinical judgment, but routine ECG monitoring prior to starting an antidepressant in every patient is not necessary.					
citalopram (Celexa®, CTP 30®, G) Tabs: 10 mg, 20 mg, 30 mg, 40 mg	Usual: 10-40 mg Maximum: 40 mg	**CNS:** sleep disturbances (insomnia, sedation), tremor, headache **CVS:** orthostatic hypotension, ECG changes **Anticholinergic:** dry mouth, sweating, constipation **GI:** nausea, vomiting, diarrhea, constipation, ↑ risk of GI bleed **Sexual disturbances:** ↓ libido, impotence, ejaculatory disturbances, anorgasmia. (likely to persist during SSRI therapy) **Hyponatremia:** can occur. (may cause fatigue or delirium) **Serotonin Syndrome:** agitation, tachycardia, tremor hyperreflexia. (combination with other serotonergic dugs also increase risk of syndrome) **Bleeding risk[5,6]:** especially when combined with ASA, NSAID or anticoagulants.	$6-11 (Regular coverage)	• [§] SSRIs have "flat" dose-response curves. For depression, most patients respond to initial lower dose. Higher doses are used for treatment of OCD. Do not ↑ dose until steady state is reached (i.e., ~4 weeks for fluoxetine, and 1-2 weeks for others). • Therapeutic effect seen after 7-28 days. • Citalopram and escitalopram have fewest drug interactions among SSRIs. • Fluoxetine is most anorexic and stimulating, has active metabolite and has long half-life. • Fluvoxamine is most nauseating, constipating and sedating among SSRIs (can be given at bedtime). • Paroxetine has most anticholinergic adverse effects & anxiety, and can cause weight gain. • Sertraline has most diarrhea and male sexual dysfunction among SSRIs. It has few drug interactions.	23-45
escitalopram (Cipralex®, Cipralax MELTZ®) Tabs: 10 mg, 20 mg Orodispersible Tabs: 10 mg, 20 mg	Usual: 10-20 mg Maximum: 20 mg (or 10 mg in elderly, patients with liver problems, on omeprazole or cimetidine)		$56-60 (Tabs: Regular coverage)		27-32
fluoxetine (Prozac®, G) Caps: 10 mg, 20 mg Solution: 20 mg/5 mL	Usual: 10-40 mg Maximum:[§] 80 mg		$15-30 (Regular coverage)		24-144 (parent); 200-330 (metabolite)
fluvoxamine (Luvox®, G) Tabs: 50 mg, 100 mg	Usual: 50-200 mg Maximum:[§] 300 mg		$7-25 (Regular coverage)		9-28
paroxetine (Paxil®, Paxil® CR, G) Tabs: 10 mg 20 mg, 30 mg, 40 mg CR Tabs: 12.5 mg, 25 mg	Usual: 10-40 mg (or 12.5-50 mg for CR tablets) Maximum:[§] 60 mg		$7-30 (Regular coverage)		3-65
sertraline (Zoloft®, G) Caps: 25 mg, 50 mg, 100 mg	Usual: 50-150 mg Maximum:[§] 200mg		$13-27 (Regular coverage)		22-36 (parent); 62-104 (metabolite)
Norepinephrine Dopamine Reuptake Inhibitors (NDRIs)					
bupropion (Wellbutrin® SR, Wellbutrin® XL, G) SR Tabs: 100 mg, 150 mg XL Tabs: 150 mg, 300 mg	Usual: 150-300 mg Maximum: 300 mg	**CNS:** sleep disturbances (insomnia, nightmares), agitation, seizures (high dose, or abrupt dose ↑), headache **CVS:** orthostatic hypotension, dizziness **GI:** ↓ appetite, anorexia	$8-37 (Regular coverage)	• SR Tabs: Max.150 mg per dose. Doses >150 mg per day should be given BID, preferably with ≥8 hours between doses. • XL Tabs: once daily dosing (AM). • Therapeutic effect seen after 7-28 days. • May ↓ seizure threshold. Contraindicated in patients with current or history of seizure disorder, bulimia or anorexia nervosa, or undergoing alcohol or benzodiazepine withdrawal. • Rarely inhibits sexual functioning.	10-14 (parent); 20-27 (metabolite)

Generic Name (Trade Name), Dosage Forms and Strengths	Usual Adult Daily Dose*	Adverse Reactions	Cost per 30 Days †	Therapeutic Considerations	Elimination Half-Life (h)
Selective Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)					
desvenlafaxine (Pristiq®) XR Tabs: 50 mg, 100 mg	Initial: 50 mg Usual: 50 mg Maximum: 100 mg	Generally dose-related. **CNS:** sleep disturbances, headache, agitation, hostility, suicidal urges **CVS:** modest, sustained ↑ in BP and HR, dizziness, orthostatic hypotension **Anticholinergic:** dry mouth, sweating, constipation **GI:** nausea **Sexual disturbances:** ↓ libido, delayed orgasm/ejaculation, anorgasmia. **Serotonin Syndrome:** agitation, tachycardia, tremor hyperreflexia. (combination with other serotornergic dugs also increase risk of syndrome)	$89 (No coverage)	• Therapeutic effect seen after 7-28 days. • Major active metabolite of venlafaxine. • Monitor BP for 2 months at each dose level. Do not use in patients with uncontrolled hypertension.	11
duloxetine (Cymbalta®) Caps: 30 mg, 60 mg	Initial: 30 mg Usual: 30-60 mg Maximum: 120 mg		$62-124 (No coverage)	• Therapeutic effect seen after 7-28 days. • Less effect on BP. Has been associated with hepatic injury. Do not use in patients with underlying liver disease, or substantial alcohol use, or severe renal insufficiency.	8-19
venlafaxine (Effexor® XR, G) XR Caps: 37.5 mg, 75 mg, 150 mg	Initial: 37.5-75 mg Usual: 75-225 mg Maximum: 375 mg		$11-32 (Regular coverage)	• Therapeutic effect seen after 7-28 days. • Monitor BP for 2 months at each dose level. Do not use in patients with uncontrolled hypertension.	9-21 (absorption half-life)
Noradrenergic/Specific Serotonergic Agents (NaSSAs)					
mirtazapine (Remeron®, Remeron®, G) Tabs: 15 mg, 30 mg, 45 mg Orally disintegrating tabs: 15 mg, 30 mg, 45 mg	Initial: 15 mg (or 7.5 mg in elderly) Usual: 15-30 mg Maximum: 60 mg	**CNS:** fatigue, sedation **Anticholingeric:** dry mouth constipation **Endocrine:** ↑ appetite, carbohydrate craving, weight gain, ↑ cholesterol **Sexual disturbance:** occasionally occurs (<2%)	$3-5 (Regular coverage)	• Therapeutic effects seen after 7-28 days. • ↓ sleep latency and ↑ sleep duration. May be of benefit in patients with marked anorexia, insomnia, or agitation. • Caution in patients with compromised liver or renal function.	20-40
Reversible Inhibitor of MAO-A (RIMA)					
moclobemide (Manerix®, G) Tabs: 100 mg, 150 mg, 300 mg	Initial: 300 mg (divided BID) Usual: 300-600 mg (some respond to 150 mg daily, but most require >450 mg) Maximum: 600 mg	**CNS:** insomnia (especially if given in the evening), headache, sedation, restlessness, anxiety, agitation **Anticholinergic:** dry mouth, blurred vision **CVS:** orthostatic hypotension, dizziness **GI:** nausea, abdominal pain, constipation	$10-20 (Regular coverage)	• Therapeutic effects seen after 7-28 days. • Take after meals to minimize tyramine-related responses (e.g., headache); avoid ingesting large quantities of tyramine-rich foods. • Hypertensive reactions may occur in patients with thyrotoxicosis or pheochromocytoma. • Enzyme inhibition is reversible (within 24 hours). • ↑ REM sleep.	1-3

Abbreviations: AM morning; **ASA** acetylsalicylic acid; **AV** atrioventricular nodal; **BID** twice daily; **BP** blood pressure; **Caps** capsules; **CNS** central nervous system; **CR** controlled-release; **CVS** cardiovascular system; **ECG** electrocardiogram; **G** generic brands available; **GI** gastrointestinal; **HR** heart rate; **max** maximum; **mg** milligrams; **mL** millilitres; **NSAID** Nonsteroidal anti-inflammatory drugs; **OCD** obsessive-compulsive disorders; **REM** rapid eye movement; **SA** sinoatrial nodal; **SR** sustained-release; **SSRI** selective serotonin reuptake inhibitor; **Tabs** tablets; **XL** or **XR** extended-release.

Footnotes:

* Dose should be individualized. Dosage adjustment may be required in patients with hepatic or renal impairment. Refer to latest product monographs and regularly review current Health Canada advisories, warnings and recalls at www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/index_e.html.

† Pricing is approximate as per PharmaCare Formulary Search on May 23, 2013 (www.health.gov.bc.ca/pharmacare/benefitslookup/) and does not include dispensing fee or additional markups. They are calculated based on the "Usual adult daily doses" in this table. "Regular coverage", also known as "regular benefit", does not require Special Authority. Regular benefit drugs may be fully or partially covered. Coverage is subject to drug price limits set by PharmaCare and to the patient's PharmaCare plan rules and deductibles. See: www.health.gov.bc.ca/pharmacare/plans/index.html and www.health.gov.bc.ca/pharmacare/policy.html for further information.

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