

Depression Specifiers³⁴

| Sleep Disturbances ³⁴ |
|----------------------------------|
| • mirtazapine |

| Cognitive Dysfunction ³⁴ | |
|-------------------------------------|--------------|
| • Vortioxetine | • Duloxetine |
| • SSRIs (vs Placebo) | • Bupropion |

| Anxious distress ³⁴ | |
|--------------------------------|----------------|
| • Paroxetine | • Escitalopram |
| • Duloxetine | • Venlafaxine |
| • Sertraline | |

| Somatic symptoms ³⁴ | |
|--------------------------------|------------------|
| Fatigue | Pain |
| • Duloxetine | • duloxetine |
| • Bupropion | • Venlafaxine |
| • SSRIs (vs Placebo) | • desvenlafaxine |

No Depression specifiers

ANY first line agent³⁴

- SSRI: citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline
- SNRI: desvenlafaxine, duloxetine, venlafaxine
- Other: Bupropion, mirtazapine, vortioxetine

Choice based on adverse effects, cost, drug interactions and other considerations

No Comorbidities

Comorbidities present

Central Nervous System

Smoking Cessation
 • Bupropion up to 300mg daily; combine with NRT (NNT=8)⁴⁶

Alcohol use disorder⁷
 • **Abstinence:** sertraline up to 200mg daily + Naltrexone NNT=4. no change in mood⁴⁵
 • **Mood:** mirtazapine 45mg daily 50% reduction in HAM-D and HAM-A scores⁶⁷

ADHD
 • Bupropion up to 450mg daily SMD -0.5 in ADHD scores⁶¹
 • Duloxetine up to 60mg daily improvement in ADHD scores (limited data)⁸

| Pain | |
|--|--|
| Chronic Low Back Pain | Duloxetine 60-120mg daily ≥30% ↓ pain inconsistent (ADR NNH~6-12) ^{19,39} |
| Osteoarthritis | Venlafaxine 150 - 225mg ↓ 30% pain in hip and knee OA in 9/18 patients ⁵⁸ Duloxetine 60 -120mg daily ↓ knee OA pain only NNT=7 (ADR NNH=17) ^{15,19,39} |
| Diabetic Peripheral Neuropathy (PN) | Duloxetine 40-120mg daily ↓ pain NNT=6 (ADR NNH@60mg =20;NNH@120mg=10) ^{37,39} Venlafaxine 150-225mg daily ↓ pain NNT=5 (limited data) ^{23,37,52} Desvenlafaxine 200-400mg daily (EXCEEDS depression dose) ³⁷ |
| Fibromyalgia | Mirtazapine to 30mg daily. Conflicting data. ↓ pain by ≥30% NNT=7-8 vs ADR NNH=9 ^{37,64} Duloxetine 60 -120mg daily ↓pain NNT=8 vs ADR NNH@60mg = 18 ;NNH@120mg=9 ^{37,39} SSRI small ↓ pain (10%) NNT=10 (low quality RCTs) ^{37,62} Venlafaxine - limited benefit (no RCT) ³⁷ |
| Chemotherapy -Induced PN | Duloxetine 60mg daily ↓ pain (-0.73 vs placebo) (NNT=5) ⁵⁶ |

Migraine Prophylaxis
 • Venlafaxine up to 150mg daily small RCT equivalent to TCA^{11,44}
 • Duloxetine 60 to 120mg daily ↓ number of headache days (limited data)⁶⁸

Cardiovascular

Heart Failure
 • Sertraline safe. No significant mood benefit⁴²

ACS
 • Escitalopram 5 -20mg daily ↓ MACE (MI) post ACS NNT=8 over 8 years³⁵
 • Sertraline Safe to use. No significant CV benefits underpowered for mood outcomes²⁷

Gastrointestinal

Liver disease
 • Hep C + Interferon: SSRIs (citalopram up to 20mg daily; weak data)³⁶

IBS (constipation and abdominal pain)
 • Paroxetine, fluoxetine, citalopram 55% ↓ global IBS symptoms (vs 33% placebo; NNT=5) over 6-12 weeks. Non-Significant vs placebo in ↓ abdominal pain^{20, 21}

Genitourinary

Loss of Libido in women
 • Bupropion 150mg daily OR=3.2 (2.1-6.3) 'meaningful improvement' (NNT=2)⁵³

Stress incontinence
 • Duloxetine QoL improvement (SMD -0.13) NNT=8 and ↓ no. of episodes (ADR NNH =7)^{26,40}

Renal

Non-Dialysis CKD
 • Sertraline to 200mg daily. no mood benefit. ↑ GI symptoms (NNH=8-9)³⁰

Dialysis ESRD
 • Sertraline to 200mg daily. ↓ QIDS-C at 12 weeks vs. CBT(-1.84, p=0.035)⁴¹

ESRD-associated Pruritis⁶
 • Sertraline 50mg (25-100mg) ↓ pruritis score in ESRD (Limited data)^{6,55}
 • mirtazapine 15mg daily(Limited data)^{6,25}

Adult Depression Antidepressant Treatment based on Efficacy and Comorbidities

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Considerations in Antidepressant Decision Making

Tracy Chin, PharmD, ACPR

Adverse Effects ^{14,54}

Headache⁶⁰

- **Most likely:** bupropion, escitalopram
- **Likely:** SSRIs, SNRIs, vortioxetine
- **Least likely:** mirtazapine

Dysrhythmia⁵⁰ and Blood Pressure¹³

- **QTc prolongation:** citalopram, escitalopram, mirtazapine (caution if baseline QTc >450ms)
- **BP/HR changes:** bupropion, SNRIs neutral: SSRI, vortioxetine, mirtazapine

Sedation⁴⁸

- **Most Sedating:** mirtazapine (esp. at low doses)
- **Possibly sedating:** SSRI, SNRI, vortioxetine
- **Activating:** bupropion

GI Disturbances⁴³

- **Nausea/Vomiting:** duloxetine, vortioxetine > SNRIs > SSRIs > mirtazapine
- **Constipation:** SNRIs, paroxetine, sertraline > bupropion, vortioxetine > SSRIs
- **Anorexia:** SNRIs > SSRIs, vortioxetine

Sexual Dysfunction^{4,16,33,49,59}

- **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^{2,57}

- **Most likely:** bupropion (1/1000; dose-related)
- **Unlikely :** SNRI, SSRI, mirtazapine, vortioxetine at therapeutic doses

↑ Weight^{22,65}

- **Most likely:** mirtazapine (+0.4 to +2.4 kg) citalopram (+0.1 to +7.1kg)
- **Less Likely to Likely :** SSRI, SNRI, vortioxetine
- **Least likely:** bupropion (-2.4kg to -0.4kg)

Withdrawal Symptoms^{17,31}

- **Most likely:** paroxetine, venlafaxine, desvenlafaxine
- **Likely:** SNRI and SSRI
- **Least likely:** fluoxetine/ vortioxetine(?)
- **Potentially None:** mirtazapine, bupropion

Drug Interactions^{32,34}

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:** escitalopram⁶⁶, sertraline (open capsule)⁶⁶, paroxetine IR⁶⁶, fluvoxamine⁶⁶, citalopram⁶⁶, mirtazapine⁶⁶
 - **DO NOT CRUSH:** desvenlafaxine SR²⁹, bupropion ER/SR^{29,47}, paroxetine CR²⁹, duloxetine beads^{29,63}, venlafaxine beads*²⁹
 - **Enteral tube considerations:** duloxetine beads^{10,63} and venlafaxine beads^{12,18} clogs enteral tubes, dilute fluoxetine liquid with water(1:1)⁹
 - **ODT available:** escitalopram²⁹, mirtazapine²⁹
 - **Commercial liquid available:** fluoxetine²⁹
- *venlafaxine liquid compound= daily dose div BID or TID and can be used in enteral tubes⁵¹

Pharmacokinetics

Absorption^{28,38}

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

Renal Dosing⁵:

| eGFR | Max Starting dose |
|------|--|
| < 60 | <ul style="list-style-type: none"> • Bupropion 150mg/d (max daily dose) • Desvenlafaxine 50mg Q2days (eGFR<30 max daily:50mg Q2d) • Paroxetine 10mg/day |
| < 30 | <ul style="list-style-type: none"> • Escitalopram 10mg/day • Sertraline 50mg/day (eGFR<15: 25mg/day) • Duloxetine 30mg/day • Venlafaxine 112.5mg/day (max daily dose) • Mirtazapine 15mg/day (max daily dose) |

Hepatic Dosing²⁴:

- Many agents ↑ T1/2 in hepatic impairment. Caution in dosing and reductions may be necessary
- Avoid: duloxetine, sertraline(?) in hepatic impairment

Cost¹

Not covered*

- *by Govt of Alberta plans
- Desvenlafaxine
- Levomilnacipran
- Vilazodone

Covered

- All SSRIs
- SNRI: duloxetine, venlafaxine
- Other: mirtazapine, bupropion, Vortioxetine

Other

- **Patient's Preference**
- **Previous Antidepressant Trials**

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