

APPENDIX C: Adjunctive medications

Second-line adjunctive therapy options

Adjunctive Agent	Level of Evidence	Dosing	Adverse Effects
Brexpiprazole*	1-3 mg	Weight gain, hyperglycemia, elevated triglycerides, EPS (appears to be less common than with aripiprazole), headache, orthostatic hypotension (rare) ¹⁹
Bupropion	...	150-300 mg	Agitation, insomnia, anorexia. Contraindicated in anorexia or bulimia nervosa and seizure disorders ¹⁹
Lithium	...	600-1200 mg (therapeutic serum levels)	Gastrointestinal discomfort, nausea, vertigo, muscle weakness and a dazed feeling that frequently disappear after stabilization of therapy ³²
Mirtazapine/mianserin	...	30-60 mg	Weight gain, sedation ¹⁹
Modafinil	...	100-400 mg	Headache, nausea, rhinitis, nervousness, diarrhea, back pain, anxiety, dizziness, dyspepsia, and insomnia ³³
Olanzapine	2.5-10 mg	Weight gain, dizziness, sedation, anticholinergic effects, hepatic aminotransferase elevation, orthostatic hypotension, increased risk of diabetes and dyslipidemia, EPS (especially akathisia) ¹⁹
Triiodothyronine	...	25-50 mcg	

*Newly approved since the 2009 Canadian Network for Mood and Anxiety Treatments (CANMAT) guidelines

Level of evidence:

.... = Meta-analysis with narrow confidence intervals and/or 2 or more RCTs with adequate sample size, preferably placebo-controlled

... = Meta-analysis with wide confidence intervals and/or 1 or more RCTs with adequate sample size,

.. = Small-sample RCTs or nonrandomized, controlled prospective studies or case series or high-quality retrospective studies,

. = Expert opinion/consensus

APPENDIX D: Special patient populations

Second-line treatment options: antenatal MDD

Mild to Moderate²¹

SSRIs:

- Citalopram
- Escitalopram
- Sertraline

Severe*

All the remaining SSRIs (except paroxetine), newer generation antidepressants and TCAs²¹

Second-line treatment options: postpartum MDD

Mild to Moderate²¹

- Citalopram
- Escitalopram
- Sertraline
- Combination SSRI + CBT or IPT

Severe*

After first-line citalopram, escitalopram, and sertraline, other antidepressants are second-choice treatments for women who are more severely depressed²¹

*Electroconvulsive therapy (ECT) can be an effective treatment for severe MDD in pregnant and postpartum patients who:

- 1) have psychotic features;
- 2) treatment-resistant patients; and,
- 3) who elect to use this modality as a matter of preference.^{14,21}

Weigh the risks and benefits of ECT with pregnant patients before recommending treatment.

Second-line treatment options: Older Adults

Mild to Severe²¹

Switch to:

- Bupropion
- Moclobemide
- Phenelzine
- Quetiapine
- Trazodone

Combine with:

- Aripiprazole
- Lithium
- Methylphenidate

- Aripiprazole (Antipsychotics, second-generation) 2 mg daily PO¹⁹
- Lithium carbonate at a dose of 600–900 mg daily¹⁹
- Methylphenidate can enhance motivation and energy but cannot improve symptoms of depression¹⁹
- Phenelzine (MAOI) 30–90 mg daily¹⁹