BUPROPION SHORTAGE: TOOL FOR SWITCHING BETWEEN AGENTS IN CANADA

The information provided below is intended to help patients and health-care providers select an alternative agent to bupropion. Doses should be individualized to optimally control the patient's health condition. Close monitoring of symptoms of the underlying condition, bupropion discontinuation syndrome and adverse effects of the selected agent may be required during the transition period.

When switching from bupropion to another psychotropic medication, a washout period is generally not required unless there is a significant interaction between the 2 agents. Gradually taper the dose of bupropion by 25% per week, to 150 mg/day for 1–2 weeks, then start the new agent at a low dose and increase slowly. A conservative approach involves tapering the dose of bupropion to 150 mg/day for 1–2 weeks, then waiting for a 1-week washout period before initiating the new agent.

A slow taper of bupropion may not be easily feasible since tablets are available only in sustained-release/extended-release form and generally should not be cut or crushed. However, 1 study reports that cutting bupropion tablets had minimal effect on drug release.[1] Alternatively, the dose may be reduced from once daily to every other day. Tapering may not be possible, depending on bupropion supply.

If bupropion is abruptly discontinued or dose-reduced, patients are at risk of experiencing discontinuation syndrome.[2] Symptoms include insomnia, dizziness, nausea and diarrhea. If untreated, symptoms usually subside within 3 weeks. Reassure patients that discontinuation syndrome is not life-threatening, and severe symptoms will usually resolve in 3 days or less. Bupropion and its active metabolites have a longer half-life than some antidepressants (bupropion: 14–21 hours; metabolites: up to 33 hours), so the symptoms may not be as severe.

Discontinuation syndrome can be reversed by restarting the antidepressant and tapering the dose more slowly. Alternatively, if a slow taper is poorly tolerated, substitute with 1 dose of fluoxetine 10–20 mg PO. If discontinuation-emergent symptoms have not resolved after several days, a 2nd dose of fluoxetine 20 mg may be taken if necessary. Consider a herbal product containing ginger if drug interactions or adverse effects limit use of other antinausea medications.

1. Cochren BE. Splitting bupropion extended-release tablets. Am J Health Syst Pharm 1999;56(6):575.

2. Warner CH, Bobo W, Warner C et al. Antidepressant discontinuation syndrome. Am Fam Physician 2006;74(3):449-56.

Drug	Indication	Initial Dose	Usual Maintenance Dose	High Dose[a]	Available Products
ALTERNATIVES, DEPRESSION					
Bupropion	Depression, first-line treatment	SR: 150 mg/day[b] XL: 150 mg/day[b]	SR: 150–300 mg/day (doses >150 mg/day should be given in divided doses) XL: 150–300 mg/day	SR: 375–450 mg/day (doses >150 mg/day should be given in divided doses) XL: 450 mg/day	SR: 150 mg XL: 150 mg, 300 mg
	Depression, augmentation of standard antidepressants	150 mg/day[b]	150–300 mg/day		
Aripiprazole[c]	Depression, augmentation of standard antidepressants		2 mg daily PO		2 mg, 5 mg, 10 mg, 15 mg, 20 mg, 30 mg
Citalopram	Depression, first-line treatment	10–20 mg/day[b]	20–40 mg/day	40 mg/day	10 mg, 20 mg, 30 mg, 40 mg
Desvenlafaxine	Depression, first-line treatment	50 mg/day	50 mg/day	100 mg/day	50 mg, 100 mg
Duloxetine	Depression, first-line treatment	30 mg/day	60 mg/day	120 mg/day	30 mg, 60 mg
Escitalopram	Depression, first-line treatment	10 mg/day[b]	10–20 mg/day	20 mg/day	10 mg, 20 mg
Fluoxetine	Depression, first-line treatment	10–20 mg/day[b]	20–40 mg/day	60–80 mg/day	10 mg, 20 mg, 40 mg, 60 mg; 20 mg/5 mL solution
Fluvoxamine	Depression, first-line treatment	50–100 mg/day[b]	150–200 mg/day	400 mg/day	50 mg, 100 mg
Mirtazapine[d]	Depression, first-line treatment	15–30 mg/day[b]	30–45 mg/day	60 mg/day	15 mg, 30 mg, 45 mg
Paroxetine	Depression, first-line treatment	IR: 10–20 mg/day[b] CR: 12.5–25 mg/day[b]	IR: 20-40 mg/day CR: 25–50 mg/day	IR: 60 mg/day CR: 75 mg/day	IR: 10 mg, 20 mg, 30 mg, 40 mg CR: 12.5 mg, 25 mg

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Drug	Indication	Initial Dose	Usual Maintenance Dose	High Dose[a]	Available Products
Quetiapine[c]	Depression, augmentation of standard antidepressants	25 mg once daily	25–100 mg once daily	150–300 mg/day	IR: 25 mg, 100 mg, 200 mg, 300 mg XR: 50 mg, 150 mg, 200 mg, 300 mg, 400 mg
Risperidone[c]	Depression, augmentation of standard antidepressants		0.5–2 mg daily PO		0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg; 1 mg/mL solution
Sertraline	Depression, first-line treatment	25–50 mg/day[b]	50–100 mg/day	150–200 mg/day	25 mg, 50 mg, 100 mg
Venlafaxine[e]	Depression, first-line treatment	37.5–75 mg/day[b]	112.5–225 mg/day	300–375 mg/day	37.5 mg, 75 mg, 150 mg
Vortioxetine[d,e]	Depression, first-line treatment	5–10 mg/day[b]	10–20 mg/day		5 mg, 10 mg, 20 mg
ALTERNATIVES, SMOKING CESSATION					
Bupropion	Smoking cessation, first-line treatment	SR: 150 mg/day PO x 3 days	SR: 150 mg BID PO × 7–12 wk		SR: 150 mg
Nicotine Replacement Therapy (NRT)	Smoking cessation, first-line treatment	Product-dependent	Product-dependent	Product-dependent	Gum, Lozenge, Patch, Spray
Varenicline	Smoking cessation, first-line treatment	0.5 mg daily PO × 3 days then BID × 4 days	0.5–1 mg BID PO × 12 wk		0.5 mg, 1 mg
ALTERNATIVES, ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD)[f]					
Bupropion	ADHD, third-line treatment	2–3 mg/kg/day PO	200–300 mg/day PO in 2 divided doses. Single doses should not exceed 150 mg		XL: 150 mg, 300 mg SR: 150 mg
Clonidine	ADHD, third-line treatment	Initial: 0.05–0.1 mg/day PO	Usual: 0.003–0.01 mg/kg/day PO (0.05–0.4 mg/day), once daily or in divided doses		0.025 mg, 0.1 mg, 0.2 mg
Imipramine[e]	ADHD, third-line treatment		6–12 y: 10–20 mg/day PO in 3–4 divided doses Adults and adolescents: 30–50 mg/day PO in 3–4 divided doses	Usual maximum: 150 mg/day PO	10 mg, 25 mg, 50 mg, 75 mg
Venlafaxine[e]	ADHD, third-line treatment	Adults: Initial: 37.5–75 mg daily PO for 1 wk	Titrate gradually to 150–300 mg daily PO	Maximum: 375 mg/day PO	37.5 mg, 75 mg, 150 mg

a. Higher doses often exceed maximum recommended doses in manufacturers' product monographs and are usually associated with increased risk of adverse effects. These doses should be used with caution in appropriately selected patients.

b. Lower initial doses (e.g., citalopram 10 mg, escitalopram 5 mg) are indicated in patients who have previously experienced side effects or who are taking multiple medications; this often applies to elderly patients.

c. Antipsychotic augmentation of standard antidepressants is not recommended for long-term use, and close monitoring for movement disorders, weight gain and cardiometabolic effects is indicated.

d. In addition to bupropion, mirtazapine and vortioxetine have been identified as having lower risk of antidepressant-associated sexual dysfunction.

e. A 1-week washout period of bupropion is recommended before initiating this drug.

f. Stimulants (amphetamine and methylphenidate-based) are usual first-line options for ADHD; atomoxetine and guanfacine are usual second-line options. Bupropion is a third-line option for ADHD; this table presents alternative third-line therapeutic options.

Information adapted from Depression, Tobacco Use Disorder: Smoking Cessation, and Attention-Deficit Disorder available from www.myrxtx.ca.

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