Bupropion Shortage

Shortages of SR and XL formulations of bupropion have been reported.

Table 1: Suppliers of bupropion[1]:

Product	Strength	DIN	Manufacturer
Mylan-Bupropion XL	150 mg	02382075	MYL
	300 mg	02382083	
Taro-Bupropion XL	150 mg	02475804	SUN
	300 mg	02475812	
Teva-Bupropion XL	150 mg	02439654	TEV
	300 mg	02439662	
Wellbutrin® XL	150 mg	02275090	VAE
	300 mg	02275104	
Bupropion SR	100 mg	02391562	SAN
	150 mg	02391570	
Odan Bupropion SR	100 mg	02275074	ODN
	150 mg	02275082	
PMS-Bupropion SR	100 mg	02325373	PMS
	150 mg	02313421	
Ratio-Bupropion SR	100 mg	02285657	RPH
Zyban®	150 mg	02238441	VAE

Health Canada Approved Indications:

Wellbutrin® SR[2]

- treatment of major depressive disorder

Wellbutrin® XL[3]

- treatment of major depressive disorder
- prevention of seasonal major depressive episodes in patients with seasonal affective disorder

Zyban®[4]

- smoking cessation in conjunction with behavioural modification; nicotine replacement therapy may also be used together

Management Options

Assess Need for Continued Pharmacological Treatment for Depression

- psychotherapies including cognitive behavioural therapy and interpersonal therapy are as effective, and in some cases may be more effective, than antidepressants for *mild to moderate* major depression.[5,6]

- patients with major depression who may be candidates for discontinuation of antidepressant therapy include[5,7]:
    - those with history of a single depressive episode that has been successfully treated and in which maintenance therapy has continued for an additional 6 to 9 months.
    - those with history of two depressive episodes that have been successfully treated and in which maintenance therapy has continued for an additional 2 to 3 years following remission of the second episode.

Pharmaceutical Alternatives

- At times the sustained release (SR) or extended release (XL) formulations may be available.
    - The SR formulation is administered once per day for daily doses ≤ 150 mg daily and twice per day for daily doses > 150 mg; no single dose should exceed 150 mg.[2]
        - For SR doses that are divided twice per day consider scheduling the second dose of the day at 14:00 to reduce possible impact on sleep.
    - The XL formulation is administered once per day.[3]
- Consider taking this opportunity to reassess the dose. Consider dose reduction for patients who are stable, especially if the dosage was originally titrated to >150 mg daily without an adequate trial (6 to 8 weeks) at daily doses of 100 mg to 150 mg.
    - For patients taking 150 mg daily, consider reducing the daily dose to 100 mg SR once daily, switching to 150 mg SR once daily, or switching to 150 mg XL once daily, depending on product availability.
- For patients in whom >150 mg daily is appropriate, when switching between SR and XL, maintain the same daily dose.[2,3] If Wellbutrin® and its generics are unavailable but Zyban® can be procured, request the prescriber to change to Zyban®. Zyban® and Wellbutrin® SR are the same tablet in terms of formulation and release pattern.[8] If the patient has third party coverage, consider investigating any restrictions such as lifetime maximums.
- Compounding pharmacies may be able to compound a product that approximates the SR formulation;[9] before referring patients, it is best to contact the compounding pharmacy to confirm ability to compound bupropion.

Therapeutic Alternatives

- Bupropion is considered a norepinephrine dopamine reuptake inhibitor (NDRI) and is the only drug available with this mechanism of action; no single alternative is preferred in every situation.
    - Bupropion exerts modest dopamine reuptake blockade as well as slight norepinephrine, histamine$_1$ and α_1 blockade properties. It has no effect on serotonin, muscarinic or α_2 receptors.[10]
- Because no antidepressants have similar neurotransmitter profiles to bupropion, determine if there are any compelling reasons the patient is on bupropion and choose an alternative agent with similar benefits (see Table 2).

Discontinuing Bupropion or Switching to an Alternative Antidepressant

- Bupropion is rarely associated with discontinuation symptoms,[11] though symptoms including dizziness, lethargy, nausea, vomiting, diarrhea, headache, fever and more may be experienced.[10]
    - When possible, if bupropion is to be discontinued, taper the dose over approximately one week. The new agent can be cross-tapered (start the new agent during the

bupropion taper). Alternatively, the new agent can be started the day following the last bupropion dose and titrated as usual.

- If the patient is not stable and has some bupropion remaining, the new agent can be started and titrated to a therapeutic dose in the presence of bupropion. Bupropion has been studied in combination with SSRIs and SNRIs in STAR*D.[12] The patient may experience more adverse effects during the period of overlap; risk versus benefit will need to be assessed.

Table 2: Potential reasons bupropion may be chosen and possible alternatives

Benefit	Possible Alternatives	Comments
Weight loss (absence of weight gain)[13]	SSRI (esp. fluoxetine), vortioxetine, nortriptyline, venlafaxine, duloxetine	If weight loss is the only indication, consider bupropion/naltrexone, orlistat, liraglutide, or metformin in combination with lifestyle and psychological strategies.[14]
Seasonal Affective Disorder[15]	Bright light therapy, fluoxetine, sertraline	
Reduced sexual dysfunction[13,16]	mirtazapine, vortioxetine	In some cases, bupropion is added to counteract sexual dysfunction of other antidepressants; no other agents are appropriate in this scenario.
Atypical depression[13]	SSRIs, RIMA, MAOIs	
Elderly patients[13]	mirtazapine (preferred), SSRI (esp. citalopram, escitalopram), venlafaxine, nortriptyline, desipramine, duloxetine	
Less sedation[10,13]	escitalopram, fluoxetine, levomilnacipran, vortioxetine	
Smoking cessation[13, 17,18]	nortriptyline	Use especially if comorbid depression (although caution if suicidal ideation, consider limiting dispense quantities)
	behavioural therapy	
	nicotine replacement	
	varenicline	Use with caution in patients with a history of past or current psychiatric illness.

MAOI = monoamine oxidase inhibitor; RIMA= reversible inhibitor of monoamine oxidase-A; SSRI= selective serotonin receptor inhibitor; TCA= tricyclic antidepressant

Prepared by Carmen Bell BSP, medSask. 06 Nov 2018 | Updated 04 Mar 2022
2018 reviewers: Dr. Alfred Remillard, College of Pharmacy & Nutrition, U of S;
Alex Crawley BSP, RxFiles; Danielle Larocque BSP, CPDPP
2022 reviewer: Dr. Katelyn Halpape, College of Pharmacy & Nutrition, U of S

References:

1. Drug Plan and Extended Benefits Branch. Saskatchewan Online Formulary Database. [homepage on the Internet]. Regina SK: Government of Saskatchewan; [cited 03 Mar 2022]. Available from: http://formulary.drugplan.health.gov.sk.ca/
2. Wellbutrin® SR [product monograph]. Bausch Health, Canada. Laval, QC H7L 4A8. 20 Jan 2022 [cited 03 Mar 2022]. Available from: https://pdf.hres.ca/dpd_pm/00064427.PDF
3. Wellbutrin® XL [product monograph]. Bausch Health, Canada. Laval, QC H7L 4A8. 20 Jan 2022 [cited 03 Mar 2022]. Available from: https://pdf.hres.ca/dpd_pm/00063455.PDF
4. Zyban® [product monograph]. Bausch Health, Canada. Laval, QC H7L 4A8. 20 Jan 2022 [cited 03 Mar 2022. Available from: https://pdf.hres.ca/dpd_pm/00064136.PDF
5. DynaMed [Internet]. Ipswich (MA): EBSCO Information Services. 1995 -2022. Record No. T116638, Major Depressive Disorder (MDD); [updated 2018 Nov 30, cited 03 Mar 2022]. Available from: https://www.dynamed.com/topics/dmp~AN~T116638. Registration and login required.
6. Kennedy S, Parikh S, Grigoriadis S. Depression. In: Therapeutics [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2022. [updated 19 Apr 2021; cited 03 Mar 2022]. Available from: http://www.myrxtx.ca. Also available in paper copy from the publisher.
7. Parikh SV, Quilty LC, Ravitz P et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 clinical guidelines for the management of adults with major depressive disorder: Section 2. Psychological treatments. Can J Psychiatry 2016;61(9):524-39
8. Email communication from Bausch Health and Valeant Canada Medical Information, Valeant_medinfo@healthconnect.ca, 02 Nov 2018
9. Phone communication with Jarron Yee, pharmacist/owner, The Medicine Shoppe Pharmacy #300, Regina SK, 20 Nov 2018.
10. Prochyshy R, Bezchlibnyk-Butler KZ, Jeffries JJ, editors. Clinical handbook of psychotropic drugs online. Hogrefe Publishing; 2022; cited 03 Mar 2022. Available at http://chpd.hogrefe.com. Subscription required.
11. Hirsch M, Birnbaum RJ. Switching antidepressant medications in adults. Post TW, ed. UpToDate. Waltham, MA: UpToDate Inc. [updated 09 Nov 2019; cited 03 Mar 2022]. Available from http://www.uptodate.com. Subscription and login required
12. Trivedi MH, Fava M, Wisniewski SR, et al; STAR*D Study Team. Medication augmentation after the failure of SSRIs for depression. N Engl J Med. 2006 Mar 23;354(12):1243-52
13. Jensen B, Regier L. Antidepressants: comparison chart. RxFiles drug comparison charts. Saskatoon, SK: University of Saskatchewan. [updated Aug 2021; accessed 03 Mar 2022]. Available from: https://www.rxfiles.ca/RxFiles/uploads/documents/members/cht-Psyc-Antidepressant.pdf
14. Jensen B, Regier L, Kosar L, et al. Weight loss approach. RxFiles drug comparison charts. Saskatoon, SK: University of Saskatchewan. [updated Feb 2022; accessed 03 Mar 2022]. Available from: https://www.rxfiles.ca/RxFiles/uploads/documents/members/Cht-weight-loss.pdf
15. DynaMed [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - 2022. Record No. T114880, Seasonal Affective Disorder; [updated 2018 Nov 30, cited 03 Mar 2022]. Available from https://www.dynamed.com/topics/dmp~AN~T114880. Registration and login required.
16. Jacobsen PL, Mahableshwarkar AR, Chen Y, et a;. Effect of vortioxetine vs. escitalopram on sexual functioning in adults with well-treated major depressive disorder experiencing SSRI-induced sexual dysfunction. J Sex Med. 2015 Oct;12(10):2036-48. doi: 10.1111/jsm.12980.
17. Selby P, deRuiter W. Tobacco use disorder: smoking cessation. In: Therapeutics [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2022. [updated 12 May 2021; cited 03 Mar 2022]. Available from: http://www.myrxtx.ca. Also available in paper copy from the publisher.
18. Regier L, Crawley A, Jensen B, et al. Tobacco use disorder / smoking cessation. RxFiles drug comparison charts. Saskatoon, SK: University of Saskatchewan. [updated Aug 2021; accessed 03 Mar 2022]. Available from: https://www.rxfiles.ca/RxFiles/uploads/documents/members/CHT-Smoking-Cessation.pdf