

## Wellbutrin® (Bupropion) Shortage

Shortages of Wellbutrin XL, Wellbutrin SR and generics have been reported.

**Table 1: Suppliers of bupropion<sup>1</sup>:**

Product	Strength	DIN	MFR
ACT Bupropion XL	150 mg	02439654	ACV
	300 mg	02439662	
Mylan-Bupropion XL	150 mg	02382075	MYL
	300 mg	02382083	
Wellbutrin XL	150 mg	02275090	VAE
	300 mg	02275104	
Bupropion SR	100 mg	02391562	SAN
	150 mg	02391570	
PMS-Bupropion SR	100 mg	02325373	PMS
	150 mg	02313421	
Ratio-Bupropion SR	100 mg	02285657	RPH
Sandoz Bupropion SR	100 mg	02275074	SDZ
	150 mg	02275082	
Wellbutrin SR	150 mg	02237825	VAE
Zyban	150 mg	02238441	VAE

### Health Canada approved indications:

Wellbutrin® SR<sup>2</sup>

- symptomatic relief of major depressive disorder

Wellbutrin® XL<sup>3</sup>

- symptomatic relief of major depressive disorder
- prevention of seasonal major depressive episodes

Zyban®<sup>4</sup>

- 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.<sup>5,6</sup>
- patients with major depression who may be candidates for discontinuation of antidepressant therapy include<sup>5,7</sup>:

- those with history of 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 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 SR or XL formulations may be available; when switching between an SR and XL product, maintain the same daily dose if possible; daily doses exceeding 150 mg of the SR formulations should be divided into two doses.
  - For patients taking bupropion 150 mg XL daily, consider switching (with prescriber approval) to 100 mg SR BID to maintain twice daily dosing.
- 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.<sup>8</sup> If the patient has third party coverage, consider investigating any restrictions –such as lifetime maximums - should the patient want to use Zyban® for smoking cessation in the future.
- Compounding pharmacies are able to compound a product that approximates the SR formulation;<sup>9</sup> before referring patients, it is best to contact to the compounding pharmacy to confirm ability to deliver compounded 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<sub>1</sub> and  $\alpha_1$  blockade properties. It has no effect on serotonin, muscarinic or  $\alpha_2$  receptors.<sup>10</sup>
- 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,<sup>11</sup> though symptoms including dizziness, lethargy, nausea, vomiting, diarrhea, headache, fever and more may be experienced.<sup>10</sup>
  - 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.<sup>12</sup> The patient may experience more adverse effects during the period of overlap;<sup>7</sup> risk versus benefit will need to be assessed.

**Table 2: Potential reasons bupropion may be chosen and possible alternatives<sup>13</sup>**

Benefit	Possible Alternatives	Comments
<b>Weight loss (absence of weight gain)</b>	SSRI (esp. fluoxetine), nortriptyline, RIMA, venlafaxine, duloxetine	If weight loss is the only indication, consider bupropion/naltrexone, orlistat, liraglutide, metformin or topiramate. <sup>14</sup>
<b>Seasonal Affective Disorder<sup>15</sup></b>	Bright light therapy, fluoxetine, sertraline	
<b>Reduced sexual dysfunction</b>	mirtazapine, citalopram, RIMA, venlafaxine	In some cases, bupropion is added to counteract sexual dysfunction of other antidepressants; no other agents are appropriate in this scenario.
<b>Atypical depression</b>	SSRIs, RIMA, MAOIs	
<b>Elderly patients</b>	SSRI (esp. citalopram, escitalopram, venlafaxine, mirtazapine, RIMA, secondary TCA, duloxetine	
<b>Less sedation<sup>9</sup></b>	escitalopram	
<b>Smoking cessation<sup>13, 16,17</sup></b>	nortriptyline	Use especially if comorbid depression.
	behavioural therapy	Best treatment in history of depression.
	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.

Thank you to reviewers: Dr. Alfred Remillard, College of Pharmacy & Nutrition, U of S;  
Alex Crawley BSP, RxFiles; Danielle Larocque BSP, CPDPP

**References:**

1. Saskatchewan Online Formulary Database. Drug Plan and Extended Benefits Branch [homepage on the Internet]. Government of Saskatchewan; [cited 26 Oct 2018]. Available from: <http://formulary.drugplan.health.gov.sk.ca/>
2. Product monograph for Wellbutrin® SR. Valeant Canada LP. Laval, QC H7L 4A8. Mar 2017.
3. RxTx [Internet]. Ottawa (ON): Canadian Pharmacists Association; 2018. CPS online: Wellburin® XL; [updated 20 Mar 2017; cited 26 Oct 2018]. Available from: <https://www.e-therapeutics.ca/>
4. RxTx [Internet]. Ottawa (ON): Canadian Pharmacists Association; 2018. CPS online: Zyban; [updated 10 Aug 2016; cited 26 Oct 2018]. Available from: <https://www.e-therapeutics.ca/>

5. DynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - 2018. Record No. 113729, Major depressive disorder; [updated 25 Oct 2018, cited 26 Oct 2018]; [about 32 screens]. Available from <http://www.dynamed.com/login.aspx?direct=true&site=DynaMed&id=113729> Registration and login required.
6. RxTx[Internet]. Ottawa (ON): Canadian Pharmacists Association; 2018. Kennedy S, Parikh S, Grigoriadis S. Depression.; [updated 01 May 2018; cited 26 Oct 2018]. Available from: <https://www.e-therapeutics.ca/>
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](mailto:Valeant_medinfo@healthconnect.ca), 02 Nov 2018
9. Phone communication with Jarron Yee, pharmacist/owner, The Medicine Shoppe Pharmacy #300, Regina SK; 306-543-5555, 20 Nov 2018.
10. Prochyshy R, Bezchlibnyk-Butler KZ, Jeffries JJ, editors. Clinical handbook of psychotropic drugs online. Hogrefe Publishing; 2018; cited 26 Oct 2018. 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. Cited 26 Oct 2018. 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: Saskatoon Health Region. [updated 01 May 2018; accessed 26 Oct 2018]. Available from: [www.RxFiles.ca](http://www.RxFiles.ca)
14. Crawley A, Jensen B, Regier L, et al. Weight loss approach. RxFiles drug comparison charts. Saskatoon, SK: Saskatoon Health Region. [updated 01 Jul 2018; accessed 26 Oct 2018]. Available from: [www.RxFiles.ca](http://www.RxFiles.ca)
15. DynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - 2018. Record No. 114880, Seasonal affective disorder; [updated 07 Jun 2016, cited 26 Oct 2018]; [about 8 screens]. Available from <http://www.dynamed.com/login.aspx?direct=true&site=DynaMed&id=114880> Registration and login required.
16. RxTx[Internet]. Ottawa (ON): Canadian Pharmacists Association; 2018. Selby P, deRuiter W. Tobacco use disorder: smoking cessation.; [updated 01 May 2018; cited 26 Oct 2018]. Available from: <https://www.e-therapeutics.ca/>
17. Regier L, Jensen B, Chan W. Tobacco / smoking cessation: pharmacotherapy. RxFiles drug comparison charts. Saskatoon, SK: Saskatoon Health Region. [updated 01 Oct 2018; accessed 26 Oct 2018]. Available from: [www.RxFiles.ca](http://www.RxFiles.ca)