

Cobalt Pharmaceuticals Inc.  
Genpharm  
Laboratoire Riva Inc.  
Novopharm Limited  
Pharmascience Inc.  
ratiopharm  
Sandoz Canada Inc.  
Wyeth Canada

**Health Canada Endorsed Important Safety Information on  
VENLAFAXINE XR**

October 23, 2008

Dear Healthcare Professional:

**SUBJECT: Safety Information Regarding Overdosage of Venlafaxine HCl Extended-Release Capsules**

Venlafaxine HCl Extended-Release Capsule manufacturers wish to provide you with important safety information regarding venlafaxine XR. Published retrospective studies<sup>1,2,3,4</sup> have reported that venlafaxine overdose may be associated with an increased risk of fatal outcome compared to that observed with Selective Serotonin Reuptake Inhibitor (SSRI) antidepressants, but lower than that for tricyclic antidepressants. Although the extent to which the finding of an increased risk of fatal outcomes can be attributed to the toxicity of venlafaxine in overdose, as opposed to some characteristics of venlafaxine-treated patients, is not clear,<sup>5</sup> post-market reports of fatal acute overdoses have been received for venlafaxine alone at doses as low as approximately 1 gram.

- Prescriptions for venlafaxine XR should be written for the smallest quantity of drug consistent with good patient management, in order to reduce the risk of overdose, particularly in patients who have more severe illness or risk factors for suicidal behaviour.
- The potential for suicide attempt in seriously depressed patients is inherent to the illness, and may persist until significant remission occurs. Clinical monitoring for suicidal ideation and/or other indicators of suicidal behaviour is recommended for all depressed patients.
- Increased risk of behavioural and emotional changes, including self-harm, has been seen with treatment with venlafaxine, as with other antidepressant drugs, and health care providers, patients, family members and/or caregivers should be vigilant for such changes.
- All antidepressants have a potential risk of fatal outcome in overdose.

Manufacturers of all extended release venlafaxine products are working with Health Canada to include this safety information in the Overdosage section in all Canadian Product Monographs for venlafaxine extended release capsules.

Managing marketed health product-related adverse reactions depends on health care professionals and consumers reporting them. Reporting rates determined on the basis of spontaneously reported post-marketing adverse reactions are generally presumed to underestimate the risks associated with health product treatments. Any case of overdose or other serious or unexpected adverse reactions in patients receiving venlafaxine XR should be reported to the manufacturer or Health Canada at the following addresses:

**Cobalt Pharmaceuticals Inc.**

6500 Kitimat Road  
Mississauga, Ontario L5N 2B8  
Tel: 1-866-254-6111  
Fax: 905-542-0478  
[www.cobaltpharma.com](http://www.cobaltpharma.com)

**Genpharm**

Drug Safety  
85 Advance Road  
Etobicoke, Ontario M8Z 2S6  
Tel: 1-800-668-3174 ext. 152  
Fax: 416-236-4363  
Email: [pharmacovigilance@genpharm.ca](mailto:pharmacovigilance@genpharm.ca)

**Laboratoire Riva Inc.**

660 Boul. Industriel  
Blainville, Quebec J7C 3V4  
Tel: 1-800-363-7988  
Fax: 450-434-2500

**Novopharm Limited**

Pharmacovigilance and Drug Safety  
30 Novopharm Court  
Toronto, Ontario M1B 2K9  
Tel: 416-291-8888 ext. 5005  
Fax: 416-335-4472  
[PhV@Novopharm.com](mailto:PhV@Novopharm.com)

**Pharmascience Inc.**

6111 Royalmount Avenue, Suite 100  
Montreal, Quebec H4P 2T4  
Tel: 1-800-363-8805  
Fax: 514-342-7764

**ratiopharm**

17800 Lapointe  
Mirabel, Quebec J7J 1P3  
Tel: 1-800-337-2584  
Fax: 1-800-313-7673  
[www.ratiopharm.ca](http://www.ratiopharm.ca)

**Sandoz Canada Inc.**

145, Jules-Leger  
Boucherville, Quebec J4B 7K8  
Tel: 1-800-343-8839 ext. 4636  
Fax: 1-888-243-6221

**Wyeth Canada**

Medical Information and Pharmacovigilance  
50 Minthorn Boulevard  
Markham, Ontario L3T 7Y2  
Tel: 1-800-461-8844  
Fax: 905-470-4385

**Any suspected adverse reaction can also be reported to:**

Canada Vigilance Program  
Marketed Health Products Directorate  
HEALTH CANADA  
Address Locator: 0701C  
Ottawa, Ontario, K1A 0K9  
Tel: 613-957-0337 or Fax: 613-957-0335  
To report an Adverse Reaction, consumers and health professionals may call toll free:  
Tel: 866-234-2345  
Fax: 866-678-6789  
[CanadaVigilance@hc-sc.gc.ca](mailto:CanadaVigilance@hc-sc.gc.ca)

The [AR Reporting Form](#) and the [AR Guidelines](#) can be found on the Health Canada web site or in *The Canadian Compendium of Pharmaceuticals and Specialties*.

[http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/ar-ei\\_form-eng.php](http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/ar-ei_form-eng.php)

[http://hc-sc.gc.ca/dhp-mps/pubs/medeff/\\_guide/2008-ar-ei\\_guide-ldir/index-eng.php](http://hc-sc.gc.ca/dhp-mps/pubs/medeff/_guide/2008-ar-ei_guide-ldir/index-eng.php)

**For other inquiries related to this communication, please contact Health Canada at:**

Marketed Health Products Directorate (MHPD)  
E-mail: [MHPD\\_DPSC@hc-sc.gc.ca](mailto:MHPD_DPSC@hc-sc.gc.ca)  
Tel: (613) 954-6522  
Fax: (613) 952-7738

Please contact the appropriate manufacturer with any questions or concerns.

Authorized by:

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Wyeth Canada

## References

1. Shah R, Uren Z, Baker A, Majeed A. Deaths from antidepressants in England and Wales 1993-1997: analysis of a new national database. *Psychological Medicine*. 2001;31:1203-1210.
2. Cheeta S, Schifano F, Oyefeso A, Webb L, Ghodse H. Antidepressant-related deaths and antidepressant prescriptions in England and Wales, 1998-2000. *British Journal of Psychiatry*. 2004;184:41-47.
3. Buckley NA, McManus PR. Fatal toxicity of serotonergic and other antidepressant drugs: analysis of United Kingdom mortality data. *BMJ*. 2002;325:1332-1333.
4. Morgan O, Griffiths C, Baker A. Fatal toxicity of antidepressants in England and Wales, 1993-2002. *Health Statistics Quarterly*. 2004;23:18-24.
5. Mines D, Hill D, Yu H, Novelli L. Prevalence of risk factors for suicide in patients prescribed venlafaxine, fluoxetine and citalopram. *Pharmacoepidemiology and Drug Safety*. 2005;14:367-372.