

Health Canada Endorsed Important Safety Information on
BOTOX and BOTOX Cosmetic (botulinum toxin type A)



Subject: Additional safety information related to BOTOX[®]/BOTOX Cosmetic[®] (botulinum toxin type A)

Dear Health Care Professional,

This letter is to update you on important safety information related to BOTOX[®] and BOTOX Cosmetic[®] and the potential risk of serious adverse effects of muscle weakness remote to the site of injection, also referred to as possible distant spread of toxin. Over the last several months, Allergan has worked closely with Health Canada to update the product monographs for BOTOX[®] and BOTOX Cosmetic[®] to include additional safety information and provide additional guidance for the optimal use of this product.

Key safety updates within the new product monographs for BOTOX[®] and BOTOX Cosmetic[®] include the following:

- The updated product monographs for BOTOX[®] and BOTOX Cosmetic[®] now include possible muscle weakness remote to the site of injection. Possible symptoms include muscle weakness, dysphagia, aspiration pneumonia, speech disorders and respiratory depression. These reactions can be fatal.
- Patients or caregivers should be advised to seek immediate medical care if swallowing, speech or respiratory disorders arise.
- BOTOX[®] and BOTOX Cosmetic[®] should only be given by physicians with the appropriate qualifications and experience in the use of BOTOX[®] and BOTOX Cosmetic[®]. The revised product monographs emphasise the need to follow the recommended dosage and frequency of administration.
- Patients with a history of underlying neurological disorders, dysphagia and/or aspiration should be treated with extreme caution. The botulinum toxin product should be used under specialist supervision in these patients and should only be used if the benefit of treatment is considered to outweigh the risk.

Based on a review of rare adverse event reports by Allergan and Health Canada, the newly updated product monographs include additional warnings and precautions for BOTOX[®] and BOTOX Cosmetic[®]. BOTOX[®] and BOTOX Cosmetic[®] share the same formulation but are marketed under different trade names, to separate between its approved therapeutic and aesthetic applications.

Muscle weakness remote to the site of injection and other serious adverse effects (e.g. dysphagia, aspiration pneumonia) have been reported rarely for BOTOX[®] in both pediatric and adult patients, and very rarely for BOTOX Cosmetic[®] in adult patients. Some cases associated with use of BOTOX[®] had a fatal outcome. There were no fatalities involved in these very rare adverse events reported following aesthetic use of BOTOX Cosmetic[®].

In reference to dosing, the product monographs state, “Generally optimum dose levels and the number of injections sites per muscle have not been established for all injections. Treatment should be initiated at the lowest effective dose. This dose can be gradually increased in subsequent treatments to the maximum recommended dose, if needed.” Recommendations on dosing guidelines and proper administration are listed for each approved indication. For instance, the BOTOX[®] monograph recommends that, to treat children suffering from spasticity associated with cerebral palsy, the dose of BOTOX[®] should generally not exceed 6 U/kg per session or 200 U over a 3-month period.

The newly updated BOTOX[®] and BOTOX Cosmetic[®] product monographs are available on the Health Canada website, by performing a search of the Drug Product Database on Health Canada’s website at: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index_e.html. To do so, enter “Botox” or “Botox Cosmetic” in the “Product Name” field and select “Search”. The PM is accessible via the “Product Monograph” box in purple below the product name that will appear on the next page.

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 serious suspected distant toxin spread or other serious or unexpected adverse reactions in patients receiving BOTOX[®] or BOTOX Cosmetic[®] should be reported to Allergan or Health Canada at the following addresses:

Allergan Canada
85 Enterprise Blvd., Suite 500
Markham, Ontario L6G 0B5
Tel: 800-668-6424 or Fax: 905-940-1902

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

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_e.html

http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/guide/ar-ei_guide-ldir_e.html

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

Marketed Health Products Directorate

E-mail: mhpd_dpdc@hc-sc.gc.ca

Tel: 613-954-6522

Fax: 613-952-7738

This communication is available on the Health Canada website at http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/_2008/index-eng.php, and on the Allergan Canada website www.allergan.ca.

Regards,

original signed by

Mark Gilmour
Director, Regulatory Affairs Allergan Canada

December 22, 2008