HEALTH REPORTS
Vol. 13 Issue 59

BLACK BOXED WARNING REQUIRED FOR BOTOX

Last spring we reported that the U.S. Food and Drug Administration (FDA) had issued an advisory regarding botulinum toxin (Botox and similar products) and was in the process of conducting further investigations into its safety. Now the FDA has come out with a much stiffer set of regulations regarding its marketing. A "black boxed warning" label must now be attached to the sale of Botox that warns of the dangers of its use.

"As the result of an ongoing safety review, FDA has notified the manufacturers of licensed botulinum toxin products of the need to strengthen warnings in product labeling – and add a boxed warning – regarding the risk of adverse events when the effects of the toxin spread beyond the site where it was injected," according to the FDA update.

Adverse report events on both adults and children lead the FDA to up its warning about products marketed as Botox and Botox Cosmetic from Allergen Inc., Myobloc sold by Solstice Neuroscience and the recently approved Dysport from Ipsen.

In children, these products are most frequently used to treat muscle spasms in cerebral palsy even though the FDA has never approved this use. What occurs with the botulinum product is that it spreads beyond its injection point and causes difficulty breathing/swallowing, muscle weakness, constipation, pneumonia and speech disorder. Hospitalized persons have needed breathing support and there are reports of deaths occurring in children.

Approved uses for adults are mainly for cosmetic improvements where small doses of the administered product bring few reports of problems. Mainly the reports of problems result when botulinum toxin is employed for the unapproved use of treating spasticity or for cervical dystonia (abnormal muscle contractions causing writhing or twisting of the body). Difficulties reported by adults include sudden loss of muscle strength, loss of bladder control, trouble breathing/swallowing, vision irregularities and speaking difficulties. Adults who have sought emergency room help often needed ventilation and unsubstantiated deaths have been reported as well.

Beyond the "black boxed warning," the FDA will now also require manufacturers to provide product information regarding the possibility of the spread of botulinum toxin beyond its local injection point. As products vary in strength, information must be provided to warn users not to interchange products from different manufacturers. A Medication Guide that explains the risks of product use to patients, their families and their caregivers must be presented as well. Finally, manufacturers will be required to submit safety data to FDA following multiple administration of the product for a specified number of adults and children with spasticity to further address the serious risk regarding distant spread of toxins and their effects.

The organization Public Citizen had petitioned FDA for stronger warnings last April and is pleased with the results. "The FDA even went beyond our petition to require companies to conduct post-marketing studies when the drug is used for the treatment of spasticity associated with cerebral palsy, an unapproved use. Although this action could have been taken by the previous administration, we hope this warning indicates that the winds of change are blowing at the FDA."

Sources: U.S. Food and Drug Administration. "Follow-up to the Feb. 8, 2008, Early Communication about an Ongoing Safety Review of Botox and Botox Cosmetics and Myobloc." April 2009. http://www.fda.gov/cder/drug/early_comm/botulinium_toxins200904.htm. Public Citizen. "FDA Grants Public Citizen Petition on Botox." April 2009. http://www.citizen.org/pressroom/release.cfm?ID=2874