



## Health

### The Botox Balance

*By Bernadine Healy M.D.*

Posted 1/14/07

Botulinum is right up there next to anthrax and smallpox on the Department of Homeland Security's short list of potential agents of bioterrorism. But modern medicine has harnessed the neurotoxin's destructive power, turning it into a veritable magic microbullet for both rare neuromuscular diseases and the most common of human afflictions, the furrowed brow. Innovation alone, however, does not explain the rapid conversion of the poison from demon to saint. This could not have happened without the Food and Drug Administration, which enabled the drug's ever expanded use and meteoric public acceptance.

The FDA first approved Botox under the name Oculinum in 1989 for treatment of two conditions, crossed eyes and eyelid tics. In almost no time, the drug was renamed Botox, and doctors from many branches of medicine—ophthalmology, neurology, rehabilitation, dermatology, plastic surgery, urology, and dentistry—quickly saw its novel and unmet patient uses. Before long, practitioners began administering Botox for numerous conditions related to overactive muscle contraction: Wry neck, back pain, bladder spasms, migraine headaches, writer's cramp, and incontinence are just a few. This was made possible because FDA-approved drugs can be used by licensed doctors "off label" according to their best judgment. That includes indications other than the ones that led to FDA approval. (Approximately 20 percent of drug prescriptions are written off label, and in fields like cancer that percentage runs higher.) In one of its most stunning off-label successes, Botox has enabled children crippled by the spastic muscle contractions of cerebral palsy to get out of their wheelchairs and onto the soccer field.

Greater fame. What emerged from this flurry of off-label use was a surprisingly positive safety record. This also encouraged greater interest in the wrinkle connection, an accidental discovery made when patients noticed that their frown lines seemed to soften after ocular injections. Initially, however, the FDA

disapproved of this particular off-label use and in 1994 denounced its promotion as an egregious example of pushing a potential toxin for cosmetic purposes. Meeting the challenge, Allergan, the makers of Botox, conducted the clinical trials that demonstrated safety and efficacy specifically for treating the glabellar lines, vertical furrows between the eyes, winning FDA approval for that purpose in 2002.

The FDA stamp of approval catapulted Botox to even wider use and greater fame. Within a year, it became one of the hottest brands in the United States, and more than 500,000 men and women had their frown lines erased-for about 120 days, anyway. That the government's premier public-health agency deemed Botox safe for casual use triggered a blast of worldwide news coverage. By the company's count, FDA approval led to more than 13,000 TV and news stories, drove 600,000 people to the Botox website, and sent 4,500 medical practitioners from all 50 states back to school to learn how to administer the treatment. The American Society of Plastic Surgeons conducted a poll that showed roughly 70 percent of Botox fence sitters became positive about treatment when they learned of the FDA imprimatur. Was that imprimatur overread? Perhaps.

With off-label use, cosmetic Botox injections involve more than the glabellar lines. When you add on the wrinkled forehead, crow's-feet, the lip area, and bands in the neck, patients are exposed to higher doses of the drug than those in the studies that led to the FDA's approval. Add to that the many injections that come with repeated use, since the drug wears off as the damaged nerve endings regrow. The same applies to therapeutic Botox use. This only highlights a recognized soft spot of any FDA safety stamp: the general lack of long-term surveillance information after drugs are approved, which is particularly important for ones that are administered repeatedly.

If truth is beauty, the beauty of Botox is that it's a powerful agent whose benefits are legion. But our knowledge is still based on short-term studies and generally low-dose exposures. We would be wise to heed the wisdom of the physician Paracelsus, the 16th-century father of drug toxicology, who said no drug is without poison-the dose makes the poison. Now is the time to aggressively initiate long-term drug evaluation studies to ensure that Botox beauty is more than skin deep.

This story appears in the January 22, 2007 print edition of U.S. News & World Report.

Copyright © 2007 U.S. News & World Report, L.P. All rights reserved.