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F.D.A. Orders Warning Label for Botox

By NATASHA SINGER

Botox and other similar antiwrinkle drugs must now carry the most stringent kind of warning label, the Food and Drug Administration said Thursday.

The F.D.A. issued that order the day after the agency approved a new drug, Dysport, that is expected to be the first real challenger to Botox in the United States. Like Botox, Dysport is an injectable drug derived from the paralytic agent botulinum toxin.

The F.D.A. said such drugs must carry warning labels explaining that the material has the potential to spread from the injection site to distant parts of the body — with the risk of serious difficulties, like problems with swallowing or breathing.

Requiring a drug to carry a box with bold-face risk information — a so-called black-box warning — is one of the strongest safety actions the F.D.A. can take. Black boxes are typically reserved for medications known to have serious or life-threatening risks. Antidepressants, for example, carry black boxes warning of the increased danger of suicidal thoughts and actions.

The F.D.A. said it would also require makers of injectable toxins to send doctors letters warning of their risks and to produce a medication guide to be given to patients at the time of injection.

In a conference call with reporters on Thursday, an F.D.A. official said that the problems had occurred mainly in patients who received overdoses of the drug for unapproved treatments, like limb spasticity in children with cerebral palsy.

Botulinum toxins are safe when administered for approved uses at approved doses, said Dr. Ellis F. Unger, an official at the agency's office of new drugs.

The agency's approval of Dysport, manufactured by Ipsen, based in Paris, portends a fierce competition in the United States toxin market of a sort that has been raging in Europe for years.

Last year, Botox had worldwide sales of about \$1.3 billion, according to its maker, Allergan. Dysport had sales of \$189 million, according to an earnings statement from Ipsen.

In the absence of serious competition, Allergan has been able to raise the drug's price annually. But Dysport, which in Europe has been priced lower than Botox, has the potential to capture up to 20 percent of the market in this country, said David M. Steinberg, an analyst at Deutsche Bank.

Injectable botulinum toxins are purified forms of the bacterial poison that causes botulism, a paralyzing disease that can be fatal. The drugs temporarily reduce or halt muscle activity.

In the last 20 years, the F.D.A. has approved Botox to treat crossed eyes, eyelid spasms, severe underarm sweating, and cervical dystonia, a neck problem that can cause severe pain and abnormal head position. Under the name Botox Cosmetic, the drug is also approved to treat frown lines.

In 2000, the agency approved a different type of the toxin, Myobloc, to treat cervical dystonia.

On Wednesday, the agency approved Dysport for frown lines and cervical dystonia.

Medicis Pharmaceutical, a company in Scottsdale, Ariz., that has the rights to sell Dysport for frown lines in the United States, said it planned to bring the drug to market within 60 days. Ipsen will market the drug in this country for the neck problem.

The new F.D.A. requirement for a black-box warning on such drugs comes 15 months after the agency received a petition from Public Citizen, a public advocacy group, calling for more substantial warnings.

In its petition, the group said that the F.D.A. had received reports of 180 serious health problems and 16 deaths connected to the injections. In a response sent to the group on Thursday, the agency said it had identified even more reports of complications, including 225 reports of problems caused by the drug spreading from the injection site to distant parts of the body.

"There would have been fewer problems caused if they had put this out a year ago," said Dr. Sidney M. Wolfe, the director of the health research group at Public Citizen.

Allergan shares fell 1.3 percent to \$46.66 on Thursday, while shares of Medicis rose more than 18 percent, to \$16.07.