

## **XEOMIN® (incobotulinumtoxinA) DATA TO BE PRESENTED AT THE 71<sup>ST</sup> ANNUAL ASSEMBLY OF THE AMERICAN ACADEMY OF PHYSICAL MEDICINE AND REHABILITATION**

### **Study Demonstrates XEOMIN Maintains Stability Without Refrigeration And Is Not Affected By Short-term Temperature Stress**

GREENSBORO, N.C., Nov. 5 /PRNewswire/ -- Merz Pharmaceuticals announced today that data from stability and clinical studies evaluating Xeomin® (incobotulinumtoxinA), a botulinum toxin type A free from accessory proteins, will be presented at the 71<sup>st</sup> Annual Assembly of the American Academy of Physical Medicine and Rehabilitation (AAPM&R) in Seattle, Wash.

The U.S. Food and Drug Administration (FDA) approved XEOMIN on July 30, 2010, for the treatment of adults with cervical dystonia (CD), to decrease the severity of abnormal head position and neck pain in both botulinum toxin-naïve and previously treated patients, and blepharospasm in adults who have been previously treated with Botox® (onabotulinumtoxinA).

#### **Stability Studies**

As part of the commercial development of XEOMIN, Merz conducted studies to assess the stability of XEOMIN and the 900 kDa neurotoxin complex which is produced by *Clostridium botulinum*. In nature, *Clostridium botulinum* produces the 150 kDa neurotoxin molecule with accessory proteins, resulting in a complex with a molecular weight of 900 kDa.

Results from a study designed to assess the stability of the 900 kDa neurotoxin complex at various pH values concluded that the 150 kDa neurotoxin molecule was released in less than one minute when exposed to physiological pH values. In the study, separation conditions were qualified by Western blot and toxin activity. (Poster 108; Eisele K.H., et al.)

In a second study, the stability of three individual batches of XEOMIN was assessed in long-term and accelerated stability studies according to the ICH Q1A(R2) guideline on stability testing of drug products. The results of this study showed that the product can be safely stored without refrigeration and is not affected by short-term temperature stress between 40°C (104°F) and 60°C (140°F). (Poster 106; Grein S., et al.)

“According to these data, the speed at which accessory proteins disassociate from the neurotoxin molecule at physiological pH suggests that the necessity of these proteins in medicinal formulations of botulinum toxin type A is questionable in influencing the therapeutic effects,” said Eric J. Pappert, M.D., Vice President of Medical Affairs, Merz Pharmaceuticals, LLC. “Additionally, results from the stability studies evaluating XEOMIN under various conditions suggest that accessory proteins are not required for the long-term maintenance of potency of this medicinal formulation of botulinum toxin type A.”

#### **Clinical Studies**

The results of studies exploring the safety and efficacy of XEOMIN in the treatment of adults with cervical dystonia and blepharospasm will also be presented:

- Poster 49: Efficacy and safety of NT 201 (XEOMIN®; Botulinum neurotoxin free from complexing proteins) in cervical dystonia (Grafe S., et al.)
- Poster 50: Efficacy and safety of NT 201 (XEOMIN®; Botulinum neurotoxin type A free from complexing proteins) for the treatment of blepharospasm: Results of a double-blind, placebo-controlled, randomized, multi-center trial (Jankovic J., et al.)
- Poster 57: Overall clinical efficacy and overall tolerability of NT 201 (Botulinum neurotoxin free from complexing proteins) (Benecke R., et al.)

#### **About XEOMIN**

In nature, *Clostridium botulinum* produces the toxin in association with accessory proteins, resulting in a 900 kDa complex. Manufacturers utilize this naturally occurring protein complex to produce therapeutic botulinum toxin products. Merz has introduced XEOMIN (incobotulinumtoxinA), manufactured using a proprietary process

that isolates the therapeutic component and eliminates accessory proteins, yielding a 150 kDa neurotoxin molecule.

More than 84,000 patients have been treated with XEOMIN worldwide since 2005. The U.S. is the 20<sup>th</sup> country to approve XEOMIN for the treatment of cervical dystonia and blepharospasm.

XEOMIN is the only botulinum toxin that does not require refrigeration prior to reconstitution. XEOMIN is available in 50-unit and 100-unit vials, which Merz believes may allow for more precise billing and reduce wastage.

## IMPORTANT SAFETY INFORMATION

### **WARNING: Distant Spread of Toxin Effect**

Postmarketing reports indicate that the effects of XEOMIN and all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. These may include asthenia, generalized muscle weakness, diplopia, blurred vision, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence and breathing difficulties. These symptoms have been reported hours to weeks after injection. Swallowing and breathing difficulties can be life threatening and there have been reports of death. The risk of symptoms is probably greatest in children treated for spasticity but symptoms can also occur in adults treated for spasticity and other conditions, particularly in those patients who have underlying conditions that would predispose them to these symptoms. In unapproved uses, including spasticity in children and adults, and in approved indications, cases of spread of effect have been reported at doses comparable to those used to treat cervical dystonia and at lower doses.

## CONTRAINDICATIONS

XEOMIN is contraindicated in patients with a known hypersensitivity to the active substance botulinum toxin type A or to any of the components in the formulation and in the presence of infection at the proposed injection site(s).

## WARNINGS AND PRECAUTIONS

- **The potency units of XEOMIN are not interchangeable with other preparations of botulinum toxin products. Therefore, units of biological activity of XEOMIN cannot be compared to or converted into units of any other botulinum toxin products.**
- Hypersensitivity reactions have been reported with botulinum toxin products (anaphylaxis, serum sickness, urticaria, soft tissue edema, and dyspnea). If serious and/or immediate hypersensitivity reactions occur further injection of XEOMIN should be discontinued and appropriate medical therapy immediately instituted.
- Treatment with XEOMIN and other botulinum toxin products can result in swallowing or breathing difficulties. Patients with pre-existing swallowing or breathing difficulties may be more susceptible to these complications. In most cases, this is a consequence of weakening of muscles in the area of injection that are involved in breathing or swallowing. When distant effects occur, additional respiratory muscles may be involved [See *Boxed Warning*]. Deaths as a complication of severe dysphagia have been reported after treatment with botulinum toxin. Dysphagia may persist for several months, and require use of a feeding tube to maintain adequate nutrition and hydration. Aspiration may result from severe dysphagia and is a particular risk when treating patients in whom swallowing or respiratory function is already compromised. These reactions can occur within hours to weeks after injection with botulinum toxin.
- **Cervical Dystonia:** Patients with smaller neck muscle mass and patients who require bilateral injections into the sternocleidomastoid muscles are at greater risk of dysphagia. Limiting the dose injected into the sternocleidomastoid muscle may decrease the occurrence of dysphagia.
- **Blepharospasm:** Injection of XEOMIN into the orbicularis oculi muscle may lead to reduced blinking and corneal exposure with possible ulceration or perforation. Lower lid injections should not be repeated if diplopia occurred with previous botulinum toxin injections.

- Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis, or neuromuscular junctional disorders (e.g., myasthenia gravis or Lambert-Eaton syndrome) should be monitored particularly closely when given botulinum toxin. Patients with neuromuscular disorders may be at increased risk of clinically significant effects including severe dysphagia and respiratory compromise from typical doses of XEOMIN.

## ADVERSE REACTIONS

**Cervical Dystonia:** The most commonly observed adverse reactions (incidence  $\geq 10\%$  of patients and twice the rate of placebo) for XEOMIN 120 Units and XEOMIN 240 Units, respectively, were: dysphagia (13%, 18%), neck pain (7%, 15%), muscle weakness (7%, 11%), and musculoskeletal pain (7%, 4%).

**Blepharospasm:** The most common adverse reactions (incidence  $\geq 10\%$  of patients and twice the rate of placebo) for XEOMIN were eyelid ptosis (19%), dry mouth (16%), visual impairment (12%), diarrhea (8%), and headache (7%).

## DRUG INTERACTIONS

Concomitant treatment of XEOMIN and aminoglycoside antibiotics, spectinomycin, or other agents that interfere with neuromuscular transmission (e.g., tubocurarine-like agents), or muscle relaxants, should be observed closely because the effect of XEOMIN may be potentiated.

## USE IN PREGNANCY

Pregnancy Category C: There are no adequate and well-controlled studies in pregnant women. XEOMIN should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Please see full prescribing information for XEOMIN, including Boxed WARNING, available at [www.XEOMIN.com](http://www.XEOMIN.com).**

### About Merz

Merz Pharmaceuticals, LLC is a part of the Merz Group of companies and was established in 1995 to develop and commercialize products for the Merz Group. Areas of therapeutic focus include Neurology, Dermatology, and Podiatry.

With a 102 year heritage, the Merz Group is known worldwide for its development of original compounds and formulations for medical professionals and consumers in 90 countries. Globally, Merz is a leader in the development of pharmaceuticals for the treatment of neurological and psychological disorders as well as for aesthetic medicine. Global research is concentrated in fields that have a strong need for therapeutic innovation such as Alzheimer's disease, Parkinson's disease, tinnitus, chronic pain conditions, addictions, and neuromuscular disturbances.

XEOMIN is a registered trademark of Merz Pharma GmbH & Co KGaA. Botox is a registered trademark of Allergan, Inc.

SOURCE: Merz Pharmaceuticals

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