



February 1, 2010

On behalf of Merz Pharma Canada, it is my great pleasure to announce that the Conseil du médicament du Québec has agreed to list Xeomin® in the following manner:

**XEOMIN  
FEBRUARY 2010 – BLEPHAROSPASM, CERVICAL DYSTONIA AND OTHER SEVERE  
SPASTIC CONDITIONS**

**Trade name:** Xeomin

**Proper name:** *Clostridium Botulinum* neurotoxin type A, free from complexing proteins

**Manufacturer:** Merz

**Dosage form:** Powder for intramuscular injection

**Strength:** 100 units

**Addition to formularies – exception drug**

**DESCRIPTION OF DRUG**

*Botulinum* neurotoxin type A blocks transmission at the neuromuscular junction, having therefore a paralyzing activity. Xeomin® is a purified version of the neurotoxin. It is indicated for the symptomatic treatment of blepharospasm, cervical dystonia and spasticity of the upper limbs in adult patients. Presently, Botox®, another *Botulinum* neurotoxin, is on the exception drug status program, under certain conditions.

**THERAPEUTIC VALUE**

**Blepharospasm**

The objective of the Roggenkämper study (2005) was to evaluate the efficacy and safety of Xeomin® compared to Botox®. This 16-week non-inferiority study grouped 256 patients with blepharospasm who had already responded to two treatment sessions with Botox®. There was non-inferiority if the upper limit of the difference confidence interval was not over 10% (or 0.8 point) in the Jankovic Rating Scale. Main results showed the following:

- No significant difference was noted in the Jankovic Rating Scale (0.22 point) between the two toxins after 3 and 16 weeks of treatment;
- Median time to onset of action and median duration of action were similar in both groups;
- Eyelid ptosis is the most frequent adverse event with both toxins. The incidence of adverse events is the same in both groups.

The *Conseil* deems acceptable the use of the Jankovic Rating Scale as well as the 10% safeguard for this indication. In the light of the results, the *Conseil* considers that the non-inferiority of Xeomin® compared to Botox® was demonstrated in spite of important loss in follow-up and also recognizes that the adverse event profile of Xeomin® is similar to the comparator's.

**Cervical dystonia**

The objective of the Benecke study (2005) was to compare the efficacy and safety of Xeomin® with that of Botox®. This 16-week non-inferiority study grouped 420 patients with cervical dystonia who had already responded to two treatment sessions with Botox®. Non-inferiority was recognized if the upper limit of the difference confidence interval in a severity scale validated for cervical dystonia was not over the fixed limit of 4% (1.3 points). Main results showed the following:

- No significant difference (0.38 point) was noted between these two toxins on the severity scale for dystonia after 28 days and 16 weeks of treatment;
- Median time to onset of action and median duration of action were similar in both groups;
- Dysphagia is the most frequent adverse event with both toxins. The incidence of adverse events is the same in both groups.

The *Conseil* deems acceptable the use of this scale as well as the 4% safeguard for this indication. In the light of the results, the *Conseil* considers that the non-inferiority of Xeomin® compared to Botox® was demonstrated.

**Other severe spastic conditions:**

Another trial (Wohlfarth 2007) studied a small group of healthy subjects and compared the amplitude and duration of paralyzing effect of an identical dose of Xeomin® or Botox® injected in a foot muscle. Results suggested that Xeomin's® efficacy to induce a targeted muscular paralysis is similar to Botox's®. However, it is hard to project these results to clinical benefits mainly because of the studied population's characteristics. The *Conseil* also accessed another study (Kanovsky 2009) which demonstrated Xeomin's® efficacy compared to a placebo for the treatment of a condition other than spasticity. In the light of these data, the *Conseil* considers it is possible to project the results of the Roggenkämper and Benecke studies to other severe spastic conditions, given these conditions' similar physiopathology, the pharmacological "familyhood" of compared toxins and Kanovsky's results.

In short, the *Conseil* recognizes Xeomin's® therapeutic value in the treatment of cervical dystonia, blepharospasm and other severe spastic conditions.

**ECONOMIC AND PHARMACOECONOMIC ASPECTS**

A vial of Xeomin® costs \$330, whereas a vial of Botox® costs \$357. From a pharmacoeconomic standpoint, and assuming that Xeomin's® and Botox's® efficacy and safety are equivalent, cost of treatment with Xeomin® is lower than Botox® in the recommended doses and for all studied medical conditions. Therefore, Xeomin® meets economic and pharmacoeconomic criteria.

**SPECIAL CONSIDERATIONS**

The *Conseil* did not list the *Botulinum* toxin in the regular section so there would be no reimbursement for aesthetic reasons.

**CONCLUSION**

Given all criteria under the law, the *Conseil* recommended that Xeomin® be added to the formularies according to the following recognized indication:

- For the treatment of cervical dystonia, blepharospasm and other severe spastic conditions.

I am very pleased that all appropriate patients will benefit from Xeomin treatment and be reimbursed.

Please do not hesitate to contact your local Merz Pharma Canada representative or me if you have any questions.

Sincerely,



Glenn Block  
President & General Manager  
Merz Pharma Canada Ltd.