MERZ
THERAPEUTICS
Better outcomes for more patients.

XEOMIN® (incobotulinumtoxinA) Pediatric Chronic Sialorrhea

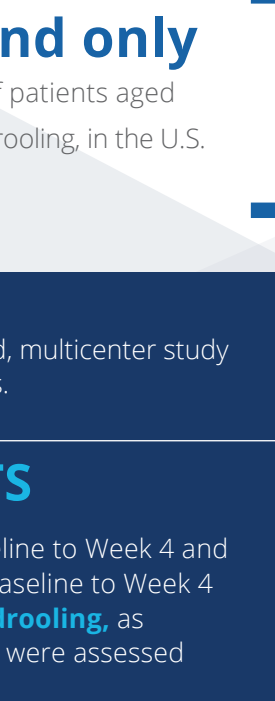
Pediatric Sialorrhea

DEFINITION: Sialorrhea, also known as drooling or ptyalis, is a debilitating symptom that occurs when there is excess saliva in the mouth beyond the lip margin.[1]

PREVALENCE:
In the U.S., an estimated
300,000
neurologically impaired children suffer from this condition commonly occuring from cerebral palsy or brain injury.[2,3]

CAUSES:
It can occur from difficulty retaining saliva inside the mouth, issues with swallowing and from problems controlling facial muscles.[4,5]

EFFECTS:
Sialorrhea can cause physical and psychosocial complications, including dehydration, odor, and social stigmatization, which can be devastating for patients and their families.[6]



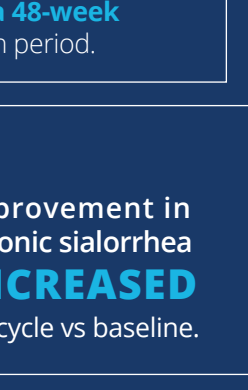
New FDA Indication

XEOMIN® (incobotulinumtoxinA) is the **first and only** neuromodulator FDA-approved for the treatment of patients aged **2 years and older with chronic sialorrhea**, or drooling, in the U.S.

Phase 3 Study

ABOUT THE STUDY: A Phase 3 prospective, randomized, double-blind, placebo-controlled, multicenter study evaluating the safety and efficacy of XEOMIN in 255 children and adolescents aged 2 - 17 years.

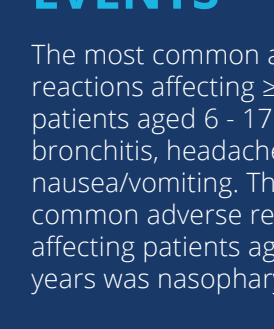
64 WEEKS
study duration



with a **16-week main period followed by three additional injections during a 48-week** open label extension period.

CO-PRIMARY ENDPOINTS

Unstimulated Salivary Flow rate (uSFR) from baseline to Week 4 and Global Impression of Change Scale (GICS) from baseline to Week 4 representing the **functional improvement in drooling,** as assessed by the caregiver. Co-primary endpoints were assessed among patients 6 - 17 years of age.



Improvement in chronic sialorrhea INCREASED with each injection cycle vs baseline.

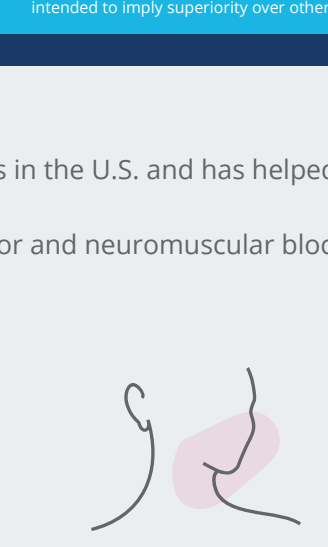
RESULTS

XEOMIN demonstrated **significantly reduced uSFR and improved GICS versus placebo** at Week 4 among patients aged 6 - 17 years, and sustained efficacy with results over 64 weeks. Efficacy in patients 2 - 5 years was comparable.

ADVERSE EVENTS

The most common adverse reactions affecting ≥1% of patients aged 6 - 17 years were bronchitis, headache and nausea/vomiting. The most common adverse reaction affecting patients aged 2 - 5 years was nasopharyngitis.

The XEOMIN Difference:



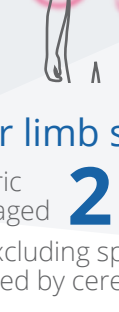
No patients demonstrated clinical resistance or secondary treatment failure due to neutralizing antibodies (NAb), supporting the importance of XEOMIN's **unique purification process** through XTRACT Technology®*.

*The direct impact of the non-therapeutic proteins on long term safety or efficacy has not been established. Information about the unique XEOMIN manufacturing process and the properties of incobotulinumtoxinA is not intended to imply superiority over other botulinum toxin type A products.

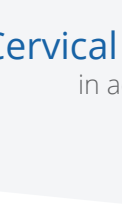
XEOMIN

XEOMIN now holds six first-line indications in the U.S. and has helped more than 3.6 million patients worldwide across various indications.

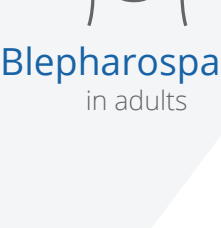
XEOMIN is an acetylcholine release inhibitor and neuromuscular blocking agent indicated for the treatment or improvement of:



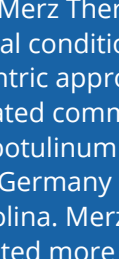
Chronic sialorrhea
in pediatric patients aged **2** YEARS AND OLDER



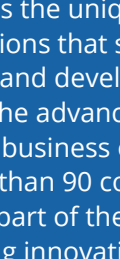
Chronic sialorrhea
in adults



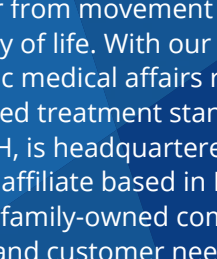
Upper limb spasticity
in adults



Upper limb spasticity
in pediatric patients aged **2** YEARS AND OLDER
excluding spasticity caused by cerebral palsy



Cervical dystonia
in adults



Blepharospasm
in adults

MERZ THERAPEUTICS
Better outcomes for more patients.

About: At Merz Therapeutics, we seek to address the unique needs of people who suffer from movement disorders, neurological conditions, and other health conditions that severely impact patients' quality of life. With our patient-centric approach, cutting-edge research and development efforts, highly-scientific medical affairs resources and dedicated commercial teams, we continue the advancement of new and individualized treatment standards, including botulinum toxin. Merz Therapeutics, a business of Merz Pharmaceuticals GmbH, is headquartered in Frankfurt, Germany and is represented in more than 90 countries, with a North America affiliate based in Raleigh, North Carolina. Merz Pharmaceuticals GmbH is part of the Merz Group, a privately held, family-owned company that has dedicated more than 110 years to developing innovations that serve unmet patient and customer needs.

Mission: Driven by our passion, we do everything to bring better outcomes to more patients. We relentlessly pursue unmet needs and engage all stakeholders to deliver meaningful value.

Merz Therapeutics is committed to ensuring XEOMIN is accessible and affordable to all patients through our MERZ CONNECT™ savings and assistance programs. Learn more at **https://www.xeomin.com/patient-savings-program**.

XEOMIN® (incobotulinumtoxinA) IMPORTANT CONSUMER SAFETY INFORMATION

Read the Medication Guide before you start receiving XEOMIN® (Zee-min) and each time XEOMIN is given to you as there may be new information. The risk information provided here is not comprehensive. To learn more:

- Talk to your health care provider or pharmacist
- Visit www.xeomin.com to obtain the FDA-approved product labeling
- Call **1-844-MYMERZ (1-844-469-6379)**

Uses

XEOMIN is a prescription medicine:

- that is injected into glands that make saliva and is used to treat long-lasting (chronic) drooling (sialorrhea) in adults and in children 2 to 17 years of age.
- that is injected into muscles and used to:
  - » treat increased muscle stiffness in the arm because of upper limb spasticity in adults.
  - » treat increased muscle stiffness in the arm in children 2 to 17 years of age with upper limb spasticity, excluding spasticity caused by cerebral palsy.
  - » treat the abnormal head position and neck pain with cervical dystonia (CD) in adults.
  - » treat abnormal spasm of the eyelids (blepharospasm) in adults.

It is not known if XEOMIN is safe and effective in children younger than:

- 2 years of age for the treatment of chronic sialorrhea
- 2 years of age for the treatment of upper limb spasticity
- 18 years of age for the treatment of cervical dystonia or blepharospasm

Warnings

XEOMIN may cause serious side effects that can be life threatening. Get medical help right away if you have any of these problems any time (hours to weeks) after injection of XEOMIN:

- **Problems swallowing, speaking, or breathing** can happen if the muscles that you use to breathe and swallow become weak. Death can happen as a complication if you have severe problems with swallowing or breathing after treatment with XEOMIN.
  - » People with certain breathing problems may need to use muscles in their neck to help them breathe and may be at greater risk for serious breathing problems with XEOMIN.
  - » Swallowing problems may last for several months, and during that time you may need a feeding tube to receive food and water. If swallowing problems are severe, food or liquids may go into your lungs. People who already have swallowing or breathing problems before receiving XEOMIN have the highest risk of getting these problems.
- **Spread of toxin effects.** In some cases, the effect of botulinum toxin may affect areas of the body away from the injection site and cause symptoms of a serious condition called botulism. The symptoms of botulism include: loss of strength and muscle weakness all over the body, double vision, blurred vision and drooping eyelids, hoarseness or change or loss of voice, trouble saying words clearly, loss of bladder control, trouble breathing, trouble swallowing.

These symptoms can happen hours to weeks after you receive an injection of XEOMIN. These problems could make it unsafe for you to drive a car or do other dangerous activities.

Do not take XEOMIN if you: are allergic to XEOMIN or any of the ingredients in XEOMIN (see below for a list of ingredients in XEOMIN), had an allergic reaction to any other botulinum toxin product such as rimabotulinumtoxinB (Myobloc®), onabotulinumtoxinA (Botox®, Botox® Cosmetic), or abobotulinumtoxinA (Dysport®) or have a skin infection at the planned injection site.

Before receiving XEOMIN, tell your doctor about all of your medical conditions, including if you:

- have a disease that affects your muscles and nerves (such as amyotrophic lateral sclerosis [ALS or Lou Gehrig's disease], myasthenia gravis or Lambert-Eaton syndrome)
- have had any side effect from any other botulinum toxin in the past
- have a breathing problem, such as asthma or emphysema
- have a history of swallowing problems or inhaling food or fluid into your lungs (aspiration)
- have drooping eyelids
- have had eye surgery
- have had surgery on your face
- are pregnant or plan to become pregnant. It is not known if XEOMIN can harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if XEOMIN passes into breast milk.

Tell your doctor about all of the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements. **Talk to your doctor before you take any new medicines after you receive XEOMIN.**

Using XEOMIN with certain other medicines may cause serious side effects. **Do not start any new medicines until you have told your doctor that you have received XEOMIN in the past. Especially tell your doctor if you:**

- have received any other botulinum toxin product in the last four months
- have received injections of botulinum toxin such as rimabotulinumtoxinB (MYOBLOC®), onabotulinumtoxinA (BOTOX®, BOTOX® COSMETIC) and abobotulinumtoxinA (DYSPORT®) in the past. Be sure your doctor knows exactly which product you received. The dose of XEOMIN may be different from other botulinum toxin products that you have received
- have recently received an antibiotic by injection or inhalation
- take muscle relaxants
- take an allergy or cold medicine
- take a sleep medicine

Ask your doctor if you are not sure if your medicine is one that is listed above.

Know the medicines you take. Keep a list of your medicines with you to show your doctor and pharmacist each time you get a new medicine.

Possible Side Effects

XEOMIN can cause serious side effects including:

- **Injury to the cornea (the clear front surface of the eye) in people treated for blepharospasm.** People who receive XEOMIN to treat spasm of the eyelid may have reduced blinking that can cause a sore on their cornea or other problems of the cornea. Call your healthcare provider or get medical care right away if you have eye pain or irritation after treatment with XEOMIN.
- **XEOMIN may cause other serious side effects including** allergic reactions. Symptoms of an allergic reaction to XEOMIN may include: itching, rash, redness, swelling, wheezing, trouble breathing, or dizziness or feeling faint. Tell your doctor or get medical help right away if you get wheezing or trouble breathing, or if you get dizzy or faint.

The most common side effects of XEOMIN in adults with chronic sialorrhea include:

- needling to have a tooth pulled (extraction)
- dry mouth
- diarrhea
- high blood pressure

The most common side effects of XEOMIN in children 2 to 17 years of age with chronic sialorrhea include:

- bronchitis
- nausea
- headache
- vomiting

The most common side effects of XEOMIN in adults with upper limb spasticity include:

- seizure
- nasal congestion, sore throat and runny nose
- dry mouth
- upper respiratory infection

The most common side effects of XEOMIN in children 2 to 17 years of age with upper limb spasticity include:

- nasal congestion, sore throat and runny nose
- bronchitis

The most common side effects of XEOMIN in adults with cervical dystonia include:

- difficulty swallowing
- neck pain
- muscle weakness
- pain at the injection site
- muscle and bone pain

The most common side effects of XEOMIN in adults with blepharospasm include:

- drooping of the eyelid
- dry eye
- vision problems
- dry mouth

These are not all the possible side effects of XEOMIN.

Call your doctor for medical advice about side effects. You may report side effects to FDA at **1-800-FDA-1088.**

General information about the safe and effective use of XEOMIN

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. You can ask your pharmacist or doctor for information about XEOMIN that is written for health professionals.

Active Ingredient: botulinum toxin type A

Inactive Ingredients: human albumin and sucrose

References

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