Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
This medicine is dispensed with a doctor's prescription only

XEOMIN® 50
Powder for solution for injection

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Active ingredient
Each 1 vial of XEOMIN 50 contains 50 LD_{50} units of botulinum toxin type A
Each 1 vial of XEOMIN 100 contains 100 LD_{50} units of botulinum toxin type A

Inactive ingredients and allergens in this medicine: See section 6 - 'Additional information'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

1. What is this medicine intended for?
- XEOMIN is intended for the symptomatic treatment of:
  - eyelid spasm (blepharospasm)
  - cervical dystonia of a predominantly rotational form (spasmodic torticollis)
  - post-stroke spasticity of the upper limb presenting with flexed wrist and clenched fist in adults
- XEOMIN is indicated for the temporary improvement in the appearance of moderate to severe vertical lines between eyebrows seen at frown (glabellar frown lines) in adults below 65 years when the severity of these lines has a significant psychological impact for the patient.

Therapeutic group: muscle relaxants

2. Before using this medicine
Do not use this medicine if:

- you are sensitive (allergic) to the active ingredient Botulinum neurotoxin type A, or to any of the other ingredients in this medicine (see section 6).
- you suffer from a generalised disorder of muscle activity (e.g. myasthenia gravis or Lambert-Eaton syndrome).
- you have an infection or inflammation at the intended injection site.

Special warnings about using this medicine
Side effects may occur from misplaced injections of Botulinum neurotoxin type A temporarily paralysing nearby muscle groups. There have been very rare reports of side effects that may be related to the spread of toxin distant from the injection site to produce symptoms consistent to Botulinum toxin type A effects (e.g. excessive muscle weakness, swallowing difficulties or accidental swallowing of food or drink into the airways). Patients who receive the recommended dose may experience excessive muscle weakness.

If the dose is too high or the injections too frequent, the risk of antibody formation may increase. Antibody formation can cause treatment with Botulinum toxin type A to fail, whatever the reason for its use.

Before using XEOMIN, tell your doctor if:
- you suffer from any type of bleeding disorder
- you take medicines that prevent the blood from clotting (e.g. coumarin, heparin, acetylsalicylic acid, clopidogrel)
- you suffer from pronounced weakness or decreased muscle volume in the muscle where you will receive the injection
- you suffer from amyotrophic lateral sclerosis (ALS), which can lead to generalised muscle decrease
- you suffer from any disease that disturbs the interaction between nerves and skeletal muscles (peripheral neuromuscular dysfunction)
- you have or have had swallowing difficulties
- you suffer or have suffered from seizures
- you have had problems with injections of Botulinum toxin type A in the past
- you are due to have surgery

Contact your doctor to receive medical attention immediately if you experience any of the following conditions:
- difficulty in breathing, swallowing or speaking
- hives, swelling including swelling of the face or throat, wheezing, feeling faint and shortness of breath (possible symptoms of severe allergic reactions) (see section 4).

Repeated injections with XEOMIN
If you have repeated injections with XEOMIN, the effect may increase or decrease. Possible reasons for this are:
- your doctor may follow a different procedure when preparing the solution for injection
- different treatment intervals
- injections into another muscle
- marginally varying effectiveness of the active ingredient of XEOMIN
- non-response/therapy failure during the treatment

Eyelid spasm (blepharospasm)
Talk to your doctor before XEOMIN is used, if:
- you have had eye surgery. Your doctor will take additional precautions.
- you are at risk of developing a disease called narrow angle glaucoma. This disease can cause the inner eye pressure to rise and may lead to damaging of your optic nerve. Your doctor will know if you are at risk.

During treatment, small punctuated bleedings may occur in the soft tissues of the eyelid. Your doctor can limit these by immediately applying gentle pressure at the injection site.
After you receive a XEOMIN injection into your eye muscle, your blinking rate may be reduced. This can lead to prolonged exposure of the transparent front part of the eye (cornea). This exposure may lead to damage to the surface and inflammation (corneal ulceration).

Cervical dystonia of a predominantly rotational form (spasmodic torticollis)
After the injection, you may develop mild to severe swallowing difficulties. This may lead to problems with breathing and you may have a higher risk of inhaling foreign substances or fluids. Foreign substances in your lungs may lead to an inflammation or infection (pneumonia). Your doctor will give you special medical treatment if needed (e.g. in the form of artificial nutrition). Swallowing difficulties can last for up to 2-3 weeks after injection, for one patient a duration of up to five months is known.
If you have been inactive for a long period of time, any activity should be started gradually after the XEOMIN injection.

Post-stroke spasticity of the upper limb presenting with flexed wrist and clenched fist in adults
XEOMIN can be used to treat this condition. XEOMIN is effective in combination with the usual treatment methods. XEOMIN should be used together with these other methods. It is unlikely that this medicine will improve the range of motion of joints where the surrounding muscles have lost the ability to stretch.
If you have been inactive for a long period of time, any activity should be started gradually after the XEOMIN injection.

The elderly
There is limited information about treatment of glabellar frown lines in patients over the age of 65. Therefore, do not use XEOMIN in patients over the age of 65 to treat glabellar frown lines.

Children and adolescents
Do not give this medicine to children and adolescents below the age of 18, as the safety and efficacy of XEOMIN in treatment of children and adolescents have not been established yet and therefore the use of XEOMIN is not recommended.

Interactions with other medicines
If you are taking or have recently taken other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:
Medicines that may increase the effect of XEOMIN:
- medicines used to treat certain infectious diseases (spectinomycin or aminoglycoside antibiotics such as neomycin, kanamycin, tobramycin).
- other medicines that relax the muscles (e.g. muscle relaxants of the tubocurarine-type). Such medicines are used, for example, in general anaesthesia. Before you have surgery, tell your anaesthetist if you have received XEOMIN.

In these cases, XEOMIN must be used carefully.
The effect of XEOMIN may be reduced by certain medicines for malaria and rheumatism (known as aminoquinolines).

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to become pregnant, consult your doctor or pharmacist before taking this medicine.
XEOMIN should not be used during pregnancy, unless your doctor decides that the necessity and potential benefit of the treatment justifies the possible risk on the foetus.
XEOMIN is not recommended if you are breast-feeding.

Driving and using machines
You should not drive or be involved in other potentially hazardous activities if drooping eyelids, weakness (asthenia), muscle weakness, dizziness or vision disorders occur.
If in doubt, ask your doctor for advice.

3. How to use this medicine?

Always use this medicine according to your doctor's instructions.
XEOMIN may only be administered by doctors with appropriate expertise and knowledge suitable for treatment with Botulinum neurotoxin type A. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.
Only your doctor will determine your dose and how you should take this medicine.

The optimum dose, frequency of use and number of injection sites will be chosen by your doctor individually for you.

The results of initial treatment with XEOMIN should be evaluated and may lead to dose adjustment until the desired therapeutic effect is achieved.
Treatment intervals will be determined by your doctor based on your actual clinical need.

If you have the impression that the effect of XEOMIN is too strong or too weak, tell your doctor. In cases where no therapeutic effect is apparent, alternative therapies should be taken into consideration.

The recommended dosage is usually:
Eyelid spasm (blepharospasm)
The recommended initial dose is up to 25 units per eye, and the final total recommended dose in follow-up treatment sessions is up to 100 units per treatment session. Usually, the first onset of effect is observed within four days after injection. The effect of each treatment session generally lasts for about 3-4 months, however, it may last significantly longer or shorter. The treatment may be repeated if necessary. Normally, no additional benefit is conferred by treating more frequently than every three months.

Cervical dystonia of a predominantly rotational form (spasmodic torticollis)
The recommended dose per single injection site is up to 50 units, and the maximum dose for the first treatment session is 200 units. Doses up to 300 units may be given to you by your doctor in subsequent courses depending on the response.
Usually, the first onset of effect is observed within seven days after injection. The effect of each treatment generally lasts for about 3-4 months, however, it may last significantly longer or shorter. Treatment intervals of less than 10 weeks are not recommended.

Post-stroke spasticity of the upper limb presenting with flexed wrist and clenched fist in adults
The recommended dose is up to 400 units per treatment session. Patients reported the onset of action 4 days after the date of the injection. An improvement of muscle tone was perceived within four weeks. The treatment generally lasted 12 weeks, however, it may last significantly longer or shorter.
The period between each treatment session should be at least 12 weeks.

Vertical lines between eyebrows seen at frown (glabellar frown lines)
When treating vertical lines between eyebrows seen at frown (glabellar frown lines), the standard total dosage is 20 units. The doctor will inject 4 units into each of the five injection sites. The doctor may increase the overall dose up to 30 units, if required for the patient's personal needs, with an interval of at least 3 months between treatments. Reduction of the vertical lines between eyebrows seen at frown generally occurs within 2 to 3 days, with the maximum effect perceived within 30 days. The effect lasts up to 4 months after the injection.

Method of administration
Reconstituted XEOMIN is intended for injections into the muscle (intramuscular administration; see information for medical professionals at the end of this leaflet).

Do not exceed the recommended dose.

If you accidentally received more XEOMIN than you were supposed to receive
Symptoms of overdose:
Symptoms of overdose are not apparent immediately after the injection and may include general weakness, drooping eyelid, double vision, breathing difficulties, speech difficulties, and paralysis of the respiratory muscles or swallowing difficulties which may lead to pneumonia.

Measures in cases of overdose:
In case you feel symptoms of overdose, or if a child has accidentally taken some of the medicine, seek medical attention immediately or ask your relatives to do so, immediately go to a hospital

emergency room and bring the medicine package with you. You may require medical supervision for up to several days and assisted ventilation.

Adhere to the treatment as recommended by your doctor.

Do not take medicines in the dark! Check the label and dose every time you take medicine. Wear glasses if you need them. If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects

As with any medicine, using XEOMIN may cause side effects in some users. Do not be alarmed by reading the list of side effects. You may not experience any of them.
An allergic reaction may occur with XEOMIN. Serious and/or immediate allergic reactions (anaphylactic reaction) or allergic reactions to the serum in the medicine (serum sickness), causing for example difficulty in breathing (shortness of breath), hives or swelling of the soft tissue (oedema), have been rarely reported. Some of these reactions have been observed following the use of conventional Botulinum toxin type A complex. They occurred when the toxin was given alone or in combination with other medicines known to cause similar reactions. These effects cannot be ruled out completely when using XEOMIN.

An allergic reaction can cause any of the following symptoms:

- difficulty with breathing, swallowing or speaking due to the swelling of the face, lips, mouth or throat.
- swelling of the hands, feet or ankles.

If you notice any of these side effects, inform your doctor immediately or ask your relatives to do so and go to the emergency room of your nearest hospital.

Usually, side effects are felt within the first week after treatment and are temporary in nature. Side effects may be related to the medicine, injection technique or both. Side effects may be restricted to the area around the injection site (e.g. localised muscle weakness, local pain, inflammation, pins and needles (paraesthesia), reduced sense of touch (hypoaesthesia), tenderness, swelling (general), swelling of the soft tissues (oedema), skin redness, itching, localised infection, haematoma, bleeding and/or bruising). Drooping eyelids may be caused as a result of the injection technique and the effect of the medicine.
The injection of the needle may cause pain. This pain or the anxiety towards needles may lead to fainting, problems with blood circulation, nausea, tinnitus (ringing/noises in the ears) or low blood pressure.

Side effects such as excessive muscle weakness or swallowing difficulties may be caused by the relaxation of muscles far from the injection site of XEOMIN. Swallowing difficulties can cause inhalation of foreign bodies resulting in lung inflammation and in some cases, death.

An allergic reaction may occur with XEOMIN. Serious and/or immediate allergic reactions (anaphylactic reaction) or allergic reactions to the serum in the medicine (serum sickness), causing for example difficulty in breathing (shortness of breath), hives or swelling of the soft tissues (oedema), have been rarely reported. Some of these reactions have been observed following the use of conventional Botulinum toxin type A complex. They occurred when the toxin was given alone or in combination with other medicines known to cause similar reactions. These effects cannot be ruled out completely when using XEOMIN.

An allergic reaction can cause any of the following symptoms:

- difficulty with breathing, swallowing or speaking due to the swelling of the face, lips, mouth or throat.
- swelling of the hands, feet or ankles.

If you notice any of these side effects, inform your doctor immediately or ask your relatives to do so and go to the emergency room of your nearest hospital.

Additional side effects
Eyelid spasm (blepharospasm)
Very common side effects - effects that appear in more than one in ten users:
Drooping eyelids

Common side effects - effects that appear in 1-10 in 100 users:
Dry eyes, vision blurred, visual impairment, dry mouth, injection site pain

Uncommon side effects - effects that appear in 1-10 in 1,000 users:
Headache, weakness of face muscle (facial paralysis), double vision, lacrimation increased, swallowing difficulties, fatigue, muscular weakness, rash

Cervical dystonia of a predominantly rotational form (spasmodic torticollis)
Very common side effects - effects that appear in more than one in ten users:
Swallowing difficulties

Common side effects - effects that appear in 1-10 in 100 users:
Neck pain, muscular weakness, musculoskeletal pain (muscle pain), musculoskeletal stiffness, muscle spasms, headache, dizziness, injection site pain, weakness, dry mouth, nausea, sweating increased, upper respiratory tract infections, feeling faint

Uncommon side effects - effects that appear in 1-10 in 1,000 users:
Speech disorders (voice disorders), shortness of breath, rash

The treatment of spasmodic torticollis may cause swallowing difficulties with varying degrees of severity. This may lead to breathing in foreign materials, which may require medical intervention. Swallowing difficulties may persist for 2-3 weeks after the injection, but has been reported in one case to last five months. Swallowing difficulties appear to be dose-dependent.

Post-stroke spasticity of the upper limb presenting with flexed wrist and clenched fist in adults
Common side effects - effects that appear in 1-10 in 100 users:
Dry mouth

Uncommon side effects - effects that appear in 1-10 in 1,000 users:
Headache, reduced sense of touch, muscular weakness, pain in extremities, weakness, musculoskeletal pain (muscle pain), swallowing difficulties, nausea

Side effects of unknown frequency (the frequency of these effects has not been established yet):
Injection site pain

Vertical lines between eyebrows seen at frown (glabellar frown lines)
These side effects have been observed with XEOMIN:

Common side effects - effects that appear in 1-10 in 100 users:
- Headache
- Mephisto sign (elevation of the outer ends of the eyebrows)

Uncommon side effects - effects that appear in 1-10 in 1,000 users:
- Acute inflammation of the upper larynx and nose (cold)
- Inflammation of the bronchia (bronchitis)
- Flu-like illness
- Drooping eyebrow
- Drooping eyelids
- Accumulation of fluid in the eyelids (eyelid oedema)

- Discomfort (eyelid/eyebrow feels heavy)
- Blurred vision
- Muscle spasm
- Eyebrow asymmetry
- Stretching feeling at injection site
- Tiredness
- Pain or bruising at injection site
- Itching
- Bruise
- Lump under the skin
- Insomnia

Effects reported post-marketing (for all indications)
These side effects were reported with unknown frequency for the use of XEOMIN since marketing, independent from injection site:
Flu-like symptoms, shrinkage of injected muscle, and hypersensitivity reactions such as swelling and swelling of the soft tissues (oedema, also at sites distant from the injection site), redness, itching, rash (local and generalised), and breathlessness.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects
You can report side effects to the Ministry of Health by following the 'Reporting Side Effects of Drug Treatment' link on the Ministry of Health home page (www.health.gov.il), which opens an online form for reporting side effects, or you can also use this link: https://sideeffects.health.gov.il

5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this and all other medicines in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by your doctor.
- Do not use the medicine after the expiry date (exp. date), which is stated on the package. The expiry date refers to the last day of that month.

Storage conditions:
- Do not store above 25°C.
- After reconstitution, store at 2°C – 8°C. Shelf-life after reconstitution: 24 hours.
  From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C – 8°C, unless reconstitution has taken place in controlled and validated aseptic conditions.

Your doctor should not use XEOMIN if the solution has a cloudy appearance or contains visible particles.

6. Additional information

In addition to the active ingredient, this medicine also contains: sucrose, human serum albumin

What the medicine looks like and contents of the pack:
The medicine is packed in a clear glass vial that contains a white-cream coloured powder. Each pack contains 1, 2, 3 or 6 vials.
Not all pack sizes may be marketed.

Registration holder's name and address: Alphamedix Ltd., 25 Bazel St., P.O. Box 10256, Petach Tikva.

Manufacturer's name and address: Merz Pharma GmbH & Co. KGAA, Germany

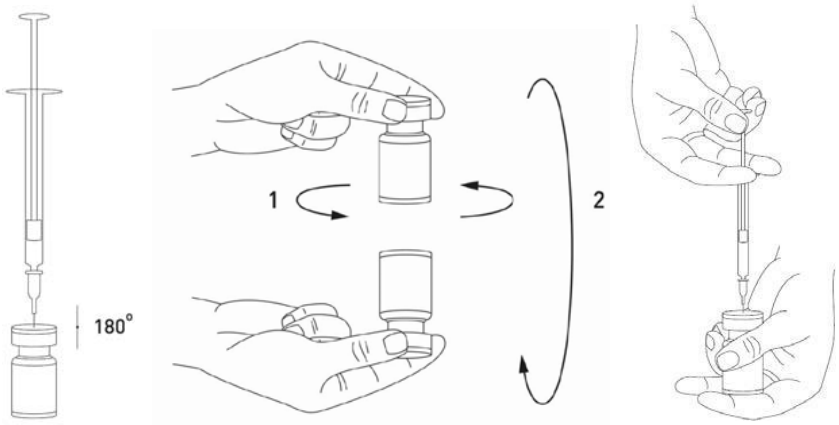
Revised in October 2024.

Registration numbers of the medicine in the Ministry of Health's National Drug Registry:
XEOMIN 50: 161-95-35383-00
XEOMIN 100: 161-96-35384-00

The following information is intended for medical professionals only (instructions for reconstitution of the solution for injection and instructions for disposal following use).

Instructions for reconstitution of the solution for injection:

XEOMIN is reconstituted prior to use with sodium chloride 9 mg/ml (0.9 %) solution for injection. XEOMIN may only be applied for its intended use to treat one patient for one session.
It is good practice to reconstitute the vial contents and prepare the syringe over plastic-lined paper towels to catch any spillage. An appropriate amount of sodium chloride solution (see dilution table) is drawn up into a syringe. A 20-27 G needle is recommended for reconstitution. After vertical insertion of the needle through the rubber stopper, the solvent is injected gently into the vial in order to avoid foam formation. Discard the vial if the vacuum does not pull the solvent into the vial. Remove the syringe from the vial and mix XEOMIN with the solvent by carefully swirling and inverting/flipping the vial – do not shake vigorously. If needed, the needle used for reconstitution should remain in the vial and the required amount of solution should be drawn up with a new sterile syringe suitable for injection.



Reconstituted XEOMIN is a clear, colourless solution.

XEOMIN must not be used if the reconstituted solution (prepared as above) has a cloudy appearance or contains floccular or particulate matter.

Care should be taken to use the correct solvent volume for the presentation chosen to prevent accidental overdose. If different vial sizes of XEOMIN are being used as part of one injection procedure, care should be taken to use the correct amount of solvent when reconstituting a particular number of units per 0.1 ml. The amount of solvent varies between XEOMIN 50 units and XEOMIN 100 units. Each syringe should be labelled accordingly.

Possible concentrations for XEOMIN 50 and 100 units are indicated in the following table:

Resulting dose in units per 0.1 ml	Solvent added (sodium chloride 9 mg/ml (0.9 %) solution for injection)	
	Vial with 50 units	**Vial with 100 units**
20 units	0.25 ml	0.5 ml
10 units	0.5 ml	1 ml
8 units	0.625 ml	1.25 ml
5 units	1 ml	2 ml
4 units	1.25 ml	2.5 ml
2.5 units	2 ml	4 ml
2 units	2.5 ml	5 ml
1.25 units	4 ml	Not applicable

Instructions for disposal
Any solution for injection that has been stored for more than 24 hours as well as any unused solution for injection should be discarded.

Procedure to follow for a safe disposal of vials, syringes and materials used
Any unused vials or remaining solution in the vial and/or syringes should be autoclaved. Alternatively, the remaining XEOMIN can be inactivated by adding one of the following solutions: 70% ethanol, 50% isopropanol, 0.1% SDS (anionic detergent), diluted sodium hydroxide solution (0.1 N NaOH), or diluted sodium hypochlorite solution (at least 0.1% NaOCl).

After inactivation used vials, syringes and materials should not be emptied and must be discarded into appropriate containers and disposed of in accordance with local requirements.

Recommendations should any incident occur during the handling of botulinum toxin type A
- Any spills of the product must be wiped up: either using absorbent material impregnated with any of the above solutions in case of the powder, or with dry, absorbent material in case of reconstituted product.
- The contaminated surfaces should be cleaned using absorbent material impregnated with any of the above solutions, then dried.
- If a vial is broken, proceed as mentioned above by carefully collecting the pieces of broken glass and wiping up the product, avoiding any cuts to the skin.
- If the product comes into contact with skin, rinse the affected area abundantly with water.
- If product gets into the eyes, rinse thoroughly with plenty of water or with an ophthalmic eyewash solution.
- If product comes into contact with a wound, cut or broken skin, rinse thoroughly with plenty of water and take the appropriate medical steps according to the dose injected.

These instructions for use, handling and disposal should be strictly followed.