Approved Patient Information Leaflet

SCHEDULING STATUS

S4

XEOMIN 50 or 100 units powder for solution for injection

Clostridium Botulinum neurotoxin type A (150 kD), free from complexing proteins

Contains sugar (sucrose: 4,7 mg per vial).

Read all of this leaflet carefully before you are given XEOMIN:

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- XEOMIN has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What XEOMIN is and what it is used for
2. What you need to know before you take XEOMIN
3. How to take XEOMIN
4. Possible side effects
5. How to store XEOMIN
6. Contents of the pack and other information

1. What XEOMIN is and what it is used for

XEOMIN is a medicine that relaxes the muscles.

XEOMIN is used in adults for the treatment of upper facial lines including the following conditions:

- vertical frown lines between the eyebrows (glabellar frown lines)
- lateral periorbital lines (crow's feet lines)
- horizontal forehead lines

XEOMIN is also used in adults for the treatment of:

- twisted neck (spasmodic torticollis)
- eyelid spasm (blepharospasm)
- increased muscle tension/uncontrollable muscle stiffness in shoulders, arms or hands (spasticity of the upper limb).

2. What you need to know before you are given XEOMIN

You should not be given XEOMIN:

- if you are allergic to Botulinum neurotoxin type A or any of the other ingredients of this medicine (see the section explaining what XEOMIN contains)
- if you suffer from generalised disorders of muscle activity (e.g. myasthenia gravis, Lambert-Eaton syndrome)
- if an infection or inflammation is present at the proposed injection site
- if you are pregnant or breastfeeding your baby.

If you are uncertain whether any of these apply to you, please discuss this with your doctor or pharmacist before being given XEOMIN.

Side effects may occur from misplaced injections of Botulinum neurotoxin

type A temporarily paralysing nearby muscle groups. There have been reports of side effects that may be related to the spread of Botulinum neurotoxin 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 doses may experience excessive muscle weakness.

If the dose is too high or the injection too frequent, the risk of antibody formation may increase. Antibody formation can cause treatment with Botulinum neurotoxin type A to fail.

Warnings and special precautions

Take special care with XEOMIN:

Talk to your doctor before taking or whilst taking XEOMIN:

- if you suffer from any type of bleeding disorders
- if you receive substances that prevent the blood from clotting (e.g. coumarin, heparin, acetylsalicylic acid, clopidogrel)
- if you suffer from pronounced weakness or decreased muscle volume in the muscle where you will receive the injection
- if you suffer from amyotrophic lateral sclerosis (ALS), which can lead to generalised muscle decrease
- if you suffer from any disease that disturbs the interaction between nerves and skeletal muscles (peripheral neuromuscular dysfunction)
- if you have or have had swallowing difficulties
- if you suffer or have suffered from seizures
- if you have had problems with injections of Botulinum neurotoxin type A

in the past

- if you are due to have surgery.

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 substance of XEOMIN
- non-response/therapy failure during the course of treatment.

Your doctor will clarify the reasons for this and discuss them with you.

If you have been inactive for a long period of time, any activity should be started gradually after the XEOMIN injection.

Contact your doctor and seek medical attention immediately if you experience any of the following:

- 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).

Twisted neck (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 two to three weeks after injection, for one patient a duration of up to five months is known.

Eyelid spasm (blepharospasm)

Talk to your doctor before XEOMIN is used, if you:

- have had an eye surgery. Your doctor will then take additional precautions.
- 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 a 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 a prolonged exposure of the transparent front part of the eye (cornea). This exposure may lead to a damaging of the surface and an inflammation (corneal ulceration).

Increased muscle tension/uncontrollable muscle stiffness in shoulder, arms or hands (spasticity of the upper limb)

XEOMIN can be used to treat increased muscle tension/uncontrollable

muscle stiffness in parts of your upper limb, e.g. your shoulder, elbow, forearm or hand. XEOMIN is effective in combination with the usual standard 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 muscle has lost its ability to stretch.

Children and adolescents

The safety and efficacy of XEOMIN for the treatment of lower and upper limb spasticity has been demonstrated in children and adolescents (age 2-17 years).

Other medicines and XEOMIN

Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines).

The effect of XEOMIN may be increased by:

- medicines to treat certain infectious diseases (spectinomycin or aminoglycoside antibiotics [e.g. neomycin, kanamycin, tobramycin])
- other medicines that relax the muscles (e.g. anaesthetic muscle relaxants). 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).

Consult your doctor, pharmacist or other healthcare professional as these medicines may interact with XEOMIN.

Pregnancy and breastfeeding:

XEOMIN must not be used during pregnancy or by mothers who are breastfeeding their babies.

If you are pregnant or breastfeeding your baby, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking XEOMIN.

Driving and using machines

You should not drive or engage in other potentially hazardous activities if drooping eyelids, weakness (asthenia), muscle weakness, dizziness, or vision disorder occur. If in doubt ask your doctor for advice.

3. How to take XEOMIN

You will not be expected to give yourself XEOMIN. It will be given to you by your doctor who is qualified to do so.

XEOMIN may only be administered by doctors with appropriate specialist knowledge of treatment with Botulinum neurotoxin type A.

The optimum dosage, frequency and number of injection sites in the treated muscle 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.

If you have the impression that the effect of XEOMIN is too strong or too weak, tell your doctor or pharmacist.

Dissolved XEOMIN is intended for injections into the muscle (intramuscular use) at various sites in your body.
Your doctor will give you the correct dose for your indicated use.

Vertical frown lines between the eyebrows (glabellar frown lines)

A reduction in the vertical lines between the eyebrows generally occurs within 2 to 3 days with the maximum effect observed on day 30, however, a comparable treatment effect can be observed from day 8 onwards. The effect lasts for up to 4 months after the injection, however, it may last longer or shorter.

Lateral periorbital lines (crow's feet lines)

A reduction in lateral periorbital lines seen at maximum smile mostly occurs within 6 days with the maximum effect observed on day 30, however, a comparable treatment effect can be observed from day 8 onwards. The effect lasts for up to 3 months after the injection, however, it may last longer or shorter. The interval between treatments should not be less than 3 months.

Horizontal forehead lines

A reduction in the horizontal forehead lines usually occurs within 7 days with the maximum effect observed on day 30, however, a comparable treatment effect can be observed from day 8 onwards. The effect lasts up to 4 months after the injection, however, it may last longer or shorter. The interval between treatments should not be less than 3 months.

Twisted neck (spasmodic torticollis)

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. The period between each treatment session should not be shorter than 6 weeks.

Eyelid spasm (blepharospasm)

Usually, the first onset of effect is observed within four days after injection. The effect of each treatment generally lasts for about 3-4 months, however, it may last significantly longer or shorter. The period between each treatment session should not be shorter than 6 weeks. The treatment can be repeated if required.

Increased muscle tension/uncontrollable muscle stiffness in shoulders, arms or hands (spasticity of the upper limb)

Patients reported the onset of action 4 days after treatment. An improvement of muscle tone was perceived within 4 weeks. In general, the treatment effect lasted 12 weeks, however, it may last significantly longer or shorter.

If you are given more XEOMIN than you require:

Symptoms of overdose are not apparent immediately after the injection and may include general weakness, drooping eyelid, double vision, breathing difficulties, speech difficulties, paralysis of the respiratory muscles or swallowing difficulties which may result in pneumonia.

Since a doctor will administer XEOMIN, he/ she will control the dosage. However, in the event of overdosage your doctor will manage the

overdosage.

In case you feel the symptoms of overdose, please seek medical emergency services immediately or ask your relatives to do so, and have yourself admitted to hospital. Medical supervision for up to several days and assisted ventilation may be necessary.

4. Possible side effects

XEOMIN can have side effects.

Not all side effects reported for **XEOMIN** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking **XEOMIN**, please consult your doctor, pharmacist or other health care provider for advice.

When treating neurological indications side effects such as excessive muscle weakness or swallowing difficulties may be caused by the relaxation of muscles distant from the injection site of XEOMIN. Swallowing difficulties can cause inhalation of foreign bodies resulting in lung inflammation and in some cases, death. Side effects such as these cannot be ruled out with the use of XEOMIN in aesthetic indications.

An allergic reaction may occur with XEOMIN. Serious immediate allergic reactions (anaphylaxis) or allergic reactions to the serum in the product (serum sickness), causing for example difficulty in breathing (dyspnoea), hives (urticaria) or swelling of the soft tissue (oedema), have been reported.

If any of the following happens, stop taking XEOMIN and tell your doctor immediately or go to the casualty department at your nearest

hospital:

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

These are very serious side effects. If you have them, you may have had a serious allergic reaction to XEOMIN. You may need urgent medical attention or hospitalisation.

Usually, side effects are observed 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 tissue (oedema), skin redness (erythema), itching, localised infection, haematoma, bleeding and/or bruising).
The injection of the needle may cause pain. This pain or the anxiety towards needles may lead to fainting, a low blood pressure, nausea or tinnitus.

Inform your doctor if you notice any of the following:

Vertical lines between the eyebrows (glabellar frown lines)

The following side effects were reported with XEOMIN:

Frequent side effects

Headache, Mephisto sign (lateral elevation of eyebrows)

Less frequent side effects

Injection site bruising, haematoma, heavy feeling of eyelid/eyebrow, drooping eyebrow, accumulation of fluid in the eyelid (eyelid oedema), itching (pruritus),

influenza like illness, tenderness, fatigue, injection site pain, muscle twitching (muscle spasms), vision blurred, drooping eyelid (eyelid ptosis), inflammation of the nose and throat (nasopharyngitis), facial asymmetry (brow asymmetry)

Lateral periorbital lines (crow's feet lines)

The following side effects were reported with XEOMIN:

Frequent side effects

Injection site haematoma, accumulation of fluid in the eyelid (eyelid oedema), dry eye

Upper facial lines

The following side effects were reported with XEOMIN:

Frequent side effects

Headache, injection site haematoma, injection site pain, injection site erythema, heavy feeling of frontal area, drooping eyelid (eyelid ptosis), dry eye, reduced sense of touch (hypoaesthesia), facial asymmetry, Mephisto sign (lateral elevation of eyebrows), nausea

Less frequent side effects

Brow ptosis

Twisted neck (spasmodic torticollis)

The following side effects were reported with XEOMIN:

Frequent side effects

Swallowing difficulties (dysphagia), dry mouth, nausea, injection site pain, weakness (asthenia), neck pain, muscular weakness, musculoskeletal pain, musculoskeletal stiffness, muscle twitching (muscle spasm), headache, feeling faint (presyncope), dizziness, upper respiratory tract infection,

sweating increased (hyperhidrosis)

Less frequent side effects

Speech disorder, voice disorder (dysphonia), shortness of breath (dyspnoea), rash

The treatment of twisted neck 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 two to three weeks after injection, but has been reported in one case to last five months. Swallowing difficulties appear to be dose-dependent.

Eyelid spasm (blepharospasm)

The following side effects were reported with XEOMIN:

Frequent side effects

Drooping eyelid (eyelid ptosis), dry eyes, headache, weakness of face muscle (facial paresis), vision blurred, visual impairment, double vision (diplopia), lacrimation increased, dry mouth, injection site pain

Less frequent side effects

Rash, swallowing difficulties (dysphagia), muscular weakness, fatigue

Increased muscle tension/uncontrollable muscle stiffness in shoulders, arms or hands (spasticity of the upper limb)

The following side effects were reported with XEOMIN:

Less frequent side effects

Swallowing difficulties (dysphagia), nausea, weakness (asthenia), pain in extremity, muscular pain (myalgia), muscular weakness, headache, reduced sense of touch (hypoaesthesia), dry mouth

Some of these side effects may be disease related.

Post-marketing experience

There have been reports of flu-like symptoms and hypersensitivity reactions, such as swelling, swelling of the soft tissue (oedema), redness, itching, rash (local and generalised), and breathlessness.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of XEOMIN.

5. How to store XEOMIN

Do not use this medicine after the expiry date which is stated on the carton and vial label after "EXP". The expiry date refers to the last day of that month.

Unopened vial: Store at or below 25 °C.

Reconstituted solution: Chemical and physical in-use stability has been demonstrated for 24 hours at 2 °C to 8 °C.

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 to 8 °C, unless reconstitution has taken place in controlled and validated aseptic conditions.

Your doctor should not use XEOMIN if the vial reconstituted according to the instructions has a cloudy appearance or contains visible particles.

For instructions on disposal, please see information for medical and healthcare professionals at the end of this leaflet.

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

6. Contents of the pack and other information

What XEOMIN contains

Each vial contains 50 or 100 units of Botulinum toxin Type A (150 kDa), free from complexing proteins.

The other ingredients are: human serum albumin and sucrose.

What XEOMIN looks like and contents of the pack

White to off-white solid.

When dissolved, XEOMIN is a clear, colourless, particle-free solution.

XEOMIN is presented in a clear vial (type 1 glass) with a grey stopper (bromobutyl rubber) and tamper-proof seal (aluminium).

50 Unit vial: The aluminium seal has a blue crimp cap and a white flip cap.

100 Unit vial: The aluminium seal has a silver coloured crimp cap and a blue flip cap.

Pack sizes of 1, 2, 3, 4 or 6 vials.

Not all pack sizes may be marketed.

Holder of the Certificate of Registration

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