Approved Professional Information for Medicines for Human Use

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 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 (see section 5.3).

Lack of interchangeability between botulinum toxin products

The potency units of XEOMIN are specific to the preparation and assay method utilised. They are not interchangeable with the 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 assessed with any other specific assay method.

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

XEOMIN 50 or 100 units powder for solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

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

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for solution for injection

White to off-white solid. When dissolved, XEOMIN is a clear, colourless, particle-free solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

XEOMIN is indicated in adults for the treatment of:

- Upper facial lines
    - Glabellar frown lines
    - Lateral periorbital lines (crow's feet)
    - Horizontal forehead lines
- Cervical dystonia (spasmodic torticollis)
- Blepharospasm
- Spasticity of the upper limb

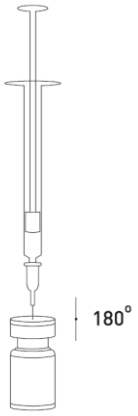
4.2 Posology and method of administration

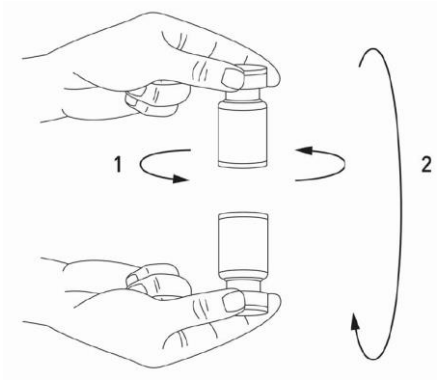
Method of administration

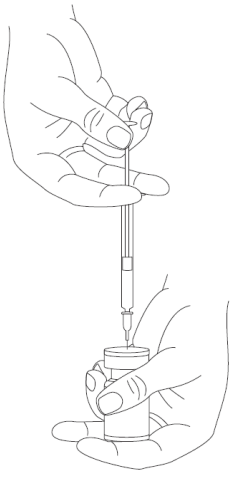
XEOMIN may only be administered by medical practitioners with suitable experience in the application of Botulinum neurotoxin type A.

XEOMIN is reconstituted prior to use with sodium chloride 9 mg/mL (0,9 %) solution for injection.

It is good practice to perform vial reconstitution and syringe preparation over plastic-lined paper towels to catch any spillage. An appropriate amount of solvent is drawn up into a syringe. A 20 - 27 G short bevel 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. The vial must be discarded 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 free of particulate matter.

XEOMIN should not be used if the reconstituted solution has a cloudy appearance or contains floccular or particulate matter.
Reconstituted XEOMIN is intended for intramuscular injection.

Aesthetic indications

Reconstituted XEOMIN is injected using a thin sterile needle (e.g. 30 - 33 gauge / 0,2 - 0,3 mm diameter / 13 mm length).

Glabellar frown lines

To reduce the risk of blepharoptosis, injections near the levator palpebrae superioris and into the cranial portion of the orbicularis oculi should be avoided. Injections into the corrugator muscle should be done in the medial portion of the muscle, and in the central portion of the muscle belly at least 1 cm above the bony edge of the eye socket.

Lateral periorbital lines (crow's feet)

Injections too close to the zygomaticus major muscle should be avoided to prevent lip ptosis.

Horizontal forehead lines

Paralyzing of lower muscle fibers by injecting XEOMIN near the orbital rim should be avoided to reduce the risk of brow ptosis.

Neurological Indications

Cervical dystonia (spasmodic torticollis)

A suitable sterile needle (e.g. 25 - 30 gauge / 0,30 – 0,50 mm diameter /

37 mm length) is used for injections into superficial muscles, and an e.g. 22 gauge / 0,70 mm diameter / 75 mm length needle may be used for injections into deeper musculature.

Blepharospasm

After reconstitution, the XEOMIN solution is injected using a suitable sterile needle (e.g. 27 - 30 gauge / 0,30 - 0,40 mm diameter / 12,5 mm length).

Spasticity of the upper limb

Reconstituted XEOMIN is injected using a suitable sterile needle (e.g. 26 gauge / 0,45 mm diameter / 37 mm length, for superficial muscles and a longer needle, e.g. 22 gauge / 0,7 mm diameter / 75 mm length, for deeper musculature).

Posology

Aesthetic indications

Possible dilutions of XEOMIN for the treatment of aesthetic indications are indicated in the following table:

Table 1: Diluent Volumes for Reconstitution of XEOMIN for the Treatment of Aesthetic Indications

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**
4 units	1,25 mL	2,5 mL
5 units	1 mL	2 mL

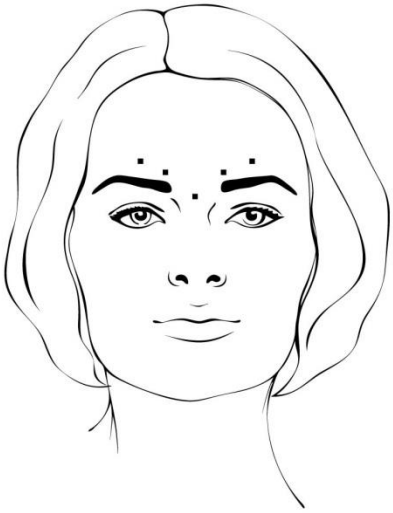
The intervals between aesthetic indications treatments should not be shorter

than 3 months.

Glabellar frown lines

Dose per injection sites: 4 units into each of the 5 injection sites: two injections in each corrugator muscle and one injection in the procerus muscle.

Total dose: 20 to 30 units may be given according to the individual needs of the patient.



Improvement in the glabellar frown lines: usually within 2 to 3 days.

Maximum effect: usually on day 30, however, a comparable treatment effect can be observed from day 8 onwards.

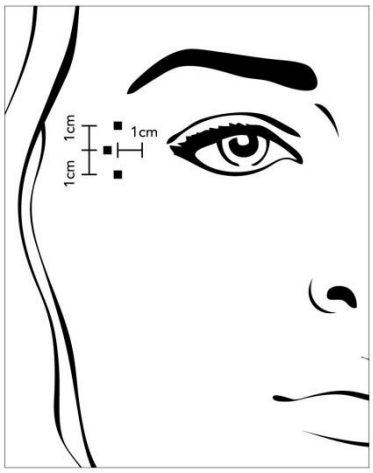
Duration of effect: up to 4 months after the injection, however, it may last longer or shorter in individual patients.

Lateral periorbital lines (crow's feet)

3-point injection scheme

Dose per injection sites: 4 units bilaterally into each of the 3 injection sites

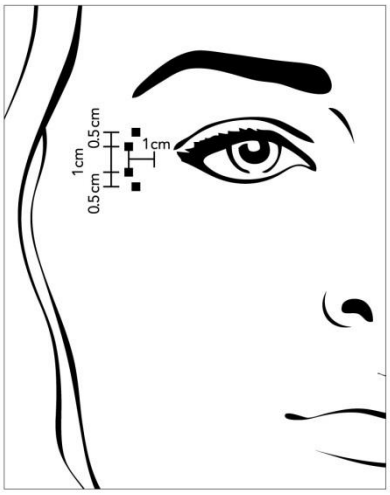
- one injection approximately 1 cm lateral from the bony orbital rim
- two injections approximately 1 cm above and below the area of the first injection.



4-point injection scheme

Dose per injection sites: 3 units bilaterally into each of the 4 injection sites

- mark the 1 cm lateral from the bony orbital rim. First two injections approximately 0,5 cm above and below this point
- two injections approximately 1 cm above and below the first marked point.



Total dose: 24 units (12 units per side) may be given.

Improvement in the lateral periorbital lines: usually within 6 days.

Maximum effect: usually on day 30, however, a comparable treatment effect can be observed from day 8 onwards.

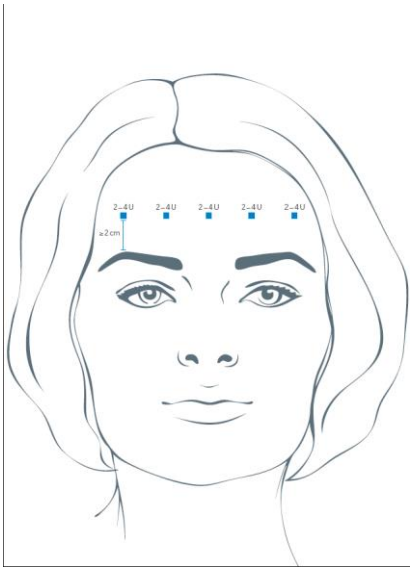
Duration of effect: up to 3 months after the injection, however, it may last longer or shorter in individual patients.

Horizontal forehead lines

Total dose: 10 to 20 units may be given according to the individual needs of the patients.

Dose per injection sites:

- 10 to 20 units into the frontalis muscle in five horizontally aligned injection sites at least 2 cm above the orbital rim
- 2 units, 3 units, or 4 units per injection point, respectively.



Improvement in the horizontal forehead lines: usually within 7 days.

Maximum effect: usually on day 30, however, a comparable treatment effect can be observed from day 8 onwards.

Duration of effect: up to 4 months after injection, however, it may last longer or shorter in individual patients.

Neurological Indications

General

The optimum dosage, frequency and number of injection sites in the treated muscle(s) should be individualised for each patient and determined by the medical practitioner.

Possible dilutions for the treatment of neurological indications are indicated in

the following table:

Table 2: Diluent Volumes for Reconstitution of XEOMIN for the Treatment of Neurological Indications

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**
40 units	0,125 mL	0,25 mL
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

Cervical dystonia (spasmodic torticollis)

Injection volume per injection site: approximately 0,1 to 0,5 mL.

Total dose: should not exceed 200 units per treatment session.

Dose: up to 300 units may be given.

No more than 50 units should be given at any single injection site.

XEOMIN is usually injected into the sternocleidomastoid, levator scapulae, splenius capitis, scalenus, and/or the trapezius muscle(s). This list is not exhaustive as any of the muscles responsible for controlling head position may require treatment.

Median time to first onset of effect: usually within seven days after injection. Duration of effect: up to 3 - 4 months, however, it may last significantly longer or shorter.

Treatment intervals should be determined based on the actual clinical need of the individual patient. Improved patient benefit may be achieved by retreating when symptoms return to a clinically significant level of discomfort and severity. Duration of action is dependent on dosing, injection technique, and other variables. Generally, the patient should be treated using the lowest effective dose at the longest clinically indicated intervals between injections.

If in individual cases the duration of effect is shorter than 12 weeks, the next injection can be given earlier, upon consideration of the risk-benefit ratio. **Injection intervals should not be shorter than 6 weeks, and one single injection given earlier than 12 weeks does not indicate a general need for regular earlier re-injection.** If an injection interval reduction is necessary, the following recommendations should be followed:

1. An objective confirmation of the necessity for an injection
2. Absence of adverse reactions to the previous injection

The dose should not be increased when the interval is reduced. In case of intervals reduction below 12 weeks, a close monitoring of adverse reaction should be performed. In a controlled clinical trial XEOMIN has been efficacious and well-tolerated when injected in intervals between 6 and 20 weeks (median: 12 weeks).

Blepharospasm

Initial dose and injection volume per injection site: 1,25 to 2,5 units (0,05 - 0,1 mL).

Dosing:

- The initial dose should not exceed 25 units per eye.
- Normally, the total dose should not exceed 100 units per treatment session.

XEOMIN is injected into the medial and lateral orbicularis oculi muscle of the upper lid and the lateral orbicularis oculi muscle of the lower lid. Additional sites in the brow area, the lateral orbicularis oculi muscle and in the upper facial area may also be injected if spasms here interfere with vision. Median time to first onset of effect: usually within four days after injection.
Duration of effect: up to 3 - 4 months, however, it may last significantly longer or shorter in individual patients.

Treatment intervals should be determined based on the actual clinical need of the individual patient. Improved patient benefit may be achieved by retreating when symptoms return to a clinically significant level of discomfort and severity. Duration of action is dependent on dosing, injection technique, and other variables. Generally, the patient should be treated using the lowest effective dose at the longest clinically indicated intervals between injections.

If in individual cases the duration of effect is shorter than 12 weeks, the next injection can be given earlier, upon consideration of the risk-benefit ratio. **Injection intervals should not be shorter than 6 weeks, and one single injection given earlier than 12 weeks does not indicate a general need for regular earlier re-injection.** If an injection interval reduction is necessary, the following recommendations should be followed:

1. An objective confirmation of the necessity for an injection

2. Absence of adverse reactions to the previous injection

The dose should not be increased when the interval is reduced. In case of intervals reduction below 12 weeks, a close monitoring of adverse reaction should be performed. In a controlled clinical trial XEOMIN has been efficacious and well-tolerated when injected in intervals between 6 and 20 weeks (median: 12 weeks).

Spasticity of the upper limb

Injection volume per injection site: approximately 0,2 to 1 mL (can be exceeded to 1,5 mL in selected cases).

The exact dosage and number of injection sites should be tailored to the individual patient based on the size, number and location of involved muscles, the severity of spasticity, and the presence of local muscle weakness.

Table 3: Standard treatment doses per muscle:

Clinical Pattern *Muscle*	**Units (Range)**	**Number of injection sites per muscle**
Flexed Wrist		
Flexor carpi radialis	25 - 100	1 - 2
Flexor carpi ulnaris	20 - 100	1 - 2
Clenched Fist		
Flexor digitorum superficialis	25 - 100	2
Flexor digitorum profundus	25 - 100	2

Flexed Elbow		
Brachioradialis	25 - 100	1 - 3
Biceps	50 - 200	1 - 4
Brachialis	25 - 100	1 - 2
Pronated Forearm		
Pronator quadratus	10 - 50	1
Pronator teres	25 - 75	1 - 2
Thumb-in-Palm		
Flexor pollicis longus	10 - 50	1
Adductor pollicis	5 - 30	1
Flexor pollicis brevis/ Opponens pollicis	5 - 30	1

This list is not exhaustive as any of the muscles of the upper limb may require treatment, e.g. shoulder.

The total recommended dose is up to 400 units per treatment session.
Median time to first onset of effect: usually within 4 days after injection.
Maximum effect: usually within 4 weeks.
Duration of effect: usually up to 12 weeks, however, it may last longer or shorter in individual patients.

Repeat treatment should generally be no more frequent than every 12 weeks. Treatment intervals should be determined based on the actual clinical need of the individual patient.

Paediatric population

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).

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients.
- Generalised disorders of muscle activity (e.g. myasthenia gravis, Lambert-Eaton syndrome).
- Infection or inflammation at the proposed injection sites.
- Pregnancy and lactation (see section 4.6)

4.4 Special warnings and precautions for use

General

Prior to administering XEOMIN the medical practitioner must familiarise himself/herself with the patient's anatomy and any alterations to the anatomy due to prior surgical procedures.

Care should be taken to ensure that XEOMIN is not injected into a blood vessel.

For the treatment of aesthetic indications: if proposed injection sites are marked with a pen, the product must not be injected through the pen marks, otherwise a permanent tattooing effect may occur.

For the treatment of cervical dystonia and spasticity of the upper limb:

XEOMIN should be injected carefully when injected at sites close to sensitive structures, such as the carotid artery, lung apices and oesophagus.

XEOMIN should be used with caution:

- if bleeding disorders of any type exist
- in patients receiving anticoagulant therapy or other substances in anticoagulant doses
- in patients with amyotrophic lateral sclerosis (ALS)

- in patients with other diseases which result in peripheral neuromuscular dysfunction
- in targeted muscles which display pronounced weakness or atrophy.

Cervical dystonia (Spasmodic torticollis)

Patients should be informed that injections of XEOMIN for the management of spasmodic torticollis may cause mild to severe dysphagia with the risk of aspiration and dyspnoea.

Medical intervention may be necessary (e.g. in the form of a gastric feeding tube).

Limiting the dose injected into the sternocleidomastoid muscle to less than 100 units may decrease the occurrence of dysphagia.

Patients with smaller neck muscle mass, or patients who require bilateral injections into the sternocleidomastoid muscles are at greater risk.

Blepharospasm

Injections near the levator palpebrae superioris should be avoided to reduce the occurrence of ptosis. Diplopia may develop as a result of Botulinum neurotoxin type A diffusion into the inferior oblique. Avoiding medial injections into the lower lid may reduce this adverse reaction.

Because of its anticholinergic effects, XEOMIN should be used with caution in patients at risk of developing narrow angle glaucoma.

Reduced blinking following injection of Botulinum neurotoxin products into the orbicularis muscle can lead to corneal exposure, persistent epithelial defect and corneal ulceration, especially in patients with cranial nerve disorders (facial nerve).

Ecchymosis easily occurs in the soft tissues of the eyelid. Immediate gentle pressure at the injection site can limit that risk.

Upper limb spasticity

New onset or recurrent seizures have been reported, typically in patients who are predisposed to experiencing these events.

Local and distant spread of toxin effect

Undesirable effects may occur from misplaced injections of Botulinum neurotoxin type A that temporarily paralyse nearby muscle groups.

There have been reports of undesirable effects that might be related to the spread of the toxin to sites distant from the injection site (see section 4.8).

Patients treated with therapeutic doses may experience excessive muscle weakness.

When treating neurological indications, some of these undesirable effects can be life threatening and there have been reports of death. Dysphagia has been reported following injection to sites other than the cervical musculature.

Patients or caregivers should be advised to seek immediate medical care if swallowing, speech or respiratory disorders occur.

Pre-existing Neuromuscular Disorders

Patients with neuromuscular disorders may be at increased risk of excessive muscle weakness. The Botulinum neurotoxin type A product should be used under specialist supervision in these patients and should only be used if the benefit of treatment is considered to outweigh the risk.

Patients with a history of dysphagia and aspiration should be treated with extreme caution when treated for neurological indications.

The treatment for aesthetic indications with XEOMIN is not recommended for patients with a history of dysphagia and aspiration.

Hypersensitivity Reactions

Hypersensitivity reactions have been reported with Botulinum neurotoxin

products. If serious (e.g. anaphylactic reactions) and/or immediate hypersensitivity reactions occur, appropriate medical therapy should be instituted.

Antibody Formation

There is a potential for immunogenicity. Too frequent doses may increase the risk of antibody formation, which can result in treatment failure even if the product is being used to treat other indications.

4.5 Interaction with other medicines and other forms of interaction

Co-administration of XEOMIN and aminoglycoside antibiotics or other medicines interfering with neuromuscular transmission, e.g. anaesthetic muscle relaxant medicines, should only be performed with caution as these medicines may potentiate the effect of the toxin.

4.6 Fertility, pregnancy and lactation

Pregnancy

XEOMIN is contraindicated during pregnancy (see section 4.3).

Studies in animals have shown reproductive toxicity.

Lactation

The use of XEOMIN is contraindicated in mothers who are breastfeeding their infants.

Fertility

There are no clinical data from the use of Botulinum neurotoxin type A. No adverse effects on male or female fertility were detected in rabbits.

4.7 Effects on ability to drive and use machines

Patients should be counselled that if asthenia, muscle weakness, vision

disorders, dizziness or drooping eyelids occur, they should avoid driving or engaging in other potentially hazardous activities.

4.8 Undesirable effects

Adverse events may take several days to become manifest. Usually, undesirable effects are observed within the first week after treatment.

Undesirable effects independent from indication

Application related undesirable effects

Localised pain, inflammation, paraesthesia, hypoaesthesia, tenderness, swelling/ oedema, erythema, itching, localised infection, haematoma, bleeding and/or bruising may be associated with the injection.
Needle related pain and/or anxiety may result in vasovagal responses, including transient symptomatic hypotension, nausea, tinnitus and syncope.

Undesirable effects of the substance class Botulinum toxin type A

Localised muscle weakness is one expected pharmacological effect of Botulinum neurotoxin type A.

Toxin spread

When treating neurological indications, side effects related to spread of toxin distant from the site of administration have been reported to produce symptoms consistent with Botulinum toxin effects (excessive muscle weakness, dysphagia, and aspiration pneumonitis with fatal outcome in some cases).

Hypersensitivity reactions

Serious and/or immediate hypersensitivity reactions including anaphylaxis, serum sickness, urticaria, soft tissue oedema, and dyspnoea have been

reported following the use of Botulinum toxin type A medicines.

Post-Marketing Experience

Flu-like symptoms and hypersensitivity reactions like swelling, oedema (also apart from injection site), erythema, pruritus, rash (local and generalized) and dyspnoea have been reported.

Undesirable effects dependent on indication

Based on clinical experience information on the frequency of adverse reactions for the individual indications is given below. The frequency categories are defined as follows:

very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); unknown (cannot be estimated from the available data).

Glabellar frown lines

Table 4: Adverse reactions based on clinical experience with glabellar frown lines

Body System	Adverse Reaction	
Infections and infestations:	Uncommon:	nasopharyngitis
Nervous system disorders:	Common:	headache
Eye disorders:	Uncommon:	eyelid oedema, vision blurred, eyelid ptosis
Vascular disorders:	Uncommon:	haematoma
Skin and subcutaneous tissue disorders:	Uncommon:	pruritus, brow ptosis

Musculoskeletal and connective tissue disorders:	Common:	Mephisto sign (lateral elevation of eyebrow)
	Uncommon:	facial asymmetry (brow asymmetry), muscle spasms (above eyebrows)
General disorders and administration site conditions:	Uncommon:	injection site bruising, influenza like illness, (local) tenderness, fatigue, injection site pain, discomfort (heavy feeling of eyelid/eyebrow)

Lateral periorbital lines (crow's feet)

Table 5: Adverse reactions based on clinical experience with crow's feet

Body System	Adverse Reaction	
Eye disorders:	Common:	eyelid oedema, dry eye
General disorders and administration site conditions:	Common:	injection site haematoma

Upper facial lines

Table 6: Adverse reactions based on clinical experience with upper facial lines

Body System	Adverse Reaction	
Nervous system disorders:	Very common:	headache
	Common:	hypoaesthesia
Eye disorders:	Common:	eyelid ptosis, dry eye
Gastrointestinal	Common:	nausea

disorders:		
Skin and subcutaneous tissue disorders	Uncommon:	brow ptosis
Musculoskeletal and connective tissue disorders:	Common:	facial asymmetry, Mephisto sign (lateral elevation of eyebrows)
General disorders and administration site conditions:	Common:	injection site haematoma, injection site pain, injection site erythema, discomfort (heavy feeling of frontal area)

Cervical dystonia (Spasmodic torticollis)

The management of spasmodic torticollis may cause dysphagia with varying degrees of severity with the potential for aspiration which may require medical intervention. Dysphagia may persist for two to three weeks after injection, but has been reported in one case to last five months. Dysphagia appears to be dose-dependent.

Table 7: Adverse reactions based on clinical experience with cervical dystonia

Body System	Adverse Reaction	
Infections and infestations:	Common:	upper respiratory tract infection
Nervous system disorders:	Common:	headache, presyncope, dizziness

	Uncommon:	speech disorder
Respiratory thoracic and mediastinal disorders:	Uncommon:	dysphonia, dyspnoea
Gastrointestinal disorders:	Very common:	dysphagia
	Common:	dry mouth, nausea
Skin and subcutaneous tissue disorders:	Common:	hyperhidrosis
	Uncommon:	rash
Musculoskeletal and connective tissue disorders:	Common:	neck pain, muscular weakness, myalgia, musculoskeletal stiffness, muscle spasms
General disorders and administration site conditions:	Common:	injection site pain, asthenia

Blepharospasm

Table 8: Adverse reactions based on clinical experience with blepharospasm

Body System	Adverse Reaction	
Nervous system disorders:	Common:	headache, facial paresis
Eye disorders:	Very common:	eyelid ptosis
	Common:	dry eyes, vision blurred, visual impairment, diplopia, lacrimation increased

Gastrointestinal disorders:	Common:	dry mouth
	Uncommon:	dysphagia
Skin and subcutaneous tissue disorders:	Uncommon:	rash
Musculoskeletal and connective tissue disorders:	Uncommon:	muscular weakness
General disorders and administration site conditions:	Common:	injection site pain
	Uncommon:	fatigue

Upper limb spasticity

Table 9: Adverse reactions based on clinical experience with upper limb spasticity

Body System	Adverse Reaction	
Nervous system disorders:	Uncommon:	headache, hypoaesthesia
Gastrointestinal disorders:	Uncommon:	dry mouth, nausea
Musculoskeletal and connective tissue disorders:	Uncommon:	muscular weakness, pain in extremity, myalgia
General disorders and administration site conditions:	Uncommon:	asthenia

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the

medicine. Healthcare professionals are asked to report any suspected adverse reactions 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

4.9 Overdose

Symptoms

Increased doses of Botulinum neurotoxin type A may result in pronounced neuromuscular paralysis distant from the injection site with a variety of symptoms. Symptoms may include general weakness, ptosis, diplopia, breathing difficulties, speech difficulties, paralysis of the respiratory muscles or swallowing difficulties which may result in aspiration pneumonia. Symptoms of overdose are not immediately apparent post-injection.

Management

In the event of overdose the patient should be medically monitored for symptoms of excessive muscle weakness or muscle paralysis. Supportive and symptomatic treatment may be necessary. Respiratory support may be required if paralysis of the respiratory muscles occurs.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological Classification/ Category and Class: A 30.5 Biologicals-Other.

Pharmacotherapeutic group: other muscle relaxants, peripherally acting agents

ATC code: M03AX01

Botulinum neurotoxin type A blocks cholinergic transmission at the neuromuscular junction by inhibiting the release of acetylcholine from peripheral cholinergic nerve terminals.

Complete recovery of endplate function/impulse transmission after intramuscular injection normally occurs within 3 - 4 months as nerve terminals sprout and reconnect with the motor endplate and the presynaptic neurotransmitter release mechanism becomes functional again.

5.2 Pharmacokinetic properties

Human pharmacokinetic studies and distribution studies cannot be conducted with Botulinum neurotoxin type A because the active substance is applied in very small quantities (picograms per injection) and because it binds rapidly and irreversibly to cholinergic nerve terminals.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Human serum albumin

Sucrose

6.2 Incompatibilities

XEOMIN must not be mixed with other medicines except those mentioned in section 6.6.

6.3 Shelf life

Unopened vial

3 years

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.

6.4 Special precautions for storage

Unopened vial

Store at or below 25 °C.

For storage conditions of the reconstituted XEOMIN, see section 6.3.

6.5 Nature and contents of container

Clear vial (type 1 glass) with a grey stopper (bromobutyl rubber) and a 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.

6.6 Special precautions for disposal and other handling

Procedure to follow for a safe disposal of vials, syringes and materials used

Any unused vials or remaining XEOMIN solution in the vial and/or syringe should be autoclaved or inactivated by adding one of the following solutions:

70 % ethanol, 50 % isopropanol, 0,1 % SDS (anionic detergent), sodium

hydroxide solution (0,1 N NaOH) or sodium hypochlorite solution (at least 0,1 % NaOCl).

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

Recommendations should any incident occur during the handling of Botulinum neurotoxin type A

- Any spills of the product must be wiped up: either using absorbent material impregnated with any of the above listed 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 listed 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.

7. HOLDER OF CERTIFICATE OF REGISTRATION

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8. REGISTRATION NUMBERS

XEOMIN 50 units powder for solution for injection: 53/30.5/0223

XEOMIN 100 units powder for solution for injection: 53/30.5/0224

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

21 January 2021

10. DATE OF REVISION OF THE TEXT