

Xeomin® (Clostridium Botulinum neurotoxin type A (150 kD), free from complexing proteins) 50/100/200 unit vials. Prescribing Information: M-XEO-UKI-0471. Please refer to the Summary of Product Characteristics (SmPC) before prescribing. **Presentation:** 50/100/200 units (U) of Clostridium Botulinum Neurotoxin type A as a powder for solution for injection. **Indications:** Treatment of blepharospasm, cervical dystonia of a predominantly rotational form (spasmodic torticollis), spasticity of the upper limb, and chronic sialorrhea due to neurological disorders in adults. **Dosage and Administration:** For intramuscular and intraglandular injection. Due to unit differences in the potency assay, unit doses for Xeomin are not interchangeable with those for other preparations of Botulinum toxin type A. Reconstitute with 0.9% sodium chloride. Xeomin may only be administered by physicians with suitable qualifications and the requisite experience in the application of Botulinum toxin type A. **Blepharospasm:** The initial recommended dose is 1.25-2.5 U per injection site, injected into the medial and lateral orbicularis oculi of the upper lid and the lateral orbicularis oculi of the lower lid. The initial dose should not exceed 25 U per eye but this can be subsequently increased. The total dose should not exceed 100 U every 12 weeks. Treatment intervals should be determined based on the actual clinical need of the individual patient. 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. **Spasmodic torticollis:** Xeomin is usually injected into the sternocleidomastoid, levator scapulae, scalenus, splenius capitis and/or the trapezius muscle(s) or any of the muscles responsible for controlling head position that may be involved. No more than 200 U should be injected for the first course of therapy. Adjustments can be made in subsequent courses depending on the response, but not exceeding a total dose of 300 U at any one treatment session. No more than 50 U should be administered at any one injection site. Treatment intervals of less than 10 weeks are not recommended. Treatment intervals should be determined based on the actual clinical need of the individual patient. **Spasticity of the upper limb:** The dose and number of injection sites should be tailored to the individual patient based on the size, number and location of muscles involved, the severity of spasticity, and the presence of local muscle weakness. The maximum total dose for the treatment of upper limb spasticity should not exceed 500 U per treatment session, and no more than 250 U should be administered to the shoulder muscles. Repeated 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. **Chronic sialorrhea:** A reconstituted solution at a concentration of 5 units/0.1 ml should be used. Inject into the parotid and submandibular glands on both sides (per treatment four injections in total).

The dose is divided with a ratio of 3:2 between the parotid and submandibular glands as follows: Parotid glands 30 U per side, Submandibular glands 20 U per side. Inject close to the centre of the gland. The recommended dose per treatment session is 100 U. Do not exceed this maximum dose. Treatment intervals should be determined based on the actual clinical need of the individual patient. Repeat treatment more frequent than every 16 weeks is not recommended. **Contraindications:** Known hypersensitivity to Botulinum neurotoxin type A or to any of the excipients, generalised disorders of muscle activity (e.g. myasthenia gravis, Lambert-Eaton syndrome) and presence of infection or inflammation at the proposed injection site. **Special warnings and precautions:** Care should be taken not to inject into blood vessels. Use with caution in patients with any bleeding disorder or receiving anticoagulant therapy or other substances that could have an anticoagulant effect. Caution in patients with pre-existing neuromuscular disorders such as patients suffering from amyotrophic lateral sclerosis, other diseases which result in peripheral neuromuscular dysfunction or where the targeted muscles display pronounced weakness or atrophy. Generally, patients with a history of aspiration or dysphagia should be treated with caution. Extreme caution should be exercised when treating these patients for cervical dystonia. Spread of Botulinum toxin type A to sites distant from the injection site has been reported. Some of these can be life threatening and there have been reports of death, some associated with dysphagia, pneumonia and/or significant debility. Patients or caregivers should be advised to seek immediate medical care if swallowing, speech or respiratory disorders arise. If serious (e.g. anaphylactic reactions) and/or immediate hypersensitivity reactions occur, appropriate medical therapy should be instituted. Too frequent doses may increase the risk of antibody formation, and possible treatment failure. Should not be used during pregnancy unless clearly necessary and the potential benefit justifies the risk. Should not be used during breast-feeding. **Blepharospasm:** Injections near the levator palpebrae superioris should be avoided to reduce the occurrence of ptosis. In order to prevent ectropion, injections into the lower lid area should be avoided, and vigorous treatment of any epithelial defect is necessary. Careful testing of corneal sensation should be performed in patients with previous eye operations. Due to its anticholinergic effects, it should be used with caution in patients at risk of developing narrow angle glaucoma. **Spasmodic torticollis:** Xeomin should be injected carefully when injecting at sites close to sensitive structures such as the carotid artery lung apices and oesophagus. 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. Limiting the dose injected into the

sternocleidomastoid muscle to less than 100 U 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.

Spasticity of the upper limb: Xeomin should be injected carefully when injecting at sites close to sensitive structures such as the carotid artery lung apices and oesophagus. Xeomin is not likely to be effective in improving range of motion at a joint affected by a fixed contracture. New onset or recurrent seizures have been reported, typically in patients who are predisposed to experiencing these events.

Chronic sialorrhea: In cases of medication-induced sialorrhea, the possibility of replacement, reduction, or even termination of the inducing medication should be considered before using Xeomin. Efficacy and safety of Xeomin in patients with medication-induced sialorrhea were not investigated. If “dry mouth” develops in association with the administration of Xeomin consider reducing the dose. A dental visit at the beginning of treatment is recommended. The dentist should be informed about sialorrhea treatment with Xeomin to be able to decide about appropriate measures for caries prophylaxis.

Interactions: No interaction studies have been performed. Concomitant use with aminoglycosides or spectinomycin requires special care. Peripheral muscle relaxants should be used with caution. 4-Aminoquinolines may reduce the effect. When used for the treatment of chronic sialorrhea, irradiation to the head and neck including salivary glands and/or co-administration of anticholinergics may increase the effect of the toxin. The treatment of sialorrhea with Xeomin during radiotherapy is not recommended.

Undesirable effects: Usually, undesirable effects are observed within the first week after treatment and are temporary in nature. Undesirable effects independent of indication include; application related undesirable effects (localised pain, inflammation, paraesthesia, hypoaesthesia, tenderness, swelling, oedema, erythema, itching, localised infection, haematoma, bleeding and/or bruising associated with injection), class related undesirable effects (localised muscle weakness), toxin spread (very rare - excessive muscle weakness, dysphagia and aspiration pneumonia with a fatal outcome in some cases), and hypersensitivity reactions (serious and/or immediate hypersensitivity reactions including anaphylaxis, serum sickness, urticaria, soft tissue oedema and dyspnoea). Needle related pain and/or anxiety may result in vasovagal responses. Management of spasmodic torticollis may cause dysphagia with varying degrees of severity. **Blepharospasm:** *Very Common:* Eyelid Ptosis, dry eyes. *Common:* Headache, facial paresis, blurred vision, visual impairment, diplopia, increased lacrimation, dry mouth, dysphagia, injection site pain, fatigue, muscular weakness. *Uncommon:* Rash. **Spasmodic torticollis:** *Very common:* Dysphagia. *Common:* Headache, presyncope, dizziness, dry mouth, nausea,

hyperhidrosis, neck pain, muscular weakness, myalgia, muscle spasms, musculoskeletal stiffness, injection site pain, asthenia, upper respiratory tract infection. *Uncommon:* Speech disorder, dysphonia, dyspnoea, rash.

Spasticity of the upper limb: *Common:* Dry mouth. *Uncommon:* Headache, hypoaesthesia, dysphagia, nausea, muscular weakness, pain in extremity, myalgia, asthenia.

Unknown: injection site pain. **Chronic sialorrhea:** *Common:* Paraesthesia, dry mouth, dysphagia. *Uncommon:* Speech disorder, gastrointestinal disorders, altered (thickened) saliva, dysgeusia. Cases of persistent dry mouth (> 110 days) of severe intensity have been reported, which could cause further complications as gingivitis, dysphagia and caries. **Post Marketing Experience:** Flu-like symptoms and hypersensitivity reactions have also been reported.

Overdose: May result in pronounced neuromuscular paralysis distant from the injection site. **Legal Category:** POM. **List Price:** 50U/vial £72.00/€110.00, 100U/vial £129.90/€195.00, 200U/Vial £259.80/€390.00. **Product Licence Number:** PL 29978/0003, PL 29978/0001, PL 29978/0004; PA1907/001/001, PA1907/001/002, PA 1907/001/003. **Marketing Authorisation Holder** Merz Pharmaceuticals GmbH, Eckenheimer Landstraße 100, 60318 Frankfurt/Main, Germany. **Date of Preparation:** June 2019. **Additional Information Available in the SmPC or on request from:** Merz Pharma UK Ltd., 260 Centennial Park, Elstree Hill South, Elstree, Hertfordshire WD6 3SR. Tel: +44 (0) 333 200 4141.

Adverse events should be reported. Reporting forms and information for United Kingdom can be found at www.mhra.gov.uk/yellowcard. Reporting forms and information for Republic of Ireland can be found at <https://www.hpra.ie/homepage/about-us/report-an-issue/human-adverse-reaction-form>. Adverse events should also be reported to Merz Pharma UK Ltd at the address above or by email to UKdrugsafety@merz.com or on +44 (0) 333 200 4143.