BOTOX (botulinum toxin type A) Glabellar and Crow's Feet Lines Abbreviated Prescribing Information

Presentation: Botulinum toxin type A (from clostridium botulinum), 50 or 100 or 200 Allergan Units/vial.

Indications: Temporary improvement in the appearance of moderate to severe vertical lines between the eyebrows seen at maximum frown (glabellar lines); moderate to severe lateral canthal lines (crow's feet lines) seen at maximum smile; moderate to severe crow's feet lines seen at maximum smile and glabellar lines seen at maximum frown when treated simultaneously in adults, when the severity of these lines has an important psychological impact for the patient.

Dosage and Administration: See Summary of Product Characteristics for full information. Do not inject into blood vessels. Botulinum toxin units are not interchangeable from one product to another. Not recommended for patients <18 years. The recommended injection volume per muscle site is 0.1 ml (4 Units). *Glabellar Lines:* Five injection sites: 2 in each corrugator muscle and 1 in the procerus muscle: total dose 20 Units. *Crow's Feet Lines:* Six injection sites: 3 in each lateral orbicularis oculi muscle: total dose 24 Units. In the event of treatment failure or diminished effect following repeat injections alternative treatment methods should be employed.

Contraindications: Known hypersensitivity to any constituent. Infection at proposed injection site(s).

Warnings/Precautions: Use not recommended in women who are pregnant, breast-feeding and/or women of childbearing potential not using contraception. The recommended dosages and frequencies of administration of BOTOX should not be exceeded due to the potential for overdose, exaggerated muscle weakness, distant spread of toxin and the formation of neutralising antibodies. Initial dosing in treatment naïve patients should begin with the lowest recommended dose for the specific indication. Prescribers and patients should be aware that side effects can occur despite previous injections being well tolerated. Caution should be exercised on the occasion of each administration. There are reports of side effects related to spread of toxin distant from injection site, sometimes resulting in death. BOTOX should only be used with extreme caution and under close supervision in patients with subclinical or clinical evidence of defective neuromuscular transmission and in patients with underlying neurological disorders. Caution in patients with underlying neurological disorder and history of dysphagia and aspiration. Patients should seek medical help if swallowing, speech or respiratory disorders arise. Previously sedentary patients should resume activities gradually. Relevant anatomy and changes due to prior surgical procedures must be understood prior to administration and injection into vulnerable anatomic structures must be avoided. Pneumothorax associated with injection procedure has been reported. Caution is warranted when injecting in proximity to the lung, particularly the apices or other vulnerable structures. Serious adverse events including fatal outcomes have been reported in patients who had received off-label injections directly into salivary glands, the oro-lingual-pharyngeal region, oesophagus and stomach. If serious and/or immediate hypersensitivity reactions occur (in rare cases), injection of toxin should be discontinued and appropriate medical therapy, such as epinephrine, immediately instituted. Procedure related injury could occur. Caution in the presence of inflammation at injection site(s), ptosis or when excessive weakness/atrophy is present in target muscle. Reports of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. New onset or recurrent seizure occurred rarely in predisposed patients, however relationship to botulinum toxin has not been established. Clinical fluctuations may occur during repeated use. Too frequent or excessive dosing can lead to antibody formation and treatment resistance. It is mandatory that BOTOX is used for one single patient treatment only during a single session. May cause asthenia, muscle weakness, somnolence, dizziness and visual disturbance which could affect driving and operation of machinery.

Interactions: Theoretically, the effect may be potentiated by aminoglycoside antibiotics or other drugs that interfere with neuromuscular transmission.

Adverse Effects: See Summary of Product Characteristics for full information on side effects. Based on controlled clinical trial data, the proportion of patients treated for glabellar lines that would be expected to experience an adverse reaction after treatment is 23% (placebo 19%). In pivotal controlled clinical trials for crow's feet lines, such events were reported in 8% (24 Units for crow's feet lines alone) and 6% (44 Units: 24 Units for crow's feet lines administered simultaneously with 20 Units for glabellar lines) of patients compared to 5% for placebo. Adverse reactions may be related to treatment, injection technique or both. In general, adverse reactions occur within the first few days following injection and are transient, but rarely persist for several months or longer. Local muscle weakness represents the expected pharmacological action. Localised pain, tenderness and/or bruising may be associated with the injection. Fever and flu syndrome have been reported.

Frequency by Indication: Defined as follows*:* Common (≥1/100 to <1/10), Uncommon (≥1/1,000 to <1/100).

Glabellar Lines (20 Units):

- *Infections and infestations.* Uncommon: Infection.
- *Psychiatric disorders.* Uncommon: Anxiety.
- *Nervous system disorders.* Common: Headache. Uncommon: Paraesthesia, dizziness.
- *Eye disorders.* Common: Eyelid ptosis. Uncommon: Blepharitis, eye pain, visual disturbance.
- *Gastrointestinal disorders.* Uncommon: Nausea, oral dryness.
- *Skin and subcutaneous tissue disorders.* Common: Erythema. Uncommon: Skin tightness, oedema (face, eyelid, periorbital), photosensitivity reaction, pruritus, dry skin.
- *Musculoskeletal and connective tissue disorders.* Common: Localised muscle weakness. Uncommon: Muscle twitching.
- *General disorders and administration site conditions.* Common: Face pain. Uncommon: Flu syndrome, asthenia, fever.

Crow's Feet Lines (24 Units):

- *Eye disorders.* Common: Eyelid oedema
- *General disorders and administration site conditions.* Common: Injection site haemorrhage*, injection site haematoma*. Uncommon: Injection site pain*, injection site paraesthesia (*procedure-related adverse reactions).

Crow's Feet Lines and Glabellar Lines (44 Units):

- *General disorders and administration site conditions.* Common: Injection site haematoma*. Uncommon: Injection site haemorrhage, injection site pain*(*procedure-related adverse reactions).

The following adverse events have been reported since the drug has been marketed for glabellar lines, crow's feet lines and other indications:

- *Cardiac disorders:* Arrhythmia, myocardial infarction.
- Ear and labyrinth disorders: Hypoacusis, tinnitus, vertigo.
- *Eye disorders:* Angle-closure glaucoma (for treatment of blepharospasm), strabismus, blurred vision visual disturbance, lagopthalmos.
- *Gastrointestinal disorders:* Abdominal pain, diarrhoea, constipation, dry mouth, dysphagia, nausea, vomiting.
- *General disorders and administration site conditions:* Denervation atrophy, malaise, pyrexia.
- *Immune system disorders:* Anaphylaxis, angioedema, serum sickness, urticaria.
- *Metabolism and nutrition disorders:* Anorexia.
- *Muscoskeletal and connective tissue disorders:* Muscle atrophy, myalgia.
- *Nervous system disorders:* Bronchial plexopathy, dysphonia, dysarthria, facial paresis, hypoaesthesia, muscle weakness, myasthenia gravis, peripheral neuropathy, paraesthesia, radiculopathy, seizures, syncope, facial palsy.
- *Respiratory, thoracic and mediastinal disorders:* Aspiration pneumonia (some with fatal outcome), dyspnea, respiratory depression, respiratory failure.
- *Skin and subcutaneous tissue disorders:* Alopecia, dermatitis psoriasiform, erythema multiforme, hyperhidrosis, madarosis, pruritus, rash.

NHS Price: 50 Units: £77.50, 100 Units: £138.20, 200 Units £276.40. **Marketing Authorization Number:** 50 Units: 426/0118, 100 Units: 426/0074, 200 Units 426/0119. **Marketing Authorization Holder:** Allergan Ltd, Marlow International, The Parkway, Marlow, Bucks, SL7 1YL, UK. **Legal Category:** POM. **Date of preparation:** June 2015.

Further information is available from: Allergan Limited, Marlow International, The Parkway, Marlow, Bucks SL7 1YL