BOTOX® (botulinum toxin type A) Forehead lines, 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) and /or; moderate to severe lateral canthal lines (crow's feet lines) seen at maximum smile and/or; moderate to severe forehead lines at maximum eyebrow elevation when the severity of the facial lines has an important psychological impact in adult patients.

DOSAGE and ADMINISTRATION: See Summary of Product Characteristics for full information on dosing and administration. Do not inject into blood vessels. Botulinum toxin units are not interchangeable from one product to another. BOTOX must only be reconstituted with sterile sodium chloride 9 mg/ml (0.9%) solution for injection. Doses recommended in Allergan Units are different from other botulinum toxin preparations. BOTOX should only be administered by an appropriately qualified healthcare practitioner with expertise in the treatment of the relevant indication and the use of the required equipment, in accordance with national guidelines. This product is for single use only and any unused solution should be discarded. The most appropriate vial size should be selected for the indication. Not recommended for patients <18 years. The recommended needle: Sterile 30 gauge needle. *Glabellar lines seen at maximum frown*: Recommended dose is 0.1ml (4 units) administered in each of the 5 injection sites (2 injections in each corrugator muscle and 1 injection in the procerus muscle for a total dose of 20 Units). In order to reduce the risk of eyelid ptosis, the maximum dose of 4 Units for each injection site as well as the number of injection sites should not be exceeded. *Crow's feet lines seen at maximum smile*: A volume of 0.1 ml (4 Units) is administered in each of the 3 injection sites per side (total of 6 injection sites) in the lateral orbicularis oculi muscle, for a total dose of 24 Units in a total volume of 0.6 ml (12 Units per side). For simultaneous treatment with glabellar lines seen at maximum frown, the dose is 24 Units for crow's feet lines seen at maximum smile and 20 Units for glabellar lines (see Administration guidance for glabellar lines) for a total dose of 44 Units in a total volume of 1.1 ml. In order to reduce the risk of eyelid ptosis, the maximum dose of 4 Units for each injection site as well as the number of injection sites should not be exceeded. *Forehead Lines seen at maximum eyebrow elevation*: A volume of 0.1 ml (4 Units) is administered in each of the 5 injection sites in the frontalis muscle, for a total dose of 20 Units in a total volume of 0.5 ml. The total dose for treatment of forehead lines (20 Units) in conjunction with glabellar lines (20 Units) is 40 Units/1.0 mL. For simultaneous treatment with glabellar lines and crow's feet lines, the total dose is 64 Units, comprised of 20 Units for forehead lines, 20 Units for glabellar lines and 24 Units for crow's feet lines. When treating adult patients for multiple indications, the maximum cumulative dose should not exceed 400 Units in a 12-week interval.

CONTRAINDICATIONS: Known hypersensitivity to botulinum toxin type A or to any of the excipients. Presence of infection at the proposed injection site(s).

SPECIAL WARNINGS AND PRECAUTIONS : 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. There are reports of side effects related to spread of toxin distant from injection site, sometimes resulting in death. The risk of symptoms is probably greatest in patients who have underlying conditions and comorbidities that would predispose them to these symptoms. Patients treated with therapeutic doses may also experience exaggerated muscle weakness. Elderly and debilitated patients should be treated with caution. Consideration should be given to the risk-benefit implications for the individual patient before embarking on treatment with BOTOX. BOTOX should only be used with extreme caution and under close supervision in patients with subclinical or clinical evidence of defective neuromuscular transmission e.g. myasthenia gravis or Lambert-Eaton Syndrome in patients with peripheral motor neuropathic diseases (e.g. amyotrophic lateral sclerosis or motor neuropathy) and in patients with underlying neurological disorders. Such patients may have an increased sensitivity to agents such as BOTOX, even at therapeutic doses, which may result in excessive muscle weakness and an increased risk of clinically significant systemic effects including severe dysphagia and respiratory compromise. The botulinum toxin 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. Patients or caregivers should be advised to seek immediate medical care if swallowing, speech or respiratory disorders arise. As with any treatment with the potential to allow previously-sedentary patients to resume activities, the sedentary patient should be cautioned to resume activity gradually. The relevant anatomy, and any alterations to the anatomy due to prior surgical procedures, must be understood prior to administering BOTOX and injection into vulnerable anatomic structures must be avoided. Pneumothorax associated with injection procedure has been reported following the administration of BOTOX near the thorax. Caution is warranted when injecting in proximity to the lung (particularly the apices) or other vulnerable anatomic structures. Serious adverse events including fatal outcomes have been reported in patients who had received off-label injections of BOTOX directly into salivary glands, the oro-lingual-pharyngeal region, oesophagus and stomach. Some patients had pre-existing dysphagia or significant debility. If such a reaction occurs further injection of BOTOX should be discontinued and appropriate medical therapy, such as epinephrine, immediately instituted. Caution should be used when BOTOX is used in the presence of inflammation at the proposed injection site(s) or when excessive weakness or atrophy is present in the target muscle. There have been reports of adverse events following administration of BOTOX involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. New onset or recurrent seizures have been reported, typically in patients who are predisposed to experiencing these events. The exact relationship of these events to botulinum toxin injection has not been established. Formation of neutralising antibodies to botulinum toxin type A may reduce the effectiveness of BOTOX treatment by inactivating the biological activity of the toxin. Clinical fluctuations during the repeated use of BOTOX (as with all botulinum toxins) may be a result of different vial reconstitution procedures, injection intervals, muscles injected and slightly differing potency values given by the biological test method used.

PREGNANCY AND LACTATION: Pregnancy: BOTOX is not recommended during pregnancy and in women of childbearing potential not using contraception. Breast-feeding: There is no information on whether BOTOX is excreted in human milk. The use of BOTOX during breast-feeding cannot be recommended. Fertility: There are no adequate data on the effects on fertility from the use of botulinum toxin type A in women of childbearing potential. Studies in male and female rats have shown fertility reductions.

DRIVING: No studies on the effects on the ability to drive and use machines have been performed. Botox may cause asthenia, muscle weakness, somnolence, dizziness and visual disturbance which could affect driving and operation of machinery.

INTERACTIONS: Theoretically, the effect of botulinum toxin may be potentiated by aminoglycoside antibiotics or spectinomycin, or other medicinal products that interfere with neuromuscular transmission.

ADVERSE REACTIONS: See Summary of Product Characteristics for full list of adverse events. In controlled clinical trials for glabellar lines seen at maximum frown, adverse events considered by the investigators to be related to BOTOX were reported in 23% (placebo 19%) of patients. In treatment cycle 1 of the pivotal controlled clinical trials for crow's feet lines seen at maximum smile, such events were reported in 8% and 6% of patients compared to 5% for placebo. In treatment cycle 1 of clinical trials for forehead lines seen at maximum eyebrow elevation, adverse events considered by the investigators to be related to BOTOX were reported in 20.6% of patients treated with 40 Units and 14.3% of patients treated with 64 Units, compared to 8.9% of patients that received 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, while generally transient, may have a duration of several months or, in rare cases, longer. Local muscle weakness represents the expected pharmacological action of botulinum toxin in muscle tissue. However, weakness of adjacent muscles and/or muscles remote from the site of injection has been reported. As is expected for any injection procedure, localised pain, inflammation, paraesthesia, hypoaesthesia, tenderness, swelling/oedema, erythema, localised infection, bleeding and/or bruising have been associated with the injection. Needle-related pain and/or anxiety have resulted in vasovagal responses, including transient symptomatic hypotension and syncope. Fever and flu syndrome have also been reported after injections of botulinum toxin. Adverse reactions reported in the clinical trials is defined as follows: Common (≥1/100 to <1/10) Glabellar lines: *Nervous system disorders (common)*: Headache. *Eye disorders (common):* Eyelid ptosis. *Skin and subcutaneous tissue disorders (common)*: Erythema. *Musculoskeletal and connective tissue disorders (common)*: Localised muscle weakness. *General disorders and administration site conditions (common)*: Face Pain. Crow's Feet Lines with or without Glabellar Lines: *General disorders and administration site conditions (common)*: Injection site haematoma (procedure-related adverse event). Forehead Lines and Glabellar Lines with or without Crow's Feet Lines: *Nervous system disorders (common)*: Headache. *Eye disorders (common):* Eyelid ptosis (The median time to onset of eyelid ptosis was 9 days following treatment). *Skin and subcutaneous tissue disorders (common):* Skin tightness, brow ptosis (The median time to onset of brow ptosis was 5 days following treatment). *Musculoskeletal and connective tissue disorders (common)*: Mephisto sign. *General disorders and administration site conditions (common)*: Injection site bruising, injection site hematoma (procedure-related adverse events).

NHS Price: 50 Units: £77.50, 100 Units: £138.20, 200 Units £276.40. **Marketing Authorization Number:** 50 Units: PL 41042/0059, 100 Units: PL 41042/0057, 200 Units PL 41042/0058. **Marketing Authorization Holder:** AbbVie Ltd, Maidenhead, Berkshire, SL6 4UB, UK . **Legal Category:** POM. **Date of preparation:** May 2023

Further information is available from: AbbVie Ltd, Maidenhead, Berkshire, SL6 4UB, UK.

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