INDICATIONS

BOTOX® is indicated for the 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 seen at maximum eyebrow elevation

when the severity of the facial lines has an important psychological impact in adult patients.

WHAT YOU CAN EXPECT FROM BOTOX®

- Patients may see improvement within 2-3 days of injection[3]
- Recommended dosing can provide long duration* of patient satisfaction (up to 6 months)[4]
- Interval between treatments must not be less than 3 months[2]

TOTAL RECOMMENDED SIMULTANEOUS DOSE

= 64U BOTOX®†

†(20U BOTOX® **(FHL)** + 24U BOTOX® **(CFL)** + 20U BOTOX® **(GL)**)

SAFETY PROFILE

BOTOX® has an extensively evaluated safety profile.[2]
Please refer to the SmPC for a full range of side effects.

*** Statistical significant favouring BOTOX® vs placebo at all visits up to Day 180 (p≤0.05).**[4,5]

BOTOX (botulinum toxin type A) Glabellar, Forehead 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. 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. Forehead Lines: Five injection sites: Each in the frontalis muscle: total dose 20 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 naive 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 outcome. 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. In clinical trials for forehead lines, adverse events considered to be related to Botox were reported in 14.3% of patients treated with 64 Units (20 Units to the frontalis with 20 Units to the glabellar complex and 24 Units to the lateral canthal lines area) 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 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).
The following represent adverse reactions that have been reported following injection of Botox for Glabellar Lines, Crow's Feet Lines with or without Glabella Lines, Forehead Lines and Glabellar Lines with or without Crow's Feet Lines.
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 and Eyelid oedema
Gastrointestinal disorders. Uncommon: Nausea, oral dryness.
Skin and subcutaneous tissue disorders. Common: Erythema. Uncommon: Skin tightness, oedema (face, periorbital), photosensitivity reaction, pruritus, dry skin, Brow Ptosis.
Musculoskeletal and connective tissue disorders. Common: Localised muscle weakness. Uncommon: Muscle twitching.
General disorders and administration site conditions. Common: Face pain, injection site bruising*, Injection site hematoma* Uncommon: Flu syndrome, asthenia, fever, Injection site haemorrhage*, Injection site pain* Injection site paraesthesia (*procedure-related adverse reaction).
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 regardless of indication:
Cardiac disorders: Arrhythmia, myocardial infarction.
Ear and labyrinth disorders: Hypoacusis, tinnitus, vertigo.
Eye disorders: Angle-closure glaucoma (for treatment of blepharospasm), eyelid ptosis, strabismus, blurred vision visual disturbance and lagophthalmos.
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.
Musculoskeletal and connective tissue disorders: Muscle atrophy, myalgia.
Nervous system disorders: Brachial plexopathy, dysphonia, dysarthria, facial paresis, hypoaesthesia, muscle weakness, myasthenia gravis, peripheral neuropathy, parasesthesia, 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, brow ptosis, 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:** October 2018.

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

Adverse events should be reported. Reporting forms and information can be found at **https://yellowcard.mhra.gov.uk**
Adverse events should also be reported to Allergan Ltd. **UK_Medinfo@allergan.com** or **01628 494026.**

References:
1. Allergan. Data on file. INT/0681/2017a. September 2017.
2. Allergan. BOTOX® Summary of Product Characteristics. October 2018.
3. Beer KR, Boyd C, Patel RK *et al*. *J Drug Dermatol* 2011;10(1):39-44.
4. Solish N, *et al*. *Dermatol Surg*. 2016;42:410–419.

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UK/0259/2018m Date of preparation: November 2018

Allergan

Indicated for **FOREHEAD LINES GLABELLAR LINES & CROW'S FEET LINES**

TRUST IN THE LEADER[1]

OPTIMAL DOSING AND ADMINISTRATION GUIDE

BOTOX® Botulinum Toxin Type A

Prescribing information can be found on the back page of this document.

TREAT **FOREHEAD LINES** (FHL), **CROW'S FEET LINES** (CFL) AND **GLABELLAR LINES** (GL) SIMULTANEOUSLY[2]

Steps for dosing and administration of BOTOX®

FOREHEAD LINES[2]

DOSING

- A volume of 0.1 ml (4 Units) is administered in each of the 5 injection sites in the frontalis muscle, for a total recommended dose of 20 Units in a total volume of 0.5 ml.
- Total recommended dose (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 recommended dose is 64 Units, comprised of 20 Units for forehead lines, 20 Units for glabellar lines and 24 Units for crow's feet lines.

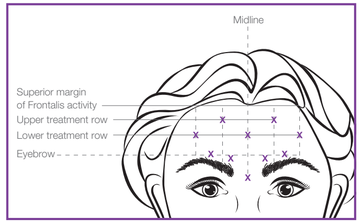


Figure 1

INJECTION

To identify the location of the appropriate injection sites in the frontalis muscle, assess the overall relationship between the size of the subject's forehead, and the distribution of frontalis muscle activity should be assessed.

The following horizontal treatment rows should be located by light palpation of the forehead at rest and maximum eyebrow elevation (see Figure 1.):

- *Superior Margin of Frontalis Activity:* approximately 1 cm above the most superior forehead crease
- *Lower Treatment Row:* midway between the superior margin of frontalis activity and the eyebrow, at least 2 cm above the eyebrow
- *Upper Treatment Row:* midway between the superior margin of frontalis activity and lower treatment row

The 5 injections should be placed at the intersection of the horizontal treatment rows with the following vertical landmarks (see Figure 1):

- On the lower treatment row at the midline of the face, and 0.5 – 1.5 cm medial to the palpated temporal fusion line (temporal crest); repeat for the other side.
- On the upper treatment row, midway between the lateral and medial sites on the lower treatment row; repeat for the other side.

CROW'S FEET LINES[2]

DOSING

- Total recommended dose: 24U in 0.6 ml (12U per side)
- 0.1 ml (4U) in each of 6 injection sites
- Injected in the lateral orbicularis oculi muscle

INJECTION

Injections should be given with the needle tip bevel up and oriented away from the eye.

The first injection (**A**) should be made approximately 1.5 to 2.0 cm temporal to the lateral canthus and just temporal to the orbital rim:

- If the lines in the crow's feet region are above and below the lateral canthus, inject as shown in Figure 2
- If the lines in the crow's feet region are primarily below the lateral canthus, inject as shown in Figure 3

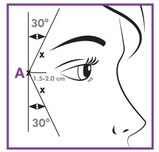


Figure 2

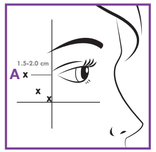


Figure 3

GLABELLAR LINES[2]

DOSING

Total recommended dose: 20U in 0.5 ml

0.1 ml (4U) in each of 5 injection sites:

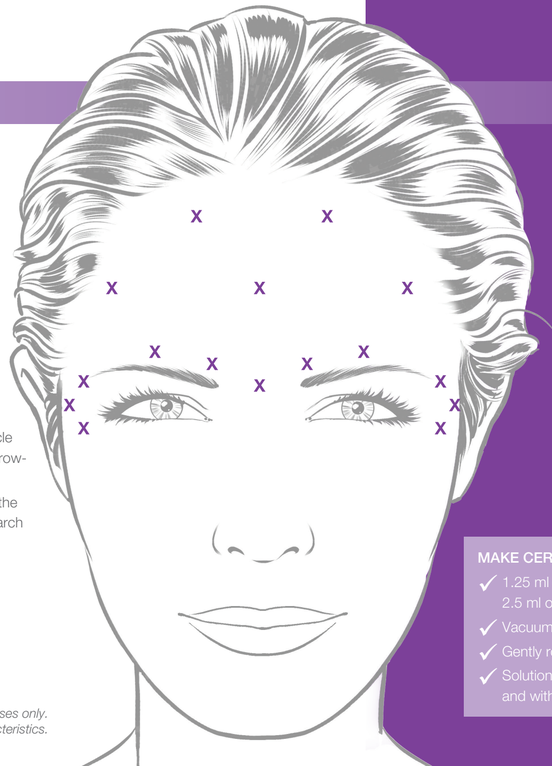
- 2 injections in each corrugator muscle
- 1 injection in the procerus muscle

INJECTION

- Before injection, place the thumb or index finger firmly below the orbital rim to prevent extravasation below the orbital rim
- Orient the needle superiorly and medially during injection

Injections near the levator palpebrae superioris muscle must be avoided particularly in patients with larger brow-depressor complexes (depressor supercilii).

Injections in the corrugator muscle must be done in the central part of that muscle, at least 1 cm above the arch of the eyebrows.



Diagrammatic representation for illustrative purposes only. Please refer to the BOTOX® Summary of Product Characteristics.

RECONSTITUTION[2]

BOTOX® is reconstituted with a sterile 0.9% preservative-free sodium chloride solution. Reconstitution should be performed in accordance with good practices and aseptic technique

1.25 ml 0.9% preservative-free sodium chloride solution

= 4U per 0.1 ml

2.5 ml 0.9% preservative-free sodium chloride solution

= 4U per 0.1 ml

MAKE CERTAIN OF THE FOLLOWING

- ✓ 1.25 ml of solvent added to 50U BOTOX® or 2.5 ml of solvent added to 100U BOTOX® slowly into the vial
- ✓ Vacuum pulled solvent into the vial (if not, discard the vial)
- ✓ Gently rotate to avoid bubble formation and denaturation
- ✓ Solution is clear, colourless to slightly yellow, and without particles

20U BOTOX® **(FHL) + 24U** BOTOX® **(CFL) + 20U** BOTOX® **(GL) = 64U** BOTOX®*

**(total recommended simultaneous dose)*