Bocouture® (Botulinum toxin type A (150 kD), free from complexing proteins) 50/100 unit vials. Prescribing information: M-BOC-UK-0067. Please refer to the Summary of Product Characteristics (SmPC) before prescribing. **Presentation:** 50/100 units of Clostridium Botulinum Neurotoxin type A, free from complexing proteins as a powder for solution for injection. **Indications:** Temporary improvement in the appearance of moderate to severe upper facial lines (glabellar frown lines, crow's feet lines, horizontal forehead lines) in adults ≥18 and <65 years when the severity of these lines has an important psychological impact for the patient. **Dosage and administration:** For intramuscular use only. Unit doses recommended for Bocouture are not interchangeable with those for other preparations of Botulinum toxin. Bocouture may only be used by physicians with suitable qualifications and proven experience in the application of Botulinum toxin. The intervals between treatments should not be shorter than 3 months. Reconstitute with 0.9% sodium chloride. ***Horizontal Forehead Lines:*** The recommended total dose range is 10 to 20 units; a total injection volume of 0.25 ml (10 units) to 0.5 ml (20 units) is injected into the frontalis muscle in five horizontally aligned injection sites at least 2 cm above the orbital rim. An injection volume of 0.05 ml (2 units), 0.075 ml (3 units) or 0.1 ml (4 units) is applied per injection point, respectively. ***Glabellar Frown Lines:*** Total recommended standard dose is 20 units. 0.1ml (4 units) into 5 injection sites (2 injections in each corrugator muscle and 1 injection in the procerus muscle). May be increased to up to 30 units. Injections near the levator palpebrae superioris and into the cranial portion of the orbicularis oculi should be avoided. ***Crow's Feet lines***: Total recommended standard dosing is 12 units per side (overall total dose: 24 units); 0.1ml (4 units) injected bilaterally into each of the 3 injection sites. Injections too close to the Zygomaticus major muscle should be avoided to prevent lip ptosis. **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 site. **Special warnings and precautions:** It should be taken into consideration that horizontal forehead lines may not only be dynamic, but may also result from the loss of dermal elasticity (e.g. associated with ageing or photodamage). In this case, patients may not respond to Botulinum toxin products. Should not be injected into a blood vessel. Not recommended for patients with a history of dysphagia and aspiration. Caution in patients with amyotrophic lateral sclerosis, peripheral neuromuscular dysfunction, or in targeted muscles displaying pronounced weakness or atrophy. Bocouture should be used with caution in patients receiving therapy that could have an anticoagulant effect, or if bleeding disorders of any type occur. Too frequent or too high dosing of Botulinum toxin type A may increase the risk of antibodies forming. Should not be used during pregnancy unless clearly necessary. Should not be used during breastfeeding. **Interactions:** Concomitant use with aminoglycosides or spectinomycin requires special care. Peripheral muscle relaxants should be used with caution. 4-aminoquinolines may reduce the effect. **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, swelling), class related undesirable effects (localised muscle weakness, blepharoptosis), and toxin spread (very rare - exaggerated muscle weakness, dysphagia, aspiration pneumonia). Hypersensitivity reactions have been reported with Botulinum neurotoxin products. ***Upper Facial Lines:*** *very common:* Headache. *Common:* Hypoaesthesia, injection site haematoma, application site pain, eyelid ptosis, dry eye, facial asymmetry, sensation of heaviness, nausea. ***Glabellar Frown Lines:*** *Common:* Headache, Muscle disorders (elevation of eyebrow). ***Crow's Feet Lines:*** *Common:* Eyelid oedema, dry eye, injection site haematoma. For a full list of adverse reactions, please consult the SmPC. **Overdose:** May result in pronounced neuromuscular paralysis distant from the injection site. Symptoms are not immediately apparent post-injection. **Legal Category:** POM. **List Price:** 50 U/vial £72.00, 50 U twin pack £144.00, 100 U/vial £229.90, 100 U twin pack £459.80. **Product Licence Number:** PL 29978/0002, PL 29978/0005 **Marketing Authorisation Holder:** Merz Pharmaceuticals GmbH, Eckenheimer Landstraße 100,60318 Frankfurt/Main, Germany. **Date of Preparation:** February 2017. **Further information available from:** Merz Pharma UK Ltd., 260 Centennial Park, Elstree Hill South, Elstree, Hertfordshire WD6 3SR. Tel: **+44 (0) 333 200 4143**

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. 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.

1. Bocouture® 50 units Summary of Product Characteristics (SmPC). March 2016. Available from: https://www.medicines.org.uk/emc/medicine/23251.
2. Bocouture® 100 units Summary of Product Characteristics (SmPC). September 2016. Available from: https://www.medicines.org.uk/emc/medicine/32426.
3. Carey, W.D., Incorrect reconstitution of incobotulinumtoxinA leads to loss of neurotoxin. J Drugs Dermatol, 2014. 13(6): p. 735-8.

M-BOC-UK-0088 Date of preparation April 2017

Further Information

- For further information on BOCOUTURE®, including the disposal of the vials please see the Summary of Product Characteristics (SmPC) at:

  50 units: https://www.medicines.org.uk/emc/medicine/23251
  100 units: https://www.medicines.org.uk/emc/medicine/32426

- medical.information@merz.com

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BOCOUTURE®
Botulinum toxin type A
free from complexing proteins

MERZ AESTHETICS

BOCOUTURE® Reconstitution Guide

Your simple 3-step guide to reconstituting BOCOUTURE®

Prescribing Information can be found on the reverse

BOCOUTURE®
Botulinum toxin type A
free from complexing proteins

BOCOUTURE®

Botulinum toxin type A
free from complexing proteins

Composition

50 Unit Vial: Active ingredient
One vial contains 50 units of Botulinum toxin type A (150 kD), free from complexing proteins.[1]
Excipients Human albumin and sucrose.

100 Unit Vial: Active ingredient
One vial contains 100 units of Botulinum toxin type A (150 kD), free from complexing proteins.[2]
Excipients Human albumin and sucrose.

Unit doses recommended for BOCOUTURE® are not interchangeable with those for other preparations of Botulinum toxin.

Storage

Unopened vial: Do not store above 25°C.[1,2]

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.[1,2]

Any solution for injection that has been stored for more than 24 hours as well as any unused solution for injection should be discarded.

Administration

Reconstituted BOCOUTURE® is intended for intramuscular injection. After reconstitution, BOCOUTURE® should be used immediately and may only be used for one treatment per patient. Reconstituted BOCOUTURE® is injected using a thin sterile needle (e.g. 30 gauge needle). BOCOUTURE® may only be applied for its intended use, to treat one patient for one session. Special care must be taken when preparing and administering the product, and when inactivating and disposing of unused solution.[1,2] If air gets into the unopened vial, e.g. by inserting an empty syringe, the powder will blow around in the vial and may settle on the glass or the stopper. This can lead to incomplete reconstitution of the powder. Please see also the SmPC for information on the disposal of unused medicinal product or waste material and for further instructions on dosing and injection.[1,2]

Reconstitution

50 units of BOCOUTURE® are reconstituted prior to use in 1.25ml unpreserved sodium chloride 9mg/ml (0.9%) solution for injection. This corresponds to a concentration of 40 units/ml.[1]

100 units of BOCOUTURE® are reconstituted prior to use in 2.5ml unpreserved sodium chloride 9mg/ml (0.9%) solution for injection. This corresponds to a concentration of 40 units/ml.[2]

Reconstitution and dilution should be performed in accordance with good clinical practice guidelines, particularly with respect to asepsis.[1,2]

It is good practice to reconstitute the vial contents and prepare the syringe over plastic-lined paper towels to catch any spillage. In order to reconstitute, an appropriate amount of sodium chloride solution is drawn up into a syringe. After vertical insertion of the needle through the rubber stopper, the sodium chloride solution is injected gently into the vial in order to avoid foam formation. A 20-27G short bevel needle is recommended for reconstitution.[1,2]

The vial must be discarded if the vacuum does not pull the solvent into the vial. Remove the syringe from the vial and mix BOCOUTURE® with the sodium chloride solution by carefully swirling and inverting 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.[1,2]

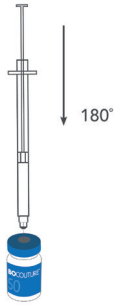
Reconstituted BOCOUTURE® is a clear, colourless solution free of particulate matter. BOCOUTURE® must not be used if the reconstituted solution (prepared as above) has a cloudy appearance or contains floccular or particulate matter.

Practical Considerations for Optimal Reconstitution[3]

- Please note these practical considerations are recommendations of the author and are based on a study demonstrating the impact of poor mixing technique.
- BOCOUTURE® reconstitution may differ from that of other Botulinum toxin type A products.
- BOCOUTURE® can be found distributed throughout the vial rather than solely at the bottom of the vial, so failure to invert the vial of BOCOUTURE® following the addition of saline may result in reconstitution of less than 100% of the available neuromodulator, possibly resulting in diminished efficacy upon injection.
- Carey's study demonstrated that improper reconstitution of BOCOUTURE®, or swirling without inversion of the vial following saline injection, can result in a significant loss of units of the neurotoxin in a clinical setting.

Reconstitution Instructions

STEP 1



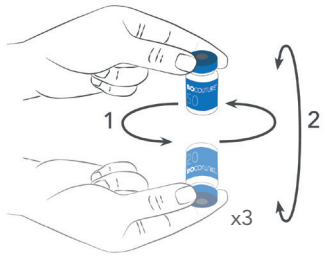
For 50 units, using a needle and suitable syringe, draw 1.25ml of unpreserved sodium chloride (0.9%) into the syringe.[1] The exposed part of the rubber stopper of the BOCOUTURE® vial should be cleaned with alcohol (70%) before the needle is inserted.

For 100 units draw 2.5ml of unpreserved sodium chloride (0.9%).[2]

After vertical insertion of a needle through the rubber stopper the solvent is injected gently into the vial in order to avoid foam formation. A 20-27 gauge short bevel needle is recommended for reconstitution.

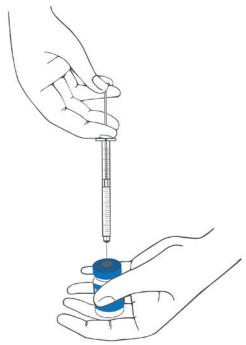
Discard the vial if the vacuum does not pull the sodium chloride solution into the vial.

STEP 2



Remove the syringe from the vial and mix BOCOUTURE® with the solvent by rotating the vial before inverting it. DO NOT shake vigorously.

STEP 3



Reconstituted BOCOUTURE® is a clear, colourless solution free of particulate matter.

Draw up the ready-to-use solution using a 20-27G needle into a syringe (the most commonly used syringe is a 1.0ml). Replace the 20-27G needle with a 30G needle for injection.