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Letybo®

Botulinum toxin type A

Package leaflet:
Information for the user
Letybo® 50 units powder for solution for injection

botulinum toxin type A

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Letybo® is and what it is used for

Letybo® contains the active substance botulinum toxin type A. It works by blocking nerve impulses to the muscles in which it has been injected. It prevents muscles from contracting, leading to a temporary paralysis.

Letybo® is used in adults less than 75 years of age to temporarily improve moderate to severe **vertical lines between the eyebrows**, when their presence has a significant psychological impact on them.

2. What you need to know before you use Letybo®

Do not use Letybo®:

- if you are allergic to botulinum toxin type A or any of the other ingredients of this medicine (listed in section 6)
- if you have muscle activity disorders, such as myasthenia gravis, Lambert-Eaton syndrome, amyotrophic lateral sclerosis
- if you have acute infection or inflammation at the proposed injection sites

Warnings and precautions

Talk to your doctor before using Letybo® if you have:

- any disorder affecting muscles and/or their direct nervous system control
- difficulties swallowing or breathing, or have had these in the past
- a bleeding disorder

If you have a history of these problems, Letybo® is not recommended for you.

Needle-related pain and/or fear of injections can lead to feeling faint due to a sudden drop in blood pressure.

Side effects due to botulinum toxin's spread away from the injection site have been reported very rarely, such as excessive muscle weakness. Swallowing and breathing difficulties are serious and can result in death.

If you have problems with your swallowing, speech or breathing, seek medical help immediately.

Children and adolescents

Children and adolescents under 18 years are not recommended to have Letybo®.

Other medicines and Letybo®

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

The following medicines could affect or be affected by Letybo®:

- medicines affecting the transfer of nerve impulses to muscles
- certain medicines used to treat bacterial infections, such as spectinomycin or those called aminoglycoside antibiotics
- other medicines containing a botulinum toxin.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby ask your doctor for advice before you receive this medicine.

Letybo® is not recommended if you are pregnant or breast-feeding, or if you are of childbearing age and not using contraception.

Driving and using machines

Botulinum toxin type A can cause weakness, dizziness and visual disturbances. Do not drive or operate machines if your ability to react is reduced.

Letybo® contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, i.e. it is essentially 'sodium-free'.

3. How to use Letybo®

The botulinum toxin unit is specific to Letybo®. This means that it is different to other botulinum toxin units and is not interchangeable with those used for other preparations of botulinum toxin.

Letybo® is only given to you by an appropriately qualified doctor who has the correct equipment for this treatment. The detailed description of the preparation of the solution and the instructions for use are described in the section "The following information is intended for healthcare professionals only" at the end of this leaflet.

The recommended dose is

20 units divided into five injections of 0.1 mL (4 units). Each injection is given into the muscles above or between the eyebrows.

Letybo® is for intramuscular use (IM use).

After the solution is reconstituted, the vial must be used only for one session per patient. Any unused solution must be discarded, as explained after section 6 in the information for healthcare professionals.

It is recommended to leave a minimum of 3 months between two treatments with Letybo®.

If you have received more Letybo® than you should

Overdoses may cause paralysis of muscles and/or nerves. Signs of overdose may not be apparent immediately after the injection.

In the event of an overdose, the doctor will monitor you for symptoms, such as general weakness or muscle paralysis. You will be admitted to hospital if symptoms of botulinum toxin type A poisoning occur, such as:

- generalised weakness
- drooping of the upper eyelid or double vision
- swallowing and speech disorders
- partial paralysis of the muscles that control your breathing.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Most side effects are mild to moderate and occur within the first few days following injection and are temporary.

Some side effects could be very serious. If you experience any of the following side effects, tell your doctor immediately or ask your relatives to tell your doctor and go to the nearest emergency room:

Uncommon, may affect up to 1 in 100 people
- drooping of the upper eyelid, eyelid spasm

Rare, may affect up to 1 in 1000 people
- eyelid sensory disorder, drooping of the brow
- bleeding in the conjunctiva
- eye pain, dry eye, visual field defect, blurred vision
- reduced sensation in the throat
- constipation
- speech sound disorder

Very rare, may affect up to 1 in 10 000 people
- muscle weakness
- difficulty in swallowing
- infection caused by breathing in food or liquid into airways or lung
- difficulty in breathing

Beside these possible side effects a severe allergic reaction could cause the following symptoms:

- difficulty swallowing, breathing or speaking due to swelling of the face, lips, mouth or throat beside these symptoms hives could occur (see section 2.)

Other known side effects can occur with the following frequencies. Please tell your doctor or pharmacist if they get serious:

Common, may affect up to 1 in 10 people
- headache
- injection site reactions

Uncommon, may affect up to 1 in 100 people
- head discomfort
- local swelling, such as of the eyelid, face, around the eyes
- injection site: pain, bruising, swelling, itching, mass, pressure
- bruising, such as around the eyes
- infection, such as viral infection of the upper airways, e.g. common cold
- Mephisto sign (raising of the outer eyebrows)

Rare, may affect up to 1 in 1000 people
- migraine
- inflammation of hair follicle
- dizziness
- abnormal sensation such as prickling, tingling and itchiness
- nausea
- dry skin, nettle-rash, itching
- face pain
- fever
- oral herpes
- increased blood potassium
- influenza like illness

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Letybo®

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.

Store and transport refrigerated (2 °C – 8 °C).

Reconstituted solution

Chemical and physical in-use stability has been demonstrated for 24 hours at 2 °C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless reconstitution/dilution (etc) has taken place in controlled and validated aseptic conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

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6. Contents of the pack and other information

What Letybo® contains

- The active substance is botulinum toxin type A.
- One vial contains 50 units botulinum toxin type A produced by *Clostridium botulinum*.
- After reconstitution each 0.1 mL of the solution contains 4 units.
- The other excipients are human albumin and sodium chloride.

What Letybo® looks like and contents of the pack

Letybo® is a white powder for solution for injection provided in a clear glass vial with a rubber stopper and aluminium tamper-proof seal.

Single pack contains one vial or two vials. Multipack contains 2 cartons, each carton contains one vial.

Multipack contains 6 cartons, each carton contains one vial.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

CROMA-PHARMA GmbH
Industriezeile 6
2100 Leobendorf
Austria

This leaflet was last revised in May 2023.

The following information is intended for healthcare professionals only:

Botulinum toxin units are not interchangeable from one product to another. Doses recommended in units are different from other botulinum toxin preparations.

The instructions for use, handling and disposal should be strictly followed.

Preparation of the solution

Reconstitution should be performed in accordance with good practice rules, particularly in the respect of asepsis.

Sodium chloride 9 mg/mL (0.9 %) solution for injection must be used as the diluent for reconstitution of Letybo® and must be added at a volume of 1.25 mL.

It is good practice to reconstitute the vial content and prepare the syringe over plastic-lined paper towels to catch any spillage. Sodium chloride 9 mg/mL (0.9 %) solution for injection is drawn up into a syringe and must be injected gently into the vial, to avoid foam/bubble formation or vigorous agitation which may cause denaturation. The vial must be discarded if the vacuum does not pull the solvent into the vial. Reconstituted Letybo® is a clear, colourless solution practically free of particulate matter. Prior to use, the vial should be visually inspected to ensure the product is free from foreign particulate matter.

Letybo® must not be used if the reconstituted solution has a cloudy appearance or contains particulate matter.

Reconstituted solution

Chemical and physical in-use stability has been demonstrated for 24 hours at 2 °C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless reconstitution / dilution (etc) has taken place in controlled and validated aseptic conditions. Any solution for injection that has been stored for more than 24 hours must be discarded. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

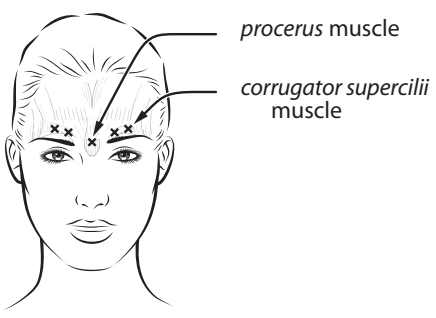
Instructions for use

Intramuscular injections should be performed using a sterile insulin or tuberculin-type syringe of 1 mL value with 0.01 mL graduation and a needle with a gauge range of 30 to 31 G.

A volume of 0.5 mL of the properly reconstituted Letybo® solution should be drawn into the sterile syringe and any air bubbles in the syringe barrel expelled. The needle used to reconstitute the medicinal product should be removed and replaced for administration.

Care should be taken to ensure that Letybo® is not injected into a blood vessel.

In order to reduce the complication of blepharoptosis, injections near the *levator palpebrae superioris* must be avoided, particularly in patients with large brow depressor complexes. When injecting into two sites of each *corrugator supercilii* muscle, the first injection should be made right above the medial margin of eyebrows. The second injection will be made approximately 1 cm above the supraorbital ridge (rigid bony boundaries palpable above the upper part of the upper eyelid) where midlines of the eyebrows meet. The injection site of the *procerus* muscle is just above the midline of the nasal bridge where horizontal wrinkles are made between the medial ends of eyebrows. When injecting into the medial ends of *corrugator supercilii* muscles and on the midlines of the eyebrows, the injection sites should be at least 1 cm away from the supraorbital ridge (rigid bony boundaries palpable above the upper part of the upper eyelid).



Injections need to be made with caution to avoid intravascular injection. Before injecting, a thumb or an index finger can be placed firmly below the orbital rim to prevent effusion of the medicinal product to this area. The needle needs to be oriented superiorly and medially.

In case of treatment failure one month after the first treatment session, i.e. in the absence of significant improvement from baseline, the following approaches may be considered:

- Analysis of the causes of failure, e.g. incorrect muscles injected, injection technique, formation of toxin neutralising antibodies, insufficient dose
- Re-evaluation of the relevance of treatment with botulinum toxin type A

In the absence of any undesirable effects secondary to a treatment session, initiation of another treatment session with at least a three-month interval between the treatment sessions is possible.

Procedure to follow for a safe disposal of vials, syringes and materials used

For safe disposal, un-reconstituted Letybo® should be reconstituted in the vial with a small amount of water and then autoclaved. Any empty vials, vials containing residual solution, syringes or spillage should be autoclaved. Alternatively, the remaining Letybo® can be inactivated with diluted sodium hydroxide solution (0.1 N NaOH) or with diluted sodium hypochlorite solution (0.5 % or 1 % NaOCl).

After inactivation used vials, syringes and materials should not be emptied and must be discarded into appropriate containers and disposed of in accordance with local requirements.

Recommendations should any incident occur during the handling of botulinum toxin

- Any spills of the product must be wiped up: either using absorbent material impregnated with a solution of sodium hypochlorite in case of the powder, or with dry, absorbent material in case of reconstituted product.
- The contaminated surfaces should be cleaned using absorbent material impregnated with a solution of sodium hypochlorite, then dried.
- If a vial is broken, proceed as mentioned above by carefully collecting the pieces of broken glass and wiping up the product, avoiding any cuts to the skin.
- If the medicinal product has had contact with the skin, wash the affected area with a solution of sodium hypochlorite then rinse abundantly with water.
- If the medicinal product has had contact with the eyes, rinse thoroughly with plenty of water or with an ophthalmic eyewash solution.
- If the medicinal product has had contact with a wound, cut or broken skin, rinse thoroughly with plenty of water and take the appropriate medical steps according to the dose exposed to.

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