WELLSTOX Injection

Prescription medicine

(Clostridium botulinum toxin type A) I.M.

【Composition】 Each vial contains:

Active ingredient: Clostridium botulinum toxin type A (separate specification) 100Units
Stabilizer: Human serum albumin ---------- 0.5mg
Isotonic agent: Sodium chloride ---------- 0.9mg

【Description】

A lyophilized white powder for injection in a colourless and transparent glass vial which should be a colourless and transparent liquid formulation when dissolved in a solvent (saline).

【Efficacy】

1. Temporary improvement of moderate to severe glabellar lines related to eyebrow wrinkle muscle (corrugator muscle) and/or procerus muscle activity in adults aged from 18 to 65
2. Temporary improvement of severe or more Lateral Canthal lines (wrinkles around the eyes) related to orbicularis oculi muscle activity in adults aged from 19 to 65

【Usage and Dosage】

1. Glabellar lines

Dilute to 100u/2.5mL (4 U/0.1 mL) with 0.9% preservative-free sterile saline solution. Use a 30-gauge needle to inject a total of 20 U of 0.1 mL each at 2 sites of the corrugator muscle and 1 site of the procerus muscle for a total of 5 sites.

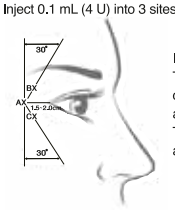
In order to reduce the complications of ptosis, avoid injections near the levator palpebrae superioris muscle, particularly in patients with larger depressor supercilii. When injecting into the inner corrugator muscle and in the midpoint between each eyebrow, it should be injected at least 1 cm above the arch of the eyebrows. Care should be taken to ensure that this drug is not injected into a blood vessel. Before injection, the thumb or index finger is to be placed firmly below the orbital rim in order to prevent extravasation below the orbital rim. The needle should be pointed upward and medially during the injection, and the injection volume must be accurate. The corrugator and orbicularis oculi muscles move the middle of the forehead to create glabellar frown lines. The procerus and depressor supercilii muscles pull the forehead down. These muscles produce frown or glabellar lines. Since the location, size, and use of muscles vary from person to person, an effective dose is determined by the overall observation of the patient's ability to actuate the injected superficial muscle.

The therapeutic effect of this drug for glabellar lines lasts for about 3 to 4 months, but the duration of effect may vary depending on the patient. The safety and efficacy of frequent administration of this drug has not been clinically evaluated and is not recommended.

2. Lateral Canthal lines

Lateral canthal lines are mainly caused by the activity of the orbicularis oculi muscle around the eyes used when blinking or closing the eyes. Strong contraction of the orbicularis oculi muscle produces a lateral fan-shaped fold (wrinkles around the eyes) originating from the lateral canthus. The distribution of these fan-shaped wrinkles is different for each patient.

Inject 0.1 mL (4 U) into 3 sites per side on the outer side of the orbicularis oculi muscle, a total of 6 sites on both sides. (total 24 U)



Inject from the outside of the eye with the inclined surface of the tip of the needle facing up.
The first site of injection is the orbital rim (marked with AX) at least 1.5-2.0 cm away from the lateral canthus toward the temple. Then, at a point 1.0 to 1.5 cm from the first site of injection, inject above and below the inside point at an angle of about 30 degrees (marked with BX and CX), respectively.
The safety and efficacy of improvement of the lateral canthal lines were evaluated for a single administration for 16 weeks.

< How to dilute >

To dissolve this lyophilized drug, use a sterile saline without the use of preservatives. The recommended diluent is 0.9% sodium chloride. Add a proper amount of diluent to a syringe of appropriate size. Since this drug denatures when foaming or similar violent agitation occurs, slowly add the diluent into the vial. If the diluent was not placed in the vial under vacuum, this vial should be discarded. The dissolution date and time should be written on the label and administered within 24 hours after dissolution. Refrigerate (2-8°C) the diluted solution. When this drug is dissolved, it should be colourless and transparent and there should be no foreign matter visible to the naked eye. Formulations for parenteral administration should be carefully inspected for foreign matter and discolouration prior to administration. As this drug and its diluent do not contain preservatives, one vial should not be used for more than 1 patient.

【Dilution table】

Added diluent(0.9% Sodium Chloride Injection)	Concentration in the dissolved state(U/0.1mL)
1.0mL	10.0U
2.0mL	5.0U
4.0mL	2.5U
8.0mL	1.25U

Caution: This diluent is calculated based on an injection of 0.1 mL. In addition, it is possible to increase or decrease the dosage by increasing or decreasing the parenteral dose. 0.05 mL (50% dosage decrement) to 0.15 mL (50% dosage increment)

【Precautions】

Since the active ingredient of this drug is botulinum toxin type A produced by Clostridium botulinum, it is necessary to understand the precautions for use and strictly follow the usage and dosage. Physicians administering this drug must have a thorough understanding of the anatomy of the eye area involving the nerve root, anatomical changes from previous surgery, and standard electromyography techniques.

The recommended dosage and frequency of administration should not be exceeded.

(a) Distant spread of toxin effect: Botulinum toxin can spread from the site of injection to other sites, causing botulinum toxin. Symptoms such as sudden muscle weakness, loss of energy, hoarseness, language disorders, stuttering, loss of bladder control, dyspnea, dysdipsia, diplopia, blurred vision and ptosis may occur. Symptoms such as dyspnea or dysdipsia can be life-threatening, and there have been reports of deaths due to the spread of toxins.

(b) Hypersensitivity reactions: Serious or immediate hypersensitivity reactions have rarely been reported with other botulinum toxin formulations. These reactions were anaphylaxis, hives, soft tissue edema, and dyspnea. An example of anaphylaxis is the use of lidocaine as a solvent, and the causative agent has not been reliably identified. If such a reaction occurs after administration of this drug, administration should be discontinued and appropriate measures should be taken.

(c) Pre-existing neuromuscular disorders

In patients with peripheral motor neuron disease (e.g. amyotrophic lateral sclerosis, motor neuropathy) or neuromuscular junction disease (e.g. myasthenia gravis, lambert-eaton syndrome), the usual dose of a botulinum toxin formulation may increase the risk of significant systemic reactions including severe dysphagia and hypopnea. According to the clinical literature of other botulinum toxin formulations, there have been rare reports of severe hypersensitivity reactions to the systemic effects of conventional doses when botulinum toxin is administered to patients with known or unknown neuromuscular disease. In some of these cases, dysphagia persisted for months and required a nasogastric tube.

(d) Due to the administration of other botulinum toxin formulations, cardiovascular adverse events, including arrhythmias and myocardial infarction, have been reported rarely, and they are fatal in some patients. Some of these have previously had risk factors, including cardiovascular disease.

(e) Non-interchangeable: It is not possible to convert units of one product to units of another, as toxin content may vary between botulinum toxin formulations.

Contraindications

(a) Patients with hypersensitivity to the ingredients of this drug

(b) Patients with systemic neuromuscular junction disorders (myasthenia gravis, lambert-eaton syndrome, amyotrophic lateral sclerosis, etc.): It has a muscle-relaxing action, which can make the disease worse for them.

(c) Pregnant women, women who may be pregnant, and lactating woman

Prudent dosing

(a) Patients taking muscle relaxants (tubocurarine chloride, dantrolene sodium, etc.): There is a possibility that muscle relaxation is promoted or the manifestation of dysphagia is increased.

(b) Patients taking drugs with muscle relaxation, such as spectinomycin hydrochloride, aminoglycoside antibiotics (gentamicin sulfate, neomycin sulfate, etc.), polypeptide antibiotics (polymyxin sulfate B, etc.), tetracycline antibiotics, lincosamides antibiotics, muscle relaxants (baclofen, etc.), anticholinergics (butyl scopolamine bromide, trihexyphenidyl hydrochloride, etc.), benzodiazepines and similar drugs (diazepam, etizolam, etc.), benzamide drugs (tiapride hydrochloride, sulpiride, etc.): There is a possibility that muscle relaxation is promoted or the manifestation of dysphagia is increased.

Adverse drug reactions

General description

After treatment with botulinum toxin, sometimes dysphagia, pneumonia and/or death related to severe lethargy or anaphylaxis have been reported rarely. In addition, adverse events of the cardiovascular system, including arrhythmias and myocardial infarction, which sometimes lead to fatal outcomes, have been rarely reported. The exact causal relationship between these adverse events and botulinum toxin has not been confirmed.

The following adverse events have been reported with other botulinum toxin formulations, and the association with botulinum toxin is unknown. In general, adverse events such as skin rash (including polymorphic red spots, hives, and psoriatic rash), itching, and allergic reactions occur within 1 week after injection and are usually temporary, but may last for several months. With regard to injection, local pain, tenderness, infection, inflammation, paresthesia, bruising, pulling at the injection site, burning sensation at the injection site, and hypertonia at the injection site and surrounding muscles may occur. The local weakness at the injection site reflects the predicted pharmacological action of botulinum toxin.

General precautions

(a) This drug contains human albumin derived from human blood. When administering a drug manufactured from human blood or plasma, infectious diseases caused by the transfer of infectious substances cannot be completely excluded. This may also apply to hitherto unknown pathogens. To reduce the risk of transmission of these infectious materials, the manufacturing process includes selection of a donor or donor site using an appropriate measurement method and removal and/or inactivation of infectious materials.

(b) The effect of this drug on the ability to operate machinery, or to drive is unpredictable due to the disease itself being treated.

Drug interaction

(a) In another botulinum toxin formulation, the efficacy of the botulinum toxin formulation was increased when combined with aminoglycoside antibiotics or drugs that interfere with muscle/neurotransmission (tubocurarine muscle relaxants). Continued use with aminoglycoside antibiotics or spectinomycin is contraindicated.
The use of polymyxin, tetracycline, or lincomycin in patients taking this drug should be used with caution.

(b) The effect of administration of other botulinum neurotoxin serotypes simultaneously or within several months is unknown.
If another botulinum toxin is administered before the effect of the previously administered botulinum toxin disappears, myoneural weakness may be exacerbated excessively.

Precautions on application

To dissolve this lyophilized drug, use a preservative-free sterile saline. The recommended diluent is 0.9% sodium chloride injection. Add a proper amount of diluent to a syringe of appropriate size. Since this drug denatures when foaming or similar violent agitation occurs at this time, slowly add the diluent into the vial. If the diluent is not put into the vial under vacuum, discard the vial. The dissolution date and time should be written on the label and administered within 24 hours after dissolution. Keep this drug dissolved during this period in a refrigerated state (2-8°C). This dissolved drug should be colourless and transparent and free from any distinct substances. As this drug and its diluent do not contain preservatives, it is not recommended to use 1 vial for more than 1 patient.

Precautions for storage and handling

This drug should be kept refrigerated (2-8°C) in an unopened state. Once this drug has dissolved, it can be refrigerated (2-8°C) for 24 hours. All vials, including expired vials, or items that have come into direct contact with the product, must be disposed of as medical waste. If inactivation of the toxin is required (e.g. leaks), it is recommended to use diluted hypochlorite (0.5 or 1%) prior to disposal as medical waste.

Information for patients

Consult your doctor with any concerns about the effects and risks of this drug. Pay attention to any signs or symptoms of adverse events. Seek medical help immediately if you have trouble swallowing, speaking, breathing, or muscle weakness after treatment. Adverse events may appear within hours or weeks after treatment.

This drug binds to receptors at the nerve endings, enters the nerve endings, and inhibits the secretion of acetylcholine, thereby blocking the conduction of the muscle nerves. When injected intramuscularly in a therapeutic dose, it produces local muscle paralysis due to its chemical denervation action. When a muscle is chemically denervated, the muscle can weaken and develop acetylcholine receptors outside the junction. As nerves are regenerated and nerve impulses can flow back to the muscles, it proves that "feeling of helplessness" is reversible.

【Storage】 Hermetic container, refrigerated (2~8°C) storage

【Packaging unit】 1vial/box(vial(100units))

【Expiry Date】 36 months from the date of manufacture

Distributed by : QH Bio

QHBIO

#322, 18, Dongjak-daero 1-gil, Dongjak-gu,
Seoul, Republic of Korea (www.qhbio.kr)

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