BTXA™

Botulinum Toxin Type A

The same origins, unlimited possibilities

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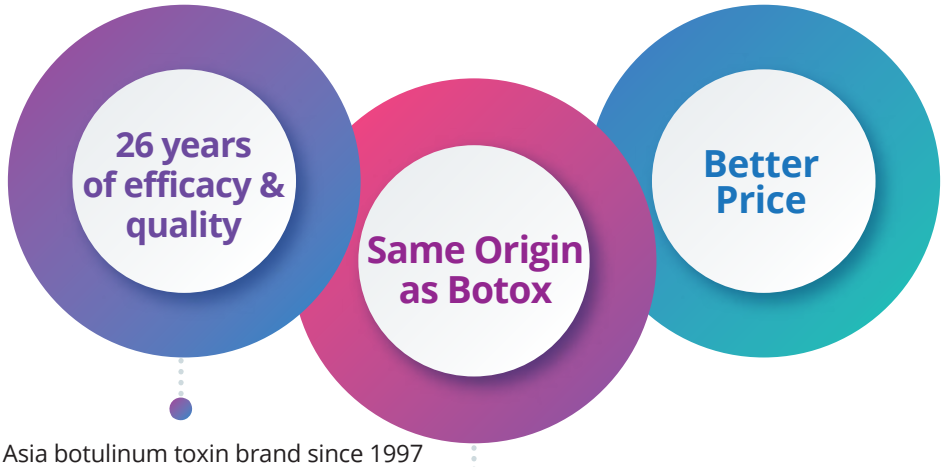
BTXA™
Botulinum Toxin Type A

Why BTXA™



- First Asia botulinum toxin brand since 1997
- Fast onset
- Good efficacy
- Long lasting

BTXA's Origin

University of Wisconsin, USA
Clostridium botulinum bacteria type A
Hall Strain developed

1970
Inventors of botulinum toxin

- Dr. Alan Scott & Oculinum™
- Prof. Sugiyama

1984
- **Dr. YC Wang**
  Donated the Clostridium botulinum Hall Strain to Dr. Ying Chun Wang

> Acute toxicity of aminoglycoside antibiotics as an aid in detecting botulism.
> Y C Wang, D H Burr, G J Korthals, and H Sugiyama
>
> This article by **Dr YC Wang** is still cited in other brand's product insert

1991
Botulinum toxin's brand

- BOTOX™
  Allergan bought Oculinum, Inc , changed the product name
- BTXA™
  Dr. Wang Developed BTXA™ in Lanzhou Biotechnique Development Co, Ltd (LBTD) China (former: Lanzhou Institute of Biological Product)

1997
- Approved & launch in South Korea

Clinical Indication of BTXA™

Cosmetic uses

Treatment of:
- Glabellar lines
- Forehead lines
- Crow's feet
- Per-oral lines & Naso-labial folds
- Neck lines
- Masseter muscle hypertrophy
- Calf muscle hypertrophy

Neurology

Ophthalmology

Gastroenterolog

Urology

Rehabilitation

Autonomic Hypersecretory Disorders

Efficacy: Comparison study with BOTOX

A Double-blind, Randomized Crossover Study of Prosigne Versus Botox in Patients With Blepharospasm and Hemifacial Spasm

FIGURE 3. Follow-up pictures of PA1 at maximum forehead frown, submitted to injection of Prosigne (left forehead side) and Botox (right forehead side) at day 0, day 30, day 60, day 120, and day 150.

Day 0 (No Injection day) | Day 60 | Day 80 | Day 120 | Day 150

FIGURE 4. Follow-up pictures of PA6 at maximum forehead frown, submitted to application of Dysport (left forehead side) and Xeomin (right forehead side) at day 0, day 60, day 90, day 120 and day 150.

Day 0 (No Injection day) | Day 30 | Day 60 | Day 120 | Day 150

Subject

Twelve (12) male patients with a mean age of 30.5 with moderate or severe hyperdynamic forehead lines on a facial wrinkle scale (FWS) , evaluation was up to day 150

Result

All patients responded In a side-to-side evaluation and no asymmetries or differences In the degree of reduction of hyperdynamic forehead lines were noted at day 30 & 60.

Conclusion: similar result in both group (BOTOX & BTXA™) in terms of efficacy, safety, tolerability, and degree of satisfaction.

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Long Term Efficacy

The Effect of long-term Treatment with Botulinum Toxin for Idiopathic Blepharospasm

Hu Xingyue, Cai Huaying, Zhang Shizheng, Shao Yuguan

Efficacy and dosage of ling term repetitive treatment for blepharospase

	Cases	Effective cases	Duration of beneficial effect (week)	Mean dosage (U)
1st session	178	160*	15.94 ± 4.56	66.87 ± 13.71
2nd session	138	134	15.54 ± 4.40	68.38 ± 14.54
3rd session	112	108	15.48 ± 4.46	70.52 ± 16.54
4th session	83	79	15.45 ± 4.48	71.58 ± 16.48
5th session	63	60	15.53 ± 4.52	70.31 ± 16.52
6th session	48	47	15.51 ± 4.37	72.75 ± 16.39

Subject
One hundred seventy eight (178) patients aged from 28 to 82 (mean 52+/- 13) , 53 patients with blepharospasm and 125 patients accompanied with segmental dystonia

Method
178 cases were followed up for 7 years with 6 sessions of BTXA topical Injections. the dosage of BTXA, therapeutic effect and duration, and side effects were compared.

Result
Mean duration of Improvement was 15-16 weeks, no significant difference between each session In the effect rate, mean dosage, and duration of Improvement.

Conclusion: Long term repeated BTXA injection for blepharospasm matinatined therapeutic effect and durtaion of improvement without incrasing dose

Quality & Safety: Post market surveillance report

Periodic Safety Update Report, BTXA (Botulinum Toxin Type A) - 50U and 100U

- 6 years continuous safety monitoring was carried out in Brazil
- During the period covered by this report, more than 300,000 cases BTXA™ treatments

>94% satisfied after 1 wk of injection

>99% satisfactory safety result

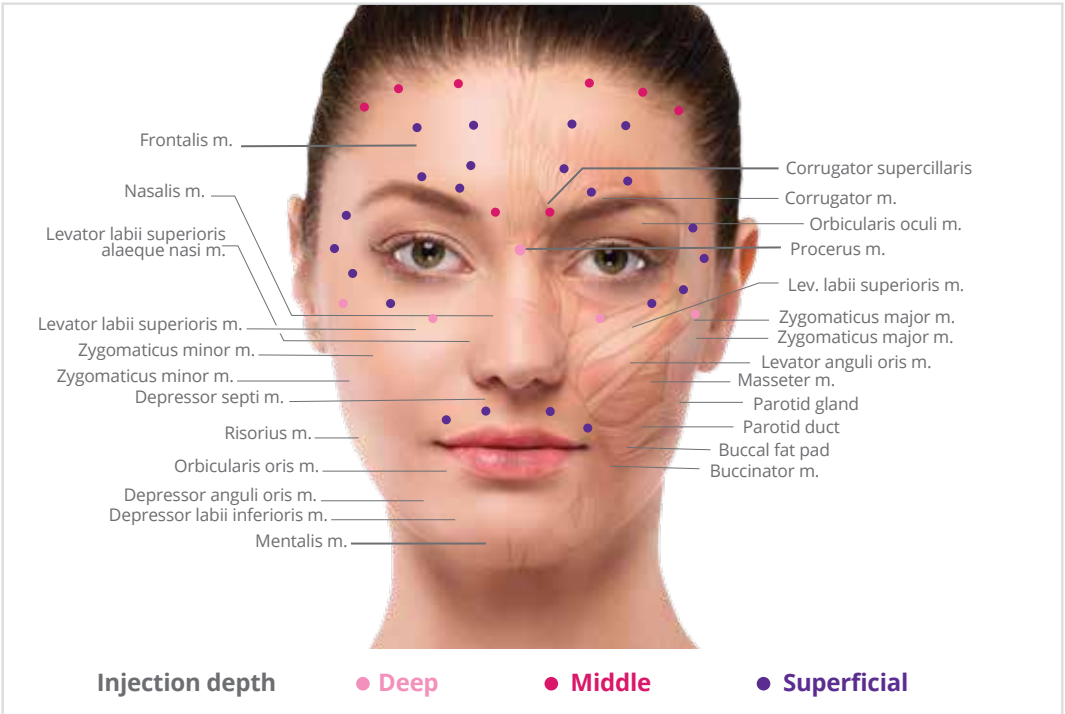
50% patient maintained satisfactory after 6 months

<1% mild adverse reactions

Injection Dosage (for reference)

Application areas		Dose per	No. of sites	Total dose	Injection depth
Forehead lines		2-4U	5-10	10-20U	SC/IM
Vertical glabellar lines		4U	4	16U	SC/IM
Horizontal glabellar lines		4U	1	4U	SC/IM
Crow's feet (each side)		2U	3 – 6	6 – 12U	SC
Perioral rhytides		1 - 2U	4	4 – 8U	Superficial
Horizontal platysmal bands (each band)		3 - 5U	3	12 – 15U	IM
Masseter muscle hypertrophy (each side)	**Man**	10 - 13U	3 – 4	30 – 15U	IM: 2 – 3 cm
	Woman	7 – 10U	3 – 4	20 - 30U	IM: 1 – 1.5 cm
Calf muscle hypertroply (each side)		5U	20 - 30	100 – 150U	IM: ~2 cm

Facial Injection Sites



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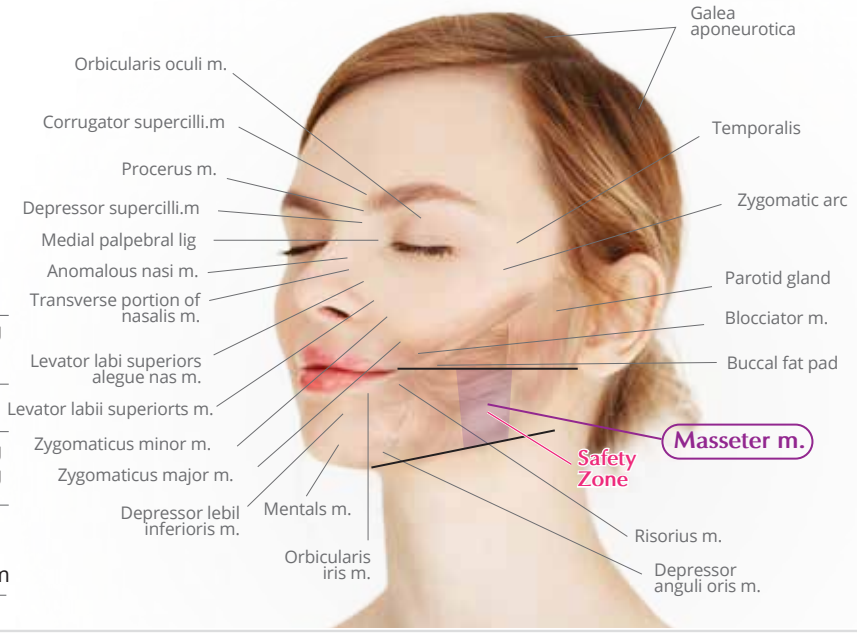
Treatment of Masseter Muscle Hypertrophy

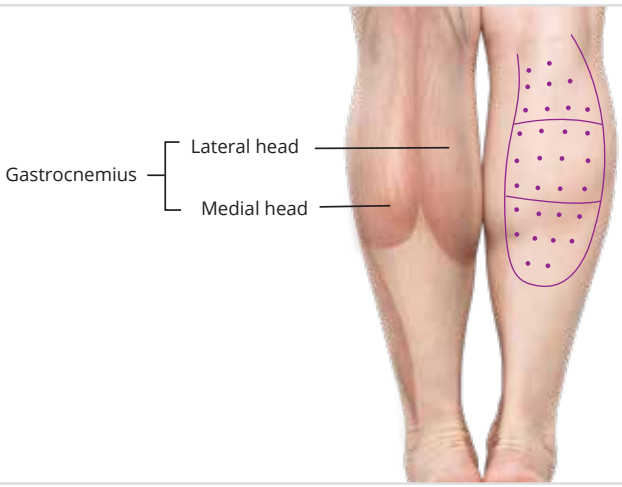
- Ask the patient to close the jaw tightly to show the masseter muscle
- Use 23G needle to inject at the deeper portion of muscle
- Avoid injection to the origin site and upper portion to prevent cheek depression
- Space the injections 2 cm apart



DOSE OF EACH SITE	Man:	10 - 13U
	Woman:	7 - 10U
NO. OF SITES	3 - 4 each side	
TTOTAL DOSE FOR EACH SIDE	Man:	30 - 40U
	Woman:	20 - 30U
DEPTH:	Intramuscular	
	Man:	2 - 3cm
	Woman:	1 - 1.5cm

Treatment of Calf Muscle Hypertrophy

- Carry out intravenous sedation with Ketamine
- Mark the outline contour of calf muscle when the patient is raising heel for tip-toeing



DOSE OF EACH SITE	5U
NO. OF SITES	20 - 30 each side
TOTAL DOSE	100 - 150U each side
DEPTH:	Intramuscular (-2 cm)

Treatment of Hyperhidrosis

Classical locations of hyperhidrosis: face, underarm, hands and feet

Before injection:

An iodine starch test can be performed to ascertain the injection areas

Steps:
1. The areas to be evaluated are covered with castor oil & iodine in a 1:9 proportion
2. The areas are sprinkled by potato starch
3. The areas of active sweating turn black

- This test should be carried out prior to regional nerve blocks or the use of topical anaesthetics.
- It is helpful to draw a grid on the skin to mark the injection fields

For palms and soles:

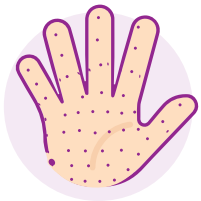
» The dose varies from patient to patient and depends on the size of the hyperhidrotic area to be injected

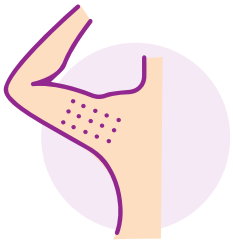
» In plantar hyperhidrosis, the lateral and medial edges of the foot may need additional injections

» The main limitation is that most patients find the injections painful and may require regional anesthesia via media ulnar nerve blocks for palms and sural and posterior tibial nerve block for soles

» Alternatively, the area can be rendered relatively pain free by prior application of anesthetic cream under occlusion iontophoretic application of lidocaine, or cryospray

Location	Dose	Concentration	Total injection sites
Palms	50 - 100U/palm	2-2.5U / 0.1ml / site	Depends on the size of the hyperhidrotic area
Soles	50 - 100U/sole	2-2.5U / 0.1ml / site	
Axillae	50U/axilla	2.5U / 0.1ml / site 5U/ 0.2ml / site	10-15 sites /axillae





Palms	Soles	Axillae
Inject intradermally	Inject intradermally	Inject intradermally
Approximate depth of 3mm	Approximate depth of 3mm	Approximate depth of 3mm and at a 45° the skin surface
Avoid intramuscular injections	Avoid intramuscular injections	Avoid intramuscular injections
Injections are scattered every 1.5 - 2cm on the palm of the hand and on the fingertips, tips and webs of hand	Injections are scattered every 1.5 - 2cm on the sole, sides of the sole and will be placed in the webs between the toes and on the tips of the toes	Injection to mutiple sites approximatel 1.5 - 2cm apart

- If injection sites are marked in ink, do not inject BTXA™ diectly through ink mark to avoid a permanent tattoo effect

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User Tips for Injection

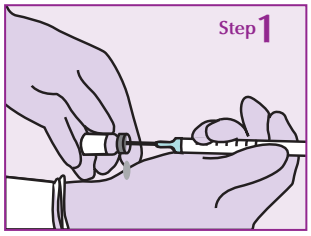
Storage condition:

	Before reconstitution	After reconstitution
Storage temperature	2°C to 8°C or -20°C to -5°C	2°C to 8°C, do not freeze
Shelf life	2 or 3 years after lyophilization	Use within 4 hours ideally

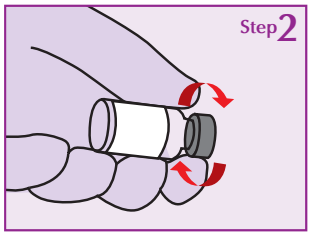
Dilution table:

Concentration (U / 0.1ml)	Volume of diluents (ml) added	
	50 U vial	100 U vial
10.0U / 0.1ml	0.5ml	1.0ml
5.0U / 0.1ml	1.0ml	2.0ml
4.0U / 0.1ml	/	2.5ml
2.5U / 0.1ml	2.0ml	4.0ml
1.25U / 0.1ml	4.0ml	8.0ml

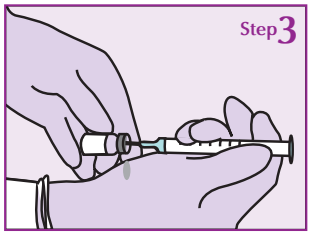
Reconstitution techniques:



Step 1:
Use a 21G needle and an appropriately sized syringe to draw up appropriate amount of 0.9% sterile saline without preservative. Insert the needle into glass vial gently and slowly inject to avoid bubble formation. Discard the vial if a vacuum does not pull the diluents into vial. Gently rotate the vial (do not vigorously shake the vial) to avoid bubble formation which may affect the potency of toxin.



Step 2:
Gently rotate the vial (do not vigorously shake the vial) to avoid bubble formation which may affect the potency of toxin.



Step 3:
Draw the mixture back into the syringe. Inject the mixture into muscle by using appropriate needle tip for injection.

Q & A

Basic injection techniques:

- Remove any make-up on the patient's skin and wipe the sites with alcohol swab. Allow to dry.
- Evaluate the bulk of muscle contraction at the proposed injection site
- After aspiration of BTXA™ solution, remove the 21G needle tip and attach a 30G needle tip in order tominimize discomfort to patient
- Clear the air bubble from the syringe using minimal agitation before injection
- Advise the patient to relax during injection

How to avoid antibody formation?

- Use minimum effective dose
- Keep at least 2 to 3 months interval between injections
- Avoid booster injection
- Inject no more than 300 units in 3 months

Post-injection:

- Press on the site with a tissue immediately after the injection for minutes to minimize bruising
- Any bruising that occurs should be treated immediately with ice pack
- No other treatments or massage unless otherwise specified
- Advise patient to take rest for 15 minutes before returning to normal activity

Effectiveness:

- The onset time is 1 to 2 days for most of the patients
- Best effect will usually be attained 1 to 4 weeks after injection
- After 3 to 4 months, effectiveness will gradually fade, but the overall efficacy of BTXA™ can be maintained for 6 to 8 months
- According to many reports, the duration of effectiveness increased after repeated injections
- Younger patients with more elastic skin will have a longer effect

Contraindications:

- × Pregnant and breast feeding women
- × Hypersensitive patients
- × Heavy forehead furrows with slight
- × Redundant facial skin
- × Unrealistic goal and expectations
- × Infection or tumor at the proposed injection sites
- × Long-term usage of anticoagulant or patients with dysfunction of blood coagulation
- × Unstable mental state
- × Patients who are taking aspirin, aminoglycosides antibiotics (eg: gentamicin), aminoquinolines, cydosporine, D-penicillamine within two weeks prior to injection

Potential risks:

Among all the cases of BTXA™ cosmetic applications, severe adverse reaction was rarely reported.

- **Bruising** — resolve in 7 to 10 days
  - Avoided by not taking aspirin prior to injection
- **Ptosis** — resolve within a few weeks
  - Avoided by injection at least 1cm above the eyebrow and no massage after injection
- Ecchymosis & oedema
- Tightening of forehead
- Mild nausea
- Pain at the injection sites
- Erythema
- Cyanosis
- Unnatural facial expression

Most side effects are transient and will disappear spontaneously after 1-2 weeks

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Botulinum Toxin Type A

BTXA™ Worldwide Market

Global Connection of BTXA™

Since 1997
BTXA™ has served in Global market

30+ Countries
BTXA™ has been successfully registered

>4 million vials
of 100U BTXA™ are sold In 2021

Other brand name:

PROSIGNE® LANTOX DITUROXAL REDUX® Lanzox® LIFTOX® BTXA Лантокс®

References:

1. Costa J, Rieder C, et al. A double-blind, randomised, crossover study of Prosigne versus Botox in patients with blepharospasm and hemifacial spasm. Clin Neuropharmacol. 2007;30:39-42. 2. Drug Safety Report-Prosigne ® (Botulinum Toxin Type A), Jan 2009, Hugh Source (Int'l) Ltd. Data on file.
3. 2007 American Society of Aesthetic Plastic Surgery (ASAPS) Cosmetic Surgery National Data Bank Statistics.
4. Talarico S, Bgatin E, Pecora CS, Ferreira LM, Orofino R, Godoy A, et al. Open-Label, Prospective, Multicenter, Multidisciplinary Phase III Study to Evaluate the Efficacy and Tolerability Prosigne (Botulinum Toxin Type A) in the Aesthetic Treatment of the Upper third of the Face in Patients with Facial Wrinkles. Data on file.

BTXA™ (BOTULINUM TOXIN TYPE A)
DESCRIPTION BTXA™ (Botulinum Toxin Type A) is a sterile, lyophilized form of purified botulinum toxin type A, produced from the crude toxin of the culture of the Hall strain of Clostridium botulinum grawn in a medium containing trypticase and yeast extract. A series of purifying procedure were taken to form a crystalline complex consisting of the active high molecular weight toxin protein and an associated hemagglutinin. After re-dissclved and dialyzed the crystalline toxin, an accurate amount of the sterile filtered (0.2 microns) toxin were added to a solution containing gelatin-dextran-sucrose, then lyophilized. Each vial of BTXA™ contains 100 or 50 units (U) of C. botulinum toxin type A, 5mg of gelatin, 25mg of dextran and 25mg of sucrose. Dilute with sterile normal saline according to different needs before using. The white loose product turns to be colortess or vellowish transparent solution after the reconstitution. One unit (U) of BTXA™ corresponds to 1 LD50 of Botulinum Toxin Type A while being intraperitoneally injected into mouse. BTXA™ could block neuromuscular conduction by inhibiting the release of acetylcholine and therefore causes local muscle flaccid paralysis.
INDICATIONS BTXA™ is indicated for the treatment of blepharospasm, hemifacial spasm in adults and some types of strabismus, especially for acute paralytic strabismus, comitant strabismus, strabismus caused by endocrine myopathy and strabismus which can not be corrected through operation.
USAGE AND DOSAGE Position for injection For blepharospasm: the injection should be taken intramuscularty at several points of upper and lower lids, i.e., taking 4 to 5 points of injection into orbicularis oculi of medial and lateral or lateral canthus temporal, For hemifacial spasm: besides the points mentioned above, three other points on middle, lower face and cheek should be given intramuscularly. BTXA™ may be given at the points of two sides of eyebrow, upper lip or the lower jaw according to the diseases. For strabismus: the BTXA™ is injected using a coaxial electrode needle with electromyographic guidance or amplifier under topical anesthesia of 0.5% Decarine. The injections into extraocular muscles are selected according to the type and position of strabismus.
Dosage For blepharospasm and hemifacial spasm: the injection could be given following above instructions. The initial dose of each point is 2.5U / 0.05ml or 2.5U / 0.1ml. If the initial treatment is considered insufficient one week later, a supplementary injection may be given. Double dose of 5U / 0.1ml could be given to recrudescent patients. But the limitation of total dose of 55 U for one injection and 200U for one month should not be exceeded. For strabismus: for vertical and horizontal muscle strabismus of less than 20 prism diopters, the initial dose into each muscle is 1.25 - 2.5U; for horizontal strabismus of 20 - 40 prism diopters, the initial dose into each muscle is 2.5U; for horizontal strabismus of 40 - 50 prism diopters, the initial dose into each muscle is 2.5U and can be increase (to 5.0 each timme) depending on the response; for persistent V cranial nerve paralysis lasted for more than one month, 1.25 - 2.5U dose could be injected into medial rectus. The injecting volume into each muscle should not exceed 0.1ml. To patients, having insufficient response, supplementary injection could be given. To recrudescent patients, the dose can be repeated or increased irregularty. But for each muscle the maximum dose should be less than 5 U / inj.
The Dilution of BTXA™ The dilution of BTXA™ with sterile normal saline should be done carefully on the basis of real needs. Following is a reference table of dilution to be recommended:

Concentration (U / 0.1ml)	Volume of Diluent (ml) Added	
	50 U vial	100 U vial
10.0U / 0.1ml	0.5 ml	1.0 ml
5.0U / 0.1ml	1.0 ml	2.0 ml
2.5U / 0.1ml	2.0 ml	4.0 ml
1.25U / 0.1ml	4.0 ml	8.0 ml

Shaking the vial gently after adding sterile normal saline to the complete dissolving. The reconstituted BTXA™ should be used at once or stored in refrigerator at 2 to 8°c and to be used within 4 hours. The container and the syringe used with the drug as wel as the residual BTXA™ solution should be disposed after sterilization.
SIDE EFFECTS Temporary ptosis of the eyelid, drawback of the lower eyelid, reduced blinking, eyelid close incompletely, weakness of facial muscles, etc. may occur to a few patients who received BTXA™ therapy for blepharospasm and hemifacial spasm. However, all the symptoms will disappear without any therapy within 3 to 8 weeks. Temporary and different degree of ptosis of the eyelid, vertical deviation and rarely mydriasis, which related to the diffusion of the toxin to the muscles adjacent, may occur to some patients who received BTXA™ therapy for strabismus. The symptoms will disappear without any therapy within a few weeks.
CONTRAINDICATIONS BTXA™ is contraindicated in individuals with anaphylactic constitution and known hypersensitivity to this preparation.
PRECAUTIONS BTXA™ must be kept, issued, registered by special person and administered only to the patients with above indications. Physicians administering especially during the treatment of strabismus, have to be trained prior, know extraocular and facial muscles anatomy and be good at lectromyographic amplifier technique. The injection procedure should be taken later to patients who have fever, acute infectious diseases and carefully to the patients with heart, liver, lung diseases, active tuberculosis, blood diseases and pregnant women. Botulinum toxin may be potentiated by aminoglycoside antibiotics (such as gentamicin). This kind of drugs should not be taken during the administration of BTXA™. BTXA™ is in low effect or without any effect to the patients in the following situations: strabismus above 50 prism diopters, fixed strabismus, Duane's syndrome due to weak lateral rectus, strabismus caused by excessively corrected operation, chronic paralysis strabismus, chronic V or III cranial nerve paralysis, serious muscle fiber contracture. 1:1000 adrenaline should be prepared in case of occasional accident. Short period of observation is recommended to the patients who just received BTXA™ injection. HOW SUPPLIED 100 U /Vial, 50 U/Vial
SHELF LIFE 3 years from the date of lyophilization.
STORAGE Store at temperature of -5 to -20'c (23 to -4°c).
MANUFACTURER Lanzhou Institute of Biological Products
SOLE AGENT Hugh Source (International) Ltd. Tel: (852) 27716622 Fax: (852) 27825249 Email: hughs@hughsource.com

BTXA™

Botulinum Toxin Type A

HUGH | Live a Healthier Life with Hugh

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