

HUTOX[®] INJ.

CLOSTRIDIUM
BOTULINUM
TOXIN TYPE A

100
UNITS



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● Main Ingredient

Clostridium botulinum type A
Neurotoxin complex (900 kD) 100 unit/vial.

● Dosage Form

Freeze-dried white powder for reconstitution with sterile, preservative-free 0.9% sodium chloride solution.

● Indication

Temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity, as well as crow's feet lines associated with orbicularis oculi muscle activity in adult patients aged 19 - 65 years old.

● Storage and Shelf life

Unopened vial of HUTOX should be stored in a refrigerator (2 to 8 °C) for up to 36 months.

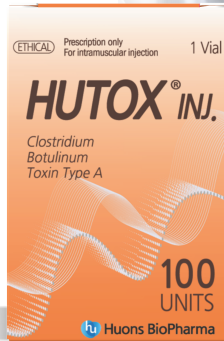
● Dilution Table

Dilution Added (Preservative-free, sterile 0.9% saline)	Resulting Dose (U/0.1mL)
1.0 mL	10.0 Units
2.0 mL	5.0 Units
2.5 mL	4.0 Units
4.0 mL	2.5 Units
8.0 mL	1.25 Units

* These dilutions are calculated for an injection volume of 0.1 ml.
Administering increased or decreased dose is also possible.

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● Clinical Trial Timeline

Hutox Inj. 100 Unit

: On-going clinical trials of expanded indications.

Glabellar Lines

: Indication Approved.

Crow's Feet Lines

: Indication Approved.

Upper Limb
Spasticity

: Indication Approved.

Benign Masseteric
Hypertrophy

: Completed Clinical Study Phase III.
Registration in progress.

Purified Type (150kDa)

: Clinical Study Phase III.

● Registration Status

Full-Range Pharmaceutical Approvals in 16 Nations.



HUTOX Specifications



Glabellar Lines Dosage & Administration

Reconstitute this product with preservative-free, sterile saline to make 100U/2.5mL (4U/O.1 mL) and using a 30-gauge needle, inject a dose of 0.1 ml into each of 5 sites, 2 in each corrugators muscle and 1 in procerus muscle, for a total of 20U.

Clinical Information

Botulinum toxin type A used for clinical improvement of moderate to severe glabellar lines was injected for a total of 20 units (U), 4 units each on the 5 areas including 2 areas of corrugator muscle and 1 area of procerus muscle. The treatment effect of glabellar lines continues for about 3-4 months.

Repeated Dose Toxicity

The administration of 180 U is feasible based on the mean weight of 60 kg. It is determined safe as it exceeds the trial dosage considering the administration frequency (3-4 months interval) and clinical trial administration (20 U).

HUTOX Identification

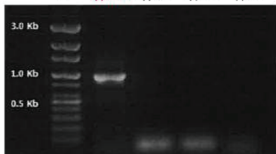
The strain was confirmed as Type A by PCR. Also, Botulinum Toxin protein showed same pattern with standard on SDS-PAGE.

Clostridium botulinum Type A



Gram positive, Rod-shaped

M Type A Type B Type E Type F



Serotyping result : Type A (PCR)

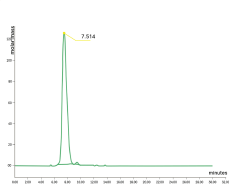
SDS-PAGE Results



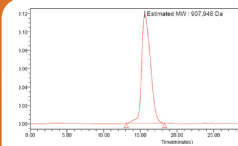
HUTOX Protein Size Comparison

The molecular weight of HUTOX protein has similar value compared with company A and B

HUTOX-903.3+4kDa

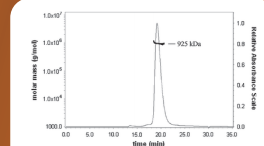


Company "A"-9079+7kDa



Ref: GIHYEOK YANG, PHD, AND HYUN HO JUNG, PHD "A New Botulinum Toxin Potentially Bioequivalent to Onabotulinumtoxin A: Are There Any Differences at All?," Dermatol Surg 2013; 39: 166-170.

Company "B"-925+45kDa

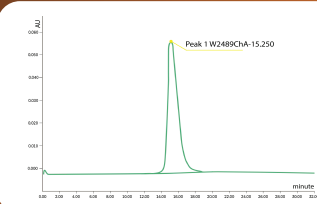


Ref: Lietzow MA, Gielow ET, Le D, Zhang J, et al. "Subunit stoichiometry of the Clostridium botulinum type A neurotoxin complex determined using denaturing capillary electrophoresis," Protein J 2008; 27: 45-49.

HUTOX Purity Comparison

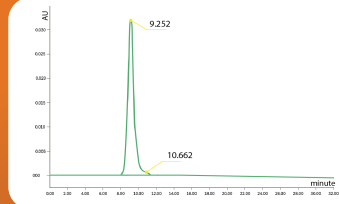
HUTOX has higher purity compared to other company's product

HUTOX - 99.8%



Peak Name	RT	Area	%Area	Height
1 Peak 1 W2489 CHA	15.250	4152357	99.81	53621
2 Peak 2 W2489 CHA	19.200	8004	0.19	209

Company "A" Purity -98.99%



Retention Time (min)	Area (AU x sec)	%Area
1 9.252	1489506	98.99
2 10.662	15157	1.01

Ref: KP 10 - 1339349

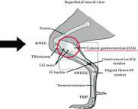
HUTOX Efficacy Comparison

HUTOX showed equivalent efficacy compared to original company A

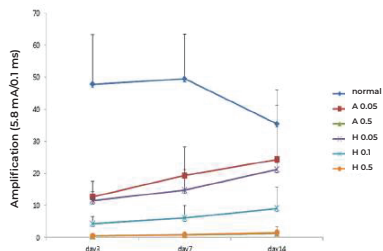
Electromyography(EMG) in mouse



Injection into Lateral gastrocnemius of mouse



	HUTOX	Company "A"
Stock concentration	900U/ml (0.5U/μl)	100U/vial (1000U/ml (0.1U/μl))
Injection concentration	0.05U/20μl/mouse 0.1U/20μl/mouse 0.5U/20μl/mouse	0.05U/20μl/mouse 0.5U/20μl/mouse
stock volume	0.05U (0.2μl) 0.1U (0.2μl) 0.5U (2μl)	0.05U (0.2μl) 0.5U (2μl)



Ref: Huons - EMG report : 2016. 18

HUTOX Pre-Clinical Study

Completed the Pre-clinical studies in Mouse, Rat and Beagle Dog.

Study Type	Route	Test System	Doses
Safety Pharmacology			
Effects on central nervous system	IM	Mouse/ICR	0, 1.5, 3, 6 U/kg
Effects on central respiratory system	IM	Rat/Sprague Dawley	0, 1.5, 3, 6 U/kg
Effects on hERG current	In vitro	HEK cell	0, 0.03, 0.3, 1.3 U/mL
Effects on cardiovascular parameters	IM	Dog/Beagle	0, 3, 10, 30 U/kg
Toxicology			
Single dose	IM	Rat/Sprague Dawley	0, 6, 30, 150 U/kg
Single dose	IM	Dog/Beagle	0, 100, 200 U/kg
Repeated dose	IM	Rat/Sprague Dawley	0, 1.5, 3, 6 U/kg/week
Repeated dose	IM	Dog/Beagle	0, 3, 10, 30 U/kg/week
Reproductive and Developmental Toxicity			
Embryo-fetal development	IM	Rat/Sprague Dawley	0, 0.16, 0.4, 1 U/kg/day
Embryo-fetal development	IM	Rabbit/New Zealand White	0, 0.05, 0.1, 0.2 U/kg/day



HUTOX Manufacturer Information

● Manufacturing Facility

Huons Biopharma Co., Ltd. located at
50 Biovalley 2-ro, Jecheon-si, Chungcheongbuk-do,
Jecheon Biovalley Complex

● Research Facility

Huons Biopharma Co., Ltd. located at
56-19, 5th floor, Gwacheon-daero 7na-gil,
Gwacheon-si, Gyeonggi-do (Galhyeon-dong)

Huons BioPharma

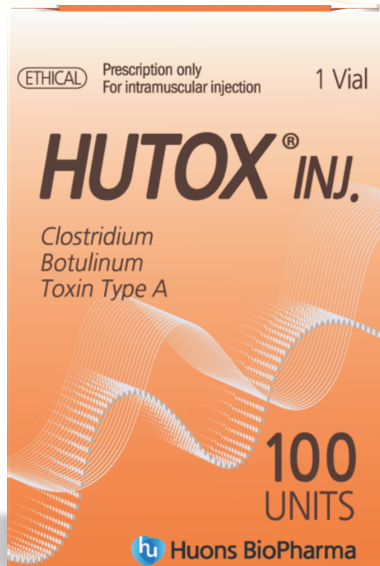


● Certifications

Huons Biopharma has successfully obtained the European Good Manufacturing Practice (EU GMP) certification for its production facility from Germany's LAVG.

Other certifications include:

- Korean Good Manufacturing Practice (GMP) Certification
- ISO 9001 Certification
- ISO 45001 Certification



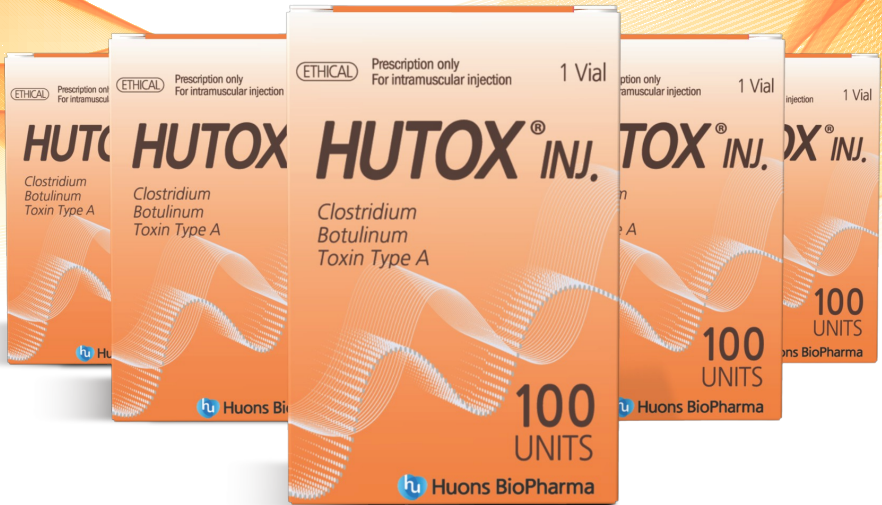
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EUROPEAN UNION
GMP

 **Huons BioPharma**

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