SUMMARY OF PRODUCT CHARACTERISTIC

QUALITATIVE AND QUANTITATIVE COMPOSITION

NABOTA vacuum dried powder for injection 200 Units (Clostridium botulinum toxin type A)

Each vial contains:

- Active ingredient: Clostridium botulinum toxin type A – 200 Units
- Stabilizing agent: Human serum albumin – 1.0 mg
- Isotonic agent: Sodium chloride – 1.8 mg

DESCRIPTION

It appears as a white to yellowish, vacuum dried powder for injection in a colorless and transparent vial. It should become colorless transparent liquid when dissolved in the diluent (physiological saline solution).

THERAPEUTIC INDICATION

1. Glabellar lines

Temporary improvement in the appearance of moderate to severe glabella lines (vertical lines between the eyebrows) associated with corrugator muscle and/or procerus muscle activities, in adults aged between 20 to 65.

2. Focal upper limb spasticity

Upper limb spasticity associated with stroke in adults aged over 18 years.

3. Lateral canthal lines (crow's feet lines)

Temporary improvement in the appearance of moderate to severe lateral canthal lines (crow's feet lines) associated with orbicularis oculi muscle activity in adults aged 18 to 65 years.

4. Blepharospasm

Treatment of benign essential blepharospasm in adults aged over 18 years.

5. Benign masseter muscle hypertrophy (square jaw)

Temporary improvement in marked* to very marked** benign masseter muscle hypertrophy in adults aged 18 to 65 years.

*Marked:

At rest, the lower face contour, including the masseter muscle, jaw, and jawline, is square, and the surface of the masseter muscle is severely convex. At maximum clenching, the lower face contour shows a severe difference compared to at rest, and the masseter muscle mass is firm or hard and palpable.

** Very marked:

At rest, the lower face contour, including the masseter muscle, jaw, and jawline, is trapezoidal,

and the surface of the masseter muscle is severely convex. At maximum clenching, the lower face contour shows a severe difference compared to at rest, and the masseter muscle is hard and palpable.

DOSAGE & ADMINISTRATION

1. Glabella lines

Reconstitute by diluting with preservative-free, sterile saline solution to make 100U/2.5 mL (4U/0.1 mL) Using a sterile 30-gauge needle, inject a dose of 0.1 mL into each of the 5 injection sites: 2 injections in each corrugator muscle and 1 injection in the procerus muscle for a total dose of 20 Units. In order to reduce the complication of ptosis, injections near the levator palpebrae superioris muscle must be avoided, particularly in patients with larger brow-depressor complexes (depressor supercilii). Injections into inner corrugators muscle and central eyebrow should be placed at least 1 cm above the bony supraorbital ridge.

Careful attention should be paid to avoid injection of this product into the blood vessel. The thumb or index finger should be placed firmly below the orbital rim in order to prevent extravasation below the orbital rim. The needle should be oriented superiorly and medially during the injection and careful attention should be paid to inject accurate volume.

Glabella facial lines arise from the activity of corrugator muscle and orbicularis oculi muscle. These muscles move the brow medially, and the procerus muscle and depressor supercilii muscle pull the brow inferiorly. This creates a frown or “furrowed brow”. The location, size, and use of the muscles vary markedly among individuals. An effective dose for facial lines is determined by gross observation of the patient’s ability to activate the superficial muscles injected. Each treatment lasts approximately three to four months. More frequent injection of this product is not recommended because the safety and efficacy are not established.

Typically the initial doses of botulinum toxin induce chemical denervation of the injected muscles one to two days after injection, increasing in intensity during the first week.

2. Focal upper limb spasticity

The exact dosage and number of injection sites may be tailored to the individual based on the size, number and location of the muscles involved, the severity of spasticity, the presence of local muscle weakness, and the patient's response to previous treatment. Clinical improvement of spasticity was observed within 4 weeks after injection, which lasted for 8 and 12 weeks.

The injection doses in the clinical study are as follows:

Muscle	**Total dose**	**Number of sites**
Biceps brachii	100 – 200 units	Up to 4 sites
Flexor digitorum profundus	15 – 50 units	1 or 2 sites
Flexor digitorum sublimis	15 – 50 units	1 or 2 sites
Flexor carpi ulnaris	10 – 50 units	1 or 2 sites
Flexor carpi radialis	15 – 60 units	1 or 2 sites

In the clinical study, doses ranging up to 360 units were divided among selected muscles.

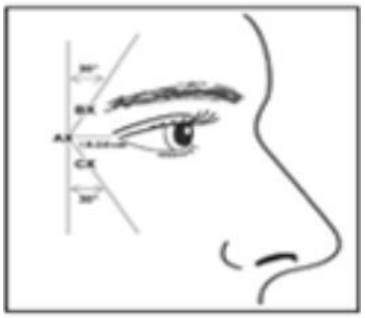
A sterile 24–30 gauge needle is used for superficial muscles, and a needle of appropriate length is used for muscle tissues. Localization of the involved muscles with techniques such as electromyographic guidance or nerve stimulation is recommended.

3. Lateral canthal lines (crow’s feet lines)

Lateral canthal lines arise largely from the activity of the orbicularis oculi muscles, which are around the eyes and responsible for blinking and eyelid closure. Forceful contraction of the orbicularis oculi results in lateral and radially oriented folds (crow's feet lines), which originate from the lateral canthus. The distribution of these radial lines differs among patients.

Injections should be given with the needle bevel tip pointed up and oriented away from the eye. Using a 30–33 gauge needle, inject a dose of 0.1 mL (4 U) into 3 sites per side (a total of 6 sites and 24 units for both sides) in the lateral orbicularis oculi muscle.

The first injection should be approximately 1.5–2.0 cm temporal to the lateral canthus and just temporal to the orbital rim. If the lines in the lateral canthus at maximum smile are above and below the lateral canthus, inject as shown in the figure.



The duration of effect of NABOTA for lateral canthal lines is approximately 3 months. The safety and efficacy of the injection interval have not been clinically evaluated.

4. Blepharospasm

For blepharospasm, reconstitute by dilution (see Dilution Table) and inject using a sterile 27–30 gauge needle without electromyographic indicator. The recommended initial dose for injection into the medial and lateral pretarsal orbicularis oculi of the upper lid and into the lateral pretarsal orbicularis oculi of the lower lid is 2.5 U (0.1 mL at each site). If blepharospasm blocks vision, injections into the medial corrugator supercilii muscle and superolateral portion of orbicularis oculi are possible. At repeat treatment sessions, the same dose as the most recent total injection dose may be injected up to 5 U per injection site (a total of 50 U).

The safety and efficacy of a single dose of NABOTA were assessed for blepharospasm for 12 weeks. The safety and efficacy of the injection interval have not been clinically evaluated.

5. Benign masseter muscle hypertrophy

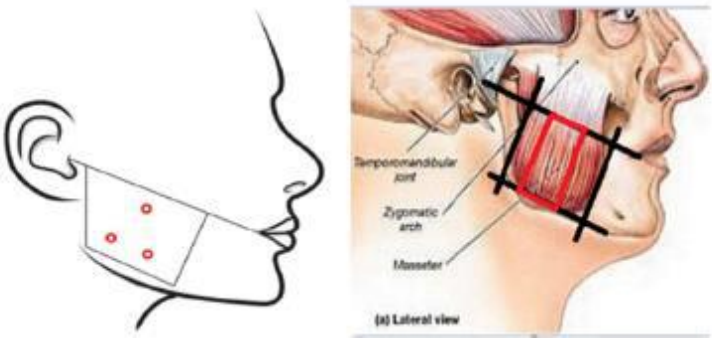
Inject a dose of 0.2 mL (8 U) into each of 3 sites on each side of the bilateral masseter muscles (a total of 6 sites and 1.2 mL (48 U) for both sides) using a 30–33 gauge needle.

Before the injection, palpate the masseter muscle to mark the anterior and posterior borders when the patient clenches their teeth.

Consider the anterior and posterior borders as left and right boundaries, respectively. Consider the line from tragus to angle of mouth to be a superior border and the mandible border line to be an inferior border and mark a zone 1 cm inside each border.

Inject into 2 sites in the inferior border of the mandible and 1 site above them corresponding to a vertex of an imaginary triangle around the most prominent bulges within the rectangle imagined by the borders (a total of 3 sites). The injection sites should be 1 cm apart.

Make sure to carefully administer the product 1 cm inward from the left/right and anterior/posterior borderlines after determining the injection sites by identifying the location of the masseter muscles and referring to the figure below, as the administration may cause discomfort in chewing and changes in facial expression when smiling. Be careful to avoid injection into the muscles around the mouth.



Injection sites of botulinum toxin for MMH and anatomical image of masseter muscle.

PREPARATION AND DILUTION TECHNIQUE

Prior to injection, reconstitute freeze-dried product with a preservative-free, sterile saline. 0.9% sodium chloride injection is the recommended diluent. Draw up the proper amount of diluent in the syringe of appropriate size. Since this product is denatured by bubbling or similar violent agitation, the diluent should be injected gently into the vial. Discard the vial if a vacuum does not pull the diluent into the vial. Record the date and time of reconstitution on the space of the label. This product should be administered within 24 hours after reconstitution. During this period, reconstituted product should be stored in a refrigerator (2-8°C). Reconstituted product should be clear, colorless and free of particulate matter. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. Because this product and the diluent do not contain any preservative, one vial of this product should be used for a single patient.

[DILUTION TABLE]

Diluent Added **(0.9% Sodium Chloride Injection)**	**Resulting dose Units per 0.1 mL**
2.0 mL	10.0 Units
4.0 mL	5.0 Units
5.0 mL	4.0 Units
8.0 mL	2.5 Units
16.0 mL	1.25 Units

Note: These dilutions are calculated for an injection volume of 0.1 mL..

A decrease or increase in the dose is also possible by administering a smaller or larger injection volume - from 0.05 mL (50% decrease in dose) to 0.15 mL (50% increase in dose.)

CONTRAINDICATIONS

A. Patients who are hypersensitive to any ingredient in the formulation of this product.

B. Patients who have neuromuscular junctional disorders (e.g., myasthenia gravis, Lambert-Eaton

syndrome or amyotrophic lateral sclerosis). The diseases may be exacerbated due to the muscle relaxation activity of this drug product.
C. Pregnant women, women of childbearing potential or nursing mothers.

ADMINISTER WITH CARE TO THE FOLLOWING PATIENTS

A. Patients under treatment with other muscle relaxants (e.g., tubocurarine chloride, dantrolene sodium, etc.) - Muscle relaxation may be potentiated or risks of dysphagia may be increased.

B. Patients under treatment with drugs with muscle relaxation activity, e.g., spectinomycin HCl, aminoglycoside antibiotics (gentamicin sulfate, neomycin sulfate, etc.), polypeptide antibiotics (polymyxin B sulfate, etc.), tetracycline antibiotics, lincomycin antibiotics (lincosamides), muscle relaxants (baclofen etc.), anti-cholinergic agents (scopolamine butylbromide, trihexylphenidil HCl, etc.), benzodiazepine and other similar drugs (diazepam, etizolam, etc.), and benzamide drugs (thiapride HCl, sulpiride, etc.). Muscle relaxation may be potentiated or risks of dysphagia may be increased.

ADVERSE REACTIONS

A. General

There have been spontaneous reports of death, sometimes associated with dysphagia, pneumonia, and/or other significant debility or anaphylaxis, after treatment with botulinum toxin. There have also been rare reports of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. The exact relationship of these events to the botulinum toxin injection has not been established. The following events have been reported in other botulinum toxin and a causal relationship to the botulinum toxin injected is unknown: skin rash (including erythema multiforme, urticaria and psoriasiform eruption), pruritus, and allergic reaction.
In general, adverse reactions occur within the first week following injection and, while generally transient, may have a duration of several months. Localized pain, tenderness, bruising, traction, swelling, hot feeling or hypertonia at injection site or adjacent muscles may be associated with the injection. Local weakness of the injected muscle(s) represents the expected pharmacological action of botulinum toxin. However, weakness of adjacent muscles may also occur due to spread of toxin. When injected to patients with blepharospasm or cervical dystonia, some muscles distant from the injection site can show increased electrophysiological jitter (rapid variation in a waveform) which is not associated with clinical weakness or other types of electrophysiological abnormalities.

B. Glabella lines

Safety of this product was evaluated in multicenter, comparative, double-blinded, randomized studies which included 268 patients aged between 20 to 65, with moderate to severe glabella lines (test

group 135, control group 133). Adverse reactions were observed in 20.00% of test group, and in 18.05% of control group.

Most of the adverse reactions were mild, and none was severe. Adverse reactions reported more than 1% in the test group of this drug, listed in the order of frequency are; ptosis (2.22%), raised eyebrows (1.48%), and vertigo (1.48%).

C. Upper limb spasticity

Safety in upper limb spasticity was evaluated in a multicenter, active-controlled, double-blind (neither the patient nor the doctor knew which treatment was given), randomized study in 197 patients aged over 18 years who were diagnosed with stroke ≥ 6 weeks before enrolment (test group (NABOTA): 99; Botox control group: 98).

Among these, adverse drug reactions related to drug treatment occurred in 3 cases in the test group (NABOTA) and 4 cases in the control group. The table below lists the reported adverse drug reactions by system organ class. The frequency of adverse drug reactions reported is defined as follows: Very Common (≥ 10%); Common (≥ 1% to < 10%); Uncommon (≥ 0.1% to < 1%); Rare (≥ 0.01% to < 0.1%); Very Rare (< 0.01%).

Table 1. Treatment-related adverse drug reactions reported in the test group (NABOTA)

System Organ Class	Common (≥ 1/100 to < 1/10)
Musculoskeletal and connective tissue disorders	Muscular weakness (1.03%, 1 case), pain in extremity (1.03%, 1 case), muscle atrophy (1.03%, 1 case)

D. Lateral canthal lines (crow's feet lines)

The safety of this product was evaluated in a multicenter, active-controlled, double-blind (neither the patient nor the doctor knew which treatment was given), randomized study in 204 patients with moderate to severe lateral canthal lines, aged ≥ 18 to ≤ 75 years.

Adverse drug reactions that related to the injection site in lateral canthal line treatment area occurred in 1 patient (0.49%, 1 each) each in the NABOTA and control drug groups, both of which were mild (NABOTA injection area: pruritus; control drug injection area: tenderness).

E. Blepharospasm

The safety of this product was evaluated in a multicenter, active-controlled, double-blind (neither the patient nor the doctor knew which treatment was given), randomized study in 230 patients aged over 18 years diagnosed with essential blepharospasm (test group (NABOTA): 117; Botox control group: 113). Adverse drug reactions related to drug treatment were observed in 11.97% (14/117, 16 cases) of the test group (NABOTA) and 13.27% (15/113, 18 cases) of the control group. The table below

lists the reported adverse reactions by system organ class.

Table 2

System organ class	Test group (NABOTA) (n=117)	Control group (n=113)
General disorders and administration site conditions		
Injection site bruising	6 (5.13%, 6 cases)	5 (4.42%, 5 cases)
Injection site swelling	2 (1.71%, 2 cases)	5 (4.42%, 5 cases)
Injection site inflammation	1 (0.85%, 1 case)	0 (0.00%, 0 cases)
Eye disorders		
Blepharitis	1 (0.85%, 2 cases)	1 (0.88%, 1 case)
Dry eye	1 (0.85%, 1 case)	0 (0.00%, 0 cases)
Eyelid ptosis	1 (0.85%, 1 case)	0 (0.00%, 0 cases)
Foreign body sensation in eyes	1 (0.85%, 1 case)	0 (0.00%, 0 cases)
Lacrimal disorder	1 (0.85%, 1 case)	0 (0.00%, 0 cases)
Neurological disorder		
Dizziness	1 (0.85%, 1 case)	0 (0.00%, 0 cases)

F. Benign Masseter Muscle Hypertrophy

Safety was evaluated in a multicenter, placebo-controlled, double-blind (neither the patient nor the doctor knew which treatment was given), randomized study in 180 male and female adults aged ≥ 18 and ≤ 65 years who wanted to improve benign masseter hypertrophy (the test group (NABOTA): 91; placebo control group: 89). Among these, adverse events related to the drug treatment occurred in 5.49% (5/91, 6 cases) of the test group (NABOTA) and 2.25% (2/89, 2 cases) of the control group. All adverse drug reactions correspond to local adverse reactions related to injection. No serious adverse drug reactions were reported. The table below lists the reported adverse drug reactions by system organ class.

System organ class	Test group (NABOTA) (n=91)	Control group (n=89)
Musculoskeletal and connective tissue disorders		
Mastication disorder	5 (5.49%, 5 cases)	1 (1.12%, 1 case)
General disorders and administration site conditions		

Injection site reaction	1 (1.10%, 1 case)	0 (0.00%, 0 cases)

G. Postmarketing surveillance results in Korea

Glabellar lines

A 4-year postmarketing surveillance of 914 patients in Korea showed an incidence of adverse events of 2.5% (23/914, 25 cases). Among these, the incidence of adverse drug reactions for which a causal relationship to this product cannot be excluded was 1.6% (15/914, 17 cases): 0.5% (5/914, 5 cases) for headache, 0.2% (2/914, 2 cases) each for eye strain and swelling around the eyes, and 0.1% (1/914, 1 case) each for chills, fatigue, facial paralysis, injection site reaction, rash/tenderness/pain at the injection site, and pruritus. No serious adverse events or serious adverse reactions were observed.

The incidence of unexpected adverse events was 1.5% (14/914, 16 cases): 0.8% (7/914, 7 cases) for headache, 0.2% (2/914, 2 cases) for eye strain and pharyngitis, and 0.1% (1/914, 1 case) each for back pain, chills, fatigue, facial paralysis, and skin wrinkles. Among these, the incidence of unexpected adverse drug reactions for which a causal relationship to this product cannot be excluded was 0.9% (8/914, 10 cases): 0.5% (5/914, 5 cases) for headache, 0.2% (2/914, 2 cases) for eye strain, and 0.1% (1/914, 1 case) each for chills, fatigue, and facial paralysis. No suspected unexpected serious adverse events or suspected unexpected serious adverse drug reactions were observed.

Adverse events from reexamination in Korea and data from spontaneous side effect reports for NABOTA were evaluated synthetically at the end of the reexamination with adverse event reporting data of all marketed drugs in Korea. As a result, the adverse events below were identified as new among the statistically significant common adverse events with NABOTA compared to all the other drugs. However, the result does not mean a causal relationship between NABOTA and these adverse events has been established.

- Skin and subcutaneous tissue: swelling around eyes (eyelids swelling)
- Nervous system headache

Upper limb spasticity

A 4-year post marketing surveillance for reexamination in 710 patients with post-stroke focal upper limb spasticity in Korea showed an incidence of adverse events of 8.31% (59/710, 81 cases). Among these, no serious adverse drug reactions were reported. Serious adverse events are listed by frequency in the table below.

		Serious adverse events 0.99% (7/710, 7 cases)
Occasional	Nervous system disorders	Seizure*, facial paralysis*

(≥0.1% to <5%)	Gastrointestinal disorders	Mechanical ileus*
	General disorders and administration site conditions	Pyrexia*
	Infections and infestations	Pneumonia*
	Injury, poisoning and procedural complications	Subdural hemorrhage*

*Unexpected serious adverse events

The unexpected adverse events and unexpected adverse drug reactions are listed by frequency in the table below.

		Unexpected adverse events regardless of causal relationship 6.06% (43/710, 62 cases)	Unexpected adverse drug reactions for which a causal relationship cannot be excluded 0.28% (2/710, 2 cases)
Occasional (≥0.1% to ≤5%)	Nervous system disorders	Seizure, Paresthesia, Headache, Tremor, Dizziness, Dementia Alzheimer's type, Facial Palsy, Hemiparesis, Parkinsonism	
	Gastrointestinal disorders	Constipation, Diarrhea, Anal hemorrhage, Stomatitis, Mechanical ileus	
	General disorders and administration site conditions	Pyrexia, Chest pain, Injection site hemorrhage, Injection site urticarial, Peripheral swelling	Injection site hemorrhage, Injection site urticaria
	Infections and infestations	Urinary tract infection, Cellulitis, Conjunctivitis, Gastroenteritis	

		Escherichia coli, Staphylococcal infection	
	Musculoskeletal and connective tissue disorders	Arthralgia, Musculoskeletal chest pain, Musculoskeletal pain, Periarthritis	
	Skin and subcutaneous tissue disorders	Blister, Eczema, Seborrhoeic dermatitis, Urticaria	
	Renal and urinary disorders	Hematuria, Hypertonic bladder, Nocturia	
	Investigations	Alanine aminotransferase increased, Aspartate aminotransferase increased, Visual field tests abnormal	
	Psychiatric disorders	Insomnia, Anxiety	
	Respiratory, thoracic and mediastinal disorders	Cough, Productive cough	
	Blood and lymphatic system disorders	Anemia	
	Endocrine disorders	Hypothyroidism	
	Eye disorders	Visual impairment	
	Hepatobiliary disorders	Nonalcoholic steatohepatitis	
	Injury, poisoning and procedural complications	Subdural hemorrhage	
	Metabolism and nutrition disorders	Hypoglycemia	
	Reproductive system and breast disorders	Menstruation irregular	

Reporting of Suspected Adverse Reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the following:

Pusat Farmakovigilans/MESO Nasional *Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif* *Badan Pengawas Obat dan Makanan* *Phone: +62-21-4244691 Ext.1079* *Email: pv-center@pom.go.id* *Website: https://e-meso.pom.go.id/ADR*	***PT Daewoong Pharmaceutical Indonesia*** *24-hour Pharmacovigilance Unit* *Phone: +62-889-7580-0212* *Email: safety_dwi@daewoong.co.kr* *Website: www.daewoong.co.id*

GENERAL PRECAUTIONS

A. This drug product contains albumin, a derivative of human blood. When a drug product derived from human blood or plasma is administered into human body, the potential of infectious diseases by transmissible agents cannot be completely excluded. It may include pathogenic agent that is still unknown. In order to minimize the risks of such infection by transmissible agents, particular cares are given to the albumin manufacturing process, including virus removal and/or inactivation processes, in addition to careful screening of donors and appropriate testing of donation units.

B. Due to the nature of the disease being treated, the effects of this drug product on the ability to drive or to operate machines cannot be predicted.

C. Glabella line/Lateral canthal lines (crow's feet lines)

Reduced blinking from botulinum toxin injection of the orbicularis muscle can lead to corneal exposure, persistent epithelial defect and corneal ulceration, especially in patients with VII nerve disorders.

Patients with skin disorders such as skin disease, infection and scars at the injection site, patients with the history of treatment of glabella part (including forehead) such as face lifting and permanent implant, patients with the history of facial nerve paralysis or the symptoms of eyelid ptosis, patients whose glabella lines cannot be satisfactorily improved with physical method since the lines are not flattened even using hands were excluded from the phase III safety and efficacy test therefore, should be warned. Injection of this product should not be more frequent than every three months and minimum effective dose should be used.

D. Upper limb spasticity

This drug product is used for the treatment of focal spasticity investigated in connection with standard treatments. It has not been shown to improve the range of motion at a joint affected by a fixed contracture.

E. Benign masseter muscle hypertrophy

Surgeries and procedures (nonmedical treatment) that may affect the masseter muscles, such as lower face contouring, high-frequency therapy, orthodontic treatment, orthognathic surgery, cosmetic procedures related to jawline lifting, and facial contouring procedures, including contour thread, were not allowed during treatment with NABOTA in the phase 3 study; therefore, caution is warranted.

F. Immunogenicity

Exposure to botulinum toxin may cause formation of neutralizing/non-neutralizing antibodies. It is known that immunogenicity is highly likely to arise from frequent treatments or use of higher doses.

PRECAUTIONS

1. Warning

Since the active ingredient of this drug product is Clostridium botulinum toxin type A which is derived from Clostridium botulinum, the information in this section should be fully understood and the recommended dosage and administration methods should be strictly followed. Physicians administering this drug product should sufficiently understand the relevant neuromuscular and/or orbital anatomy of the area involved and any alterations to the anatomy due to prior surgical procedures, and standard electromyographic techniques. The recommended dosages and administration frequencies should not be exceeded.

A. Spread of Toxin Effect

The effects of botulinum toxin products may spread from the area of injection and produce negative symptoms. The symptoms may include asthenia, generalized muscle weakness, dysphonia, dysarthria, stuttering, urinary incontinence, breathing difficulties, dysphagia, diplopia, blurred vision, and ptosis. Swallowing and breathing difficulties can be life threatening and there have been reports of death related to spread of toxin effects. The risk of symptoms is probably greatest in children treated for spastic cerebral palsy, but symptoms can also occur in adults treated for spastic cerebral palsy and other conditions. Cases of the above adverse reactions have occurred at doses comparable to those used to treat cervical dystonia and at lower doses.

B. Hypersensitivity Reactions

Serious and/or immediate hypersensitivity reactions have been reported in other botulinum toxin product. These reactions include anaphylaxis, urticaria, soft tissue edema and dyspnea. One fatal case of anaphylaxis has been reported in which lidocaine was used as a diluent, and consequently, the causal agent was not reliably determined. If such a reaction occurs, further injection of this drug product should be discontinued and appropriate medical therapy should be immediately instituted.

C. Pre-Existing Neuromuscular Disorders

Individuals with peripheral motor neuropathic diseases (e.g., amyotrophic lateral sclerosis or motor neuropathy) or neuromuscular junction disorders (e.g., myasthenia gravis or Lambert-Eaton syndrome) may be at increased risk of clinically significant systemic effects, including severe dysphagia and respiratory compromise from typical doses of this product. Published medical literatures with other botulinum toxin product have reported rare cases of administration of a botulinum toxin to patients with known or unrecognized neuromuscular disorders where patients have shown serious hypersensitivity to systemic effects of typical clinical doses. In some cases, dysphagia lasted several months and placement of a gastric feeding tube was required.

D. Dysphagia

Dysphagia is a commonly reported adverse event following treatment of cervical dystonia patients with all botulinum toxins. In these patients, there are reports of rare cases of dysphagia severe enough to warrant the insertion of a gastric feeding tube. There are also rare case reports where subsequent to the finding of dysphagia a patient developed aspiration pneumonia and died.

E. There have also been reports of adverse reactions with other botulinum toxin product, involving cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. Some of these patients had risk factors including cardiovascular disease.

F. During administration of other botulinum toxin product for treatment of strabismus, retrobulbar hemorrhages sufficient to compromise retinal circulation have occurred owing to penetration of the needle into areas surrounding eyes. It is recommended that appropriate instruments to decompress the orbit be accessible. Ocular (globe) penetrations by needles have also occurred. An ophthalmoscope to diagnose this condition should be available. Inducing paralysis in one or more extraocular muscles may produce spatial disorientation, double vision or past-pointing. Covering the affected eye may alleviate these symptoms.

G. Blepharospasm

Reduced blinking from injection of botulinum toxin into orbicularis muscle can lead to corneal exposure, persistent epithelial defect and corneal ulceration, especially in patients with VII nerve

disorders. In the use of other botulinum toxin product for treatment of blepharospasm, one case of corneal perforation in an aphakic eye requiring corneal grafting has occurred because of this effect. Careful testing of corneal sensation in eyes previously operated upon should be conducted and injection into the lower lid area should be avoided to reduce the risk of ectropion. Vigorous treatment of any epithelial defect should be employed. This may require protective drops, ointment, therapeutic soft contact lenses, or closure of the eye by patching or other means.

H. Lack of Interchangeability between Botulinum Toxin Products

Since the potency units of botulinum toxin are specific to individual products, they are not interchangeable with other botulinum toxin product. Therefore, units of biological activity of botulinum toxin cannot be compared or converted into units of any other botulinum toxin product assessed with other specific assay method.

I. Injections In or Near Vulnerable Anatomic Structures

Care should be taken when injecting in or near vulnerable anatomic structures. Serious adverse events including fatal outcomes have been reported in patients who had received botulinum toxin injected directly into salivary glands, the oro-lingual-pharyngeal region, esophagus and stomach (Safety and effectiveness have not been established for indications pertaining to these injection sites). Pneumothorax associated with injection procedure has been reported following the administration of botulinum toxin near the thorax. Caution is warranted when injecting in proximity to the lung, particularly the apices.

J. Pulmonary Effects of Botulinum Toxin in Patients with Compromised Respiratory Status Treated for Spasticity or for Detrusor Overactivity associated with a Neurologic Condition

In patients with upper limb spasticity and respiratory disorder, upper respiratory tract infections and reduced lung function (decrease in Forced Vital Capacity [FVC] ≥15%) were reported more frequently when administered with other botulinum toxin products, compared to placebo. Reduced lung functions (decrease in Forced Vital Capacity [FVC] ≥15%) were also reported in patients treated with other botulinum toxin products for detrusor overactivity associated with a neurologic condition.

K. Bronchitis and Upper Respiratory Tract Infections in Patients Treated for Spasticity

Bronchitis was reported more frequently as an adverse reaction in patients treated for upper limb spasticity with botulinum toxin, compared to placebo. In patients with reduced lung function treated for upper limb spasticity, upper respiratory tract infections were also reported more frequently as adverse reactions in patients treated with botulinum toxin compared to placebo

DRUG INTERACTIONS

A. The effects of botulinum toxin products are generally potentiated by concomitant use of aminoglycoside antibiotics or other drugs that interfere with neuromuscular transmission, e.g. tubocurarine-type muscle relaxants. Concomitant use of aminoglycosides or spectinomycin is contraindicated. Polymyxin, tetracycline and lincomycin should be carefully used in patients injected with this product.

B. The effects of administering different botulinum neurotoxin serotypes at the same time or within several months are unknown. Excessive neuromuscular weakness may be exacerbated by administration of another botulinum toxin product before the effects of a previously administered botulinum toxin disappear.

PREGNANCY & BREASTFEEDING

There are no adequate and well-controlled studies in pregnant women. An effect of this drug on maternal condition and embryofetal development was assessed following intramuscular injection of this drug (0.5, 1, 4 U/kg) into pregnant rats during the period of organogenesis (days 6 to 16 of gestation). As a result, stooped toes, paralytic gait, and curling of toes were observed in mother rats and osteopenia in fetuses in the 4U/kg dose group, but there was no statistical significance.

It is not known whether botulinum toxin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when this product is administered to a nursing woman. Administration of this product is not recommended during pregnancy or lactation.

PEDIATRIC USE

Safety and effectiveness in children and adolescents below the age of 20 years were not investigated for improvement of glabella lines.

The safety and efficacy of upper limb spasticity have not been established in children and adolescents under the age of 18 years.

NON CLINICAL SAFETY PROFILE

Non-clinical data reveal no special hazard for humans based on conventional studies for acute and repeat dose toxicity.

<u>Reproduction toxicity</u>

The potential impact of NABOTA on fertility has not been investigated in animals. In pregnant rats, daily intramuscular injections of 0.5, 1, or 4 Units/kg during the period of organogenesis (from gestation days 6 to 16), did not induce significant test article-related toxicological effects on the dams and on embryo-fetal development. Effects on peri-/postnatal development have not been evaluated.

OVERDOSAGE

Signs and symptoms of overdose are not apparent immediately after injection. Should accidental injection or oral intake occur, the person should be medically supervised for up to several weeks for signs or symptoms of systemic weakness or muscle paralysis. An antitoxin may be used in the event of immediate knowledge of overdose or wrong administration. The antitoxin will not reverse any botulinum toxin-induced muscle weakness effects already appeared by the time of antitoxin administration.

If the muscles of the oropharynx and esophagus are affected, aspiration may occur which may lead to development of aspiration pneumonia. If the respiratory muscles become paralyzed or sufficiently weakened, intubation and assisted respiration may be required until recovery takes place. Supportive care could involve the need for a tracheostomy and/or prolonged mechanical ventilation, in addition to other general supportive care. These patients should be considered for further medical evaluation and appropriate medical therapy immediately instituted, which may include hospitalization.

PRECAUTIONS IN STORAGE & HANDLING

Unopened vials of this drug product should be stored in a refrigerator (2-8°C). Reconstituted product may be stored in a refrigerator (2-8°C) for up to 24 hours after reconstitution. For safe disposal, all vials including expired vials or equipment directly contacted with the drug should be disposed as medical waste. If inactivation is required (e.g. spillages), use of dilute hypochlorite solution (0.5% or 1%) before disposal as medical waste is recommended.

PATIENT INFORMATION

Patients should be encouraged to consult with their doctor about any and all concerns over effectiveness and/or risks of this product. Careful attention should be paid to potential signs or symptoms of adverse reactions. Call your doctor or get immediate medical help if you experience any unusual symptoms after treatment with this product, including difficulty in swallowing, speaking or breathing, or muscle weakness. Such adverse reactions may happen hours to weeks after injection of this product.

This product blocks neuromuscular transmission by binding to acceptor sites on motor nerve terminals, entering the nerve terminals, and inhibiting the release of acetylcholine. When injected intramuscularly at therapeutic doses, this product produces partial chemical denervation of the muscle resulting in a localized reduction in muscle activity. In addition, the muscle may atrophy, axonal sprouting may occur, and extra junctional acetylcholine receptors may develop. There is evidence that reinnervation of the muscle may occur, thus slowly reversing muscle denervation produced by this product.

EXPERT INFORMATION

1) Pharmacological action

NABOTA blocks neuromuscular transmission by binding to receptor sites on motor nerve terminals, entering the nerve terminals, and inhibiting the release of acetylcholine.

2) Clinical studies

Lateral canthal lines

(Phase III study) An active-controlled, double-blind, randomized, multicenter study was conducted in 204 male and female adult patients (aged 18 to 75 years) who wanted to improve moderate to severe lateral canthal lines (LCLs).

The subjects were randomized to receive either NABOTA or another botulinum toxin drug to the right or left LCL. The results showed that the improvement rate of LCLs at maximum smile 4 weeks after administration as assessed by the investigator was 65.02% (132/203 subjects) at the NABOTA injection site and 62.56% (127/203 subjects) at the other botulinum toxin injection sites. The lower limit of the 95% confidence interval for the difference in the improvement rate of LCLs between the two injection sites was −0.91%, so the effectiveness of NABOTA was noninferior compared to the other botulinum toxin drug.

(Extension study) A single-arm, open-label, multicenter extension study was conducted in 109 adults who participated in the abovementioned phase 3 clinical trials and wanted to improve moderate to severe LCLs or glabellar lines (GLs). Subjects received a single dose of 24 U in the LCLs and 20 U in the GLs. The improvement rate of LCLs at maximum smile 4 weeks after administration as assessed by the investigator was similar to that observed in the phase 3 study.

Benign Masseter Muscle Hypertrophy

(Phase III study) A double-blind, randomized, placebo-controlled, multicenter study was conducted in 180 male and female adult patients aged 18 years or over who wanted to improve benign masseter muscle hypertrophy.

(Extension study) Open-label extension study with the subjects who completed the core study among the 180 randomized subjects.

A total of 114 subjects (study group (NABOTA-NABOTA): 48 subjects; control group (placebo-NABOTA): 66 subjects) who provided informed consent were enrolled in the OLE study (Open Label Extension Phase, 24 weeks). Among the 114 enrolled subjects, a total of 111 subjects (study group: 45 subjects; control group: 66 subjects) completed the OLE study, as 3 subjects were withdrawn from the study.

The study showed that the maximum improvement effect was seen at week 12 after the initial administration of the study drug (NABOTA®) compared to baseline. After the second treatment, the improvement showed a trend similar to the initial treatment in the mean change and percent change in bilateral masseter muscle thickness at maximum clenching and at rest, percent change in lower face volume, overall subject satisfaction, and proportions of subjects with MMHS $\leq$ 3 and MMHS-

S ≤ 3 at all measurement points.

Focal Upper Limb Spasticity

(Phase III study) An active-controlled, double-blind, randomized, multi-center study was conducted in 197 male and female adult patients (aged 18 years or older) who wanted to improve post stroke upper limb spasticity.

The total of 197 subjects were randomized, and 97 subjects in the NABOTA group and 98 subjects in the BOTOX group were evaluated.

The study showed that in the primary endpoint, the changes in MAS score of wrist flexor muscle tension at Week 4 after administration as assessed by the investigator were 1.44±0.72 points for the NABOTA® group and 1.46±0.77 points for the BOTOX® group, and the difference between the treatment groups was found to be 0.0129 point (95% CI: [-0.2062, 0.2319]). Since the upper limit of the 97.5% one-sided confidence interval of the difference in changes was 0.2319 and this value is lower than 0.45, which is the maximum recognized as clinically non-inferior, it was proved that the study drug, NABOTA Inj., was not inferior to the comparator, Botox Inj.

Blepharospasm

(Phase III study) A randomized, double-blind, active-controlled, multi-center study was conducted in 208 adult patients (NABOTA® group: 117 subjects, BOTOX® group: 113 subject) aged 18 years or older who wanted to improve benign essential blepharospasm.

The study showed that the improvement rate in the severity of spams of the patients assessed using Scott's scale at Week 4 after IP administration compared to before administration, between the two treatment groups was 0.04% [two-sided 95% CI (-5.21, 5.29)] which was greater than the non-inferiority margin of -10%, it was determined that the effect of NABOTA® was non-inferior to that of BOTOX®. Additionally, the difference in the improvement rate between the two groups seen in the sensitivity analysis adjusted by stratification factors was 0.05% [two-sided 95% CI (-4.65, 4.74)], indicating no statistically significant difference between the groups (p=0.9847), and the lower limit of the two-sided 95% CI (i.e., lower limit of the one-sided 97.5% CI) was -4.65%, which was greater than -10%. These results demonstrated that the efficacy of the NABOTA® group was non-inferior to that of the BOTOX® group.

PACKAGE

Box, 1 vial @ 200 Units

STORAGE & EXPIRY DATE

Store at 2-8°C in hermetic container, 36 months from the date of manufacture

Reconstituted product may be stored in a refrigerator (2-8°C) for up to 24 hours after reconstitution

Reg. No.

HARUS DENGAN RESEP DOKTER

Pada proses pembuatannya bersinggungan dengan bahan bersumber babi

MANUFACTURER

Daewoong Pharmaceutical Co., Ltd, 35-14, Jeyakgongdan 4-Gil, Hyangnam-Eup, Hwaseong-Si, Gyeonggi-Do, Korea

IMPORTED by

DAEWOONG PHARMACEUTICAL INDONESIA

PT Daewoong Pharmaceutical Indonesia

Cikarang, Indonesia

Informasi Produk Untuk Pasien

NABOTA
Toksin Botulinum Tipe A
Serbuk Injeksi 200 Unit

Nama Obat

NABOTA

Bentuk Sediaan

Serbuk injeksi

Apa yang terkandung dalam Obat?

Tiap vial mengandung:

- Zat aktif: toksin *Clostridium botulinum tipe A* – 200 Units
- Zat penstabil: Serum albumin manusia – 1.0 mg
- Zat isotonik: Natrium klorida – 1.8 mg

Pemerian obat

Serbuk injeksi, berwarna putih hingga kekuningan. Ketika dilarutkan dalam pelarut (larutan garam fisiologis), menjadi larutan jernih yang tidak berwarna.

Untuk apa Obat digunakan?

- Nabota diberikan untuk perbaikan sementara pada tampilan garis kerutan pada wajah berupa garis vertikal antara alis (garis glabella) sedang sampai parah pada pasien dewasa usia 20 sampai 65 tahun.
- Spastisitas atau kekakuan otot pada anggota gerak tubuh bagian atas yang berhubungan dengan stroke pada pasien dewasa diatas 18 tahun.
- Perbaikan sementara pada tampilan garis-garis kerutan disekitar mata sedang hingga parah yang terkait dengan aktivitas otot orbikularis okuli (otot di sekitar mata) pada orang dewasa berusia 18 hingga 65 tahun.
- Pengobatan blefarospasme esensial (kejang atau kedutan kelopak mata yang tidak terkontrol) pada orang dewasa berusia di atas 18 tahun.
- Perbaikan sementara pada otot masseter (rahang persegi) yang kentara* hingga sangat kentara** pada orang dewasa berusia 18 hingga 65 tahun.

*Yang kentara:

Pada saat istirahat, kontur wajah bagian bawah termasuk otot masseter, rahang, dan garis rahang, menunjukkan bentuk persegi, dan permukaan otot masseter sangat cembung. Saat mengepalkan tangan secara maksimal, kontur wajah bagian bawah menunjukkan perbedaan yang parah dibandingkan saat istirahat, dan massa otot masseter terasa kencang atau keras dan teraba.

** Sangat kentara:

Pada saat istirahat, kontur wajah bagian bawah, termasuk otot masseter, rahang, dan garis rahang, menunjukkan bentuk trapesium, dan permukaan otot masseter sangat cembung. Saat mengepalkan tangan secara maksimal, kontur wajah bagian bawah menunjukkan perbedaan yang mencolok dibandingkan saat istirahat, dan otot masseter keras dan teraba.

Berapa banyak dan seberapa sering obat ini boleh digunakan?

Nabota hanya boleh disuntikkan oleh dokter dengan pengalaman dan keterampilan mengenai cara penggunaan obat ini.

Dokter yang akan memutuskan jumlah obat yang diperlukan pada kondisi pasien.

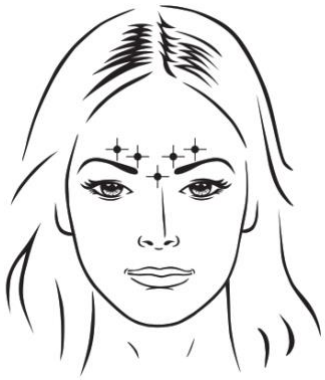
Metode dan rute administrasi

Nabota disuntikkan pada otot Anda (intramuskular). Nabota disuntikkan langsung pada area yang dimaksud; dokter Anda biasanya akan menyuntikkan **Nabota pada beberapa titik dalam area yang dimaksud.**

Informasi umum tentang dosis

- Jumlah suntikan untuk setiap otot dan dosis berbeda-beda tergantung indikasi. Untuk itu, dokter Anda akan menentukan berapa banyak, seberapa sering, dan pada otot mana Nabota akan diberikan. Direkomendasikan agar dokter Anda menggunakan dosis efektif terendah.
- Dosis untuk orang usia lanjut sama dengan dosis orang dewasa.

Dosis Nabota dan durasi dari efeknya akan berbeda-beda tergantung pada kondisi pengobatan. Di bawah ini adalah detail dari kondisi-kondisi tersebut.



Untuk mengatasi Garis Glabella

Dosis total yang diperlukan: 20 unit, diberikan pada 5 area penyuntikan yaitu pada bagian otot korugator dan otot procerus seperti pada gambar.

Tiap pengobatan berlangsung sekitar 3 sampai 4 bulan. Penyuntikan produk ini yang lebih sering tidak dianjurkan karena keamanan dan khasiat belum diketahui.

Untuk spastisitas atau kekakuan otot pada anggota gerak tubuh bagian atas

Dokter yang akan menentukan jumlah dosis dan area penyuntikan sesuai dengan kondisi pasien, termasuk tingkat kekakuan otot dan respons terhadap pengobatan sebelumnya. Anda akan mulai merasakan efek mulai dari 4 minggu setelah penyuntikan dan dapat bertahan selama 8 hingga 12 minggu.

Untuk garis kerutan disekitar mata

Dokter Anda akan menyuntikkan obat ke otot di sekitar sudut luar mata. Penyuntikan umumnya dilakukan pada 3 titik di setiap sisi mata. Efek pengobatan biasanya mulai terasa setelah penyuntikan dan dapat bertahan hingga sekitar 3 bulan.

Untuk blefarospasme atau mata kedutan

Dokter Anda akan menyuntikkan obat di area otot sekitar kelopak mata atas dan bawah. Jika kedutan pada kelopak mata cukup berat hingga mengganggu penglihatan, dokter dapat memberikan suntikan tambahan pada area alis atau sekitar mata sesuai kebutuhan. Tiap pengobatan dapat berlangsung sekitar 12 minggu.

Untuk hipertrofi otot masseter pada rahang kotak

Dosis total yang diperlukan adalah 48 unit pada area penyuntikan yaitu otot bilateral masseter di area rahang.

Pada keadaan apa Pasien tidak diperbolehkan menggunakan obat ini?

1. Jika pasien alergi terhadap komponen yang ada dalam produk ini

2. Jika pasien mengalami gangguan pada persambungan otot dan saraf
3. Wanita hamil, wanita yang kemungkinan hamil atau wanita menyusui

Pencegahan Umum

Konsultasikan dengan dokter Anda sebelum menggunakan Nabota:

- Apabila Anda memiliki atau pernah mengalami **masalah kulit** di area yang akan disuntik, seperti penyakit kulit, infeksi, atau bekas luka.
- Apabila Anda pernah menjalani **operasi pada wajah atau dahi** yang memengaruhi otot, termasuk operasi pengencangan wajah atau pemasangan implan permanen.
- Apabila Anda memiliki **riwayat kelumpuhan saraf wajah** atau mengalami **kelopak mata turun (ptosis)**.
- Apabila Anda memiliki **garis di antara alis (garis glabela)** yang tidak dapat diratakan meskipun ditekan dengan tangan.
- Apabila Anda memiliki **keterbatasan gerak sendi** akibat kontraktur yang bersifat permanen.
- Apabila Anda pernah menjalani **tindakan bedah atau prosedur nonmedis** yang dapat memengaruhi otot rahang, seperti pembentukan kontur wajah bagian bawah, terapi frekuensi tinggi, perawatan untuk merapikan gigi/ortodonti, operasi rahang, prosedur kecantikan berkaitan dengan pengencangan garis rahang, termasuk pemasangan benang tarik/benang kontur.
- Apabila Anda memiliki **riwayat penyakit yang berkaitan dengan sistem kekebalan tubuh (imun)**.
- Apabila Anda menderita **penyakit otot** atau penyakit kronis yang memengaruhi otot, seperti miastenia gravis atau *sindrom Lambert-Eaton*.
- Apabila Anda menderita **penyakit sistem saraf**, seperti *amyotrophic lateral sclerosis* (ALS) atau neuropati motorik.
- Apabila Anda menderita **distonia servikal** atau gangguan otot leher yang menyebabkan posisi kepala tidak normal.
- Apabila Anda menderita **penyakit kardiovaskular** (penyakit jantung dan pembuluh darah), termasuk gangguan irama jantung (aritmia) atau pernah mengalami serangan jantung.

Peringatan dan Perhatian

Konsultasikan dengan dokter apabila Anda memiliki pertanyaan atau kekhawatiran mengenai manfaat dan risiko penggunaan produk ini. Perhatikan apabila muncul gejala yang tidak biasa setelah penyuntikan.

Segera cari pertolongan medis jika Anda mengalami kesulitan menelan, berbicara, bernapas, atau kelemahan otot, karena gejala tersebut dapat muncul beberapa jam hingga beberapa minggu setelah penyuntikan.

Produk ini bekerja dengan mengurangi aktivitas otot sementara, sehingga otot menjadi lebih rileks. Efek ini akan berangsur hilang seiring waktu.

Penggunaan produk ini harus sesuai dengan petunjuk dokter dan tidak boleh dilakukan terlalu sering.

Efek toksin botulinum dapat menyebar dari area suntikan dan menimbulkan gejala yang tidak diinginkan, seperti kelelahan atau kelemahan tubuh, kelemahan otot menyeluruh, gangguan suara, gangguan bicara, gagap, sulit menahan buang air kecil, kesulitan bernapas, kesulitan menelan, penglihatan ganda, penglihatan kabur, serta kelopak mata turun. Risiko ini dapat meningkat pada pasien dengan kondisi medis tertentu yang membuatnya lebih rentan terhadap efek tersebut.

Apabila terjadi reaksi alergi serius setelah penggunaan produk ini, seperti reaksi anafilaksis, biduran, pembengkakan jaringan lunak, atau sesak napas, segera hubungi dokter atau fasilitas kesehatan. Pemberian suntikan lanjutan harus dihentikan.

Penggunaan toksin botulinum pada area mata, termasuk untuk pengobatan mata juling atau kedutan kelopak mata yang tidak terkontrol, dapat meningkatkan risiko gangguan mata, seperti penurunan frekuensi kedipan, iritasi permukaan mata, penglihatan ganda, atau cedera mata. Untuk mencegah hal ini, Anda mungkin memerlukan perawatan seperti tetes mata, salep mata, atau penutup mata atau perlindungan lainnya. Dokter Anda akan memberitahukan apabila hal-hal tersebut diperlukan

Penyuntikan toksin botulinum harus dilakukan dengan sangat hati-hati, terutama pada area tubuh yang sensitif. Pada lokasi tertentu, efek samping serius bahkan berisiko mengancam jiwa dapat terjadi. Penyuntikan di area dekat dada juga dapat memengaruhi fungsi paru-paru. Oleh karena itu, prosedur ini harus dilakukan oleh dokter yang berpengalaman dan dengan kehati-hatian tinggi.

Pada pasien dengan gangguan pernapasan atau yang menjalani pengobatan spastisitas, penggunaan toksin botulinum dapat meningkatkan risiko infeksi saluran pernapasan dan

penurunan fungsi paru. Pasien dengan kondisi tersebut memerlukan pemantauan khusus selama pengobatan. Dokter akan menilai manfaat dan risiko sebelum pemberian serta memberikan penjelasan apabila diperlukan pemeriksaan atau tindakan tambahan.

Apa yang perlu diperhatikan jika menggunakan obat ini?

Jika Anda mengalami gejala berikut ini, segera konsultasikan kepada dokter

1. Kelemahan otot secara umum, gagap, gangguan berkemih, kesulitan bernafas, kesulitan menelan, pandangan kabur dan lain-lain.
2. Jika terjadi reaksi alergi
3. Kesulitan menelan
4. Gangguan pada jantung
5. Riwayat gangguan otot-saraf / neuromuscular

Efek samping apa yang mungkin terjadi?

Seperti semua obat pada umumnya, obat ini dapat menyebabkan efek samping, meskipun tidak semua orang mengalaminya. Secara umum, efek samping terjadi dalam beberapa hari pertama setelah penyuntikan.

Seperti yang diperkirakan pada prosedur penyuntikan lainnya, rasa nyeri/terbakar/tersengat, bengkak, kelemahan otot, kelelahan, dan atau memar dapat diasosiasikan dengan penyuntikan.

Efek samping dapat diklasifikasikan menjadi kategori-kategori berikut, tergantung dari seberapa sering efek samping ini terjadi:

Sangat sering	≥10%
Sering	≥1% dan <10%
Tidak sering	≥0.1% dan <1%
Jarang	≥0.01% dan <0.1%
Sangat jarang	<0.01%

Dibawah ini adalah daftar efek samping yang bervariasi tergantung pada bagian tubuh dimana NABOTA disuntikka. Apabila efek samping ini menjadi serius, atau apabila Anda merasakan efek samping yang tidak tertera dalam leaflet ini, beritahukan pada dokter atau apoteker Anda.

Injeksi (suntikan) untuk garis-garis dahi (garis glabellar)

Sering	• Kelopak mata terkulai • Kenaikan alis • Vertigo

Injeksi (suntikan) pada spastisitas / kekakuan otot tungkai atas

Sering	• Kelemahano tot • Nyeri pada anggota tubuh bagian atas • Penghilangan massa otot

Injeksi (suntikan) pada kontraksi otot kelopak mata yang tidak normal (*blefarospasme*)

Sering	• Reaksi pada lokasi injeksi (memar, bengkak, peradangan)
Tidak sering	• Radang pada kelopak mata • Mata kering • Mata mengantuk • Sensasi benda asing • Gangguan sistem air mata • Pusing

Injeksi (suntikan) pada otot masseter (rahang persegi)

Sering	• Ganggunan mengunyah • Reaksi pada Lokasi injeksi

Pelaporan efek samping

Jika Anda mengalami efek samping, beritahukan dokter atau apoteker Anda. Hal ini termasuk efek samping yang mungkin terjadi yang belum tercantum di leaflet ini.

Anda dapat juga melaporkan keluhan efek samping atau kondisi tidak nyaman tersebut secara langsung ke Industri Farmasi melalui kontak berikut:

PT Daewoong Pharmaceutical Indonesia
Unit Farmakovigilans 24 Jam
Telepon: +62-889-7580-0212
Email: safety_dwi@daewoong.co.kr

Dengan melaporkan efek samping, Anda dapat membantu menyediakan informasi keamanan lebih lanjut dari obat ini.

Obat dan Makanan apa yang harus dihindari jika menggunakan obat ini?

1. Obat relaksan otot seperti tubokurarin klorida, natrium dantrolene
2. Antibiotik golongan aminoglikosida (gentamisin sulfat, neomisin sulfat), antibiotic golongan peptide (polimiksin B sulfat, antibiotik tetrasiklin, antibiotic linkomisin
3. Obat antikolinergik seperti skopolamin butilbromida, triheksifenidil, benzodiazepine dan lain-lain

4. Penggunaan bersamaan produk toksin botulinum lain.

Apakah boleh digunakan pada wanita hamil dan menyusui?

Tidak

Apakah boleh digunakan pada anak-anak?

Tidak

Tanda dan gejala kelebihan dosis

Tanda dan gelaja kelebihan dosis tidak terlihat dengan jelas segera setelah penyuntikan. Jika terjadi kelemahan otot, kesulitan bernapas, segera hubungi dokter atau unit pelayanan kesehatan terdekat.

Apakah boleh mengendarai dan menjalankan mesin selama menggunakan obat ini?

Efek obat ini terhadap kemampuan konsentrasi saat mengendarai dan menjalankan mesin tidak diketahui

Bagaimana cara menyimpan obat ini?

Vial obat yang belum dibuka harus disimpan dalam lemari es (2-8°C); masa kadaluarsa adalah 36 bulan setelah tanggal produksi yang tertera pada kemasan.

Obat yang telah dilarutkan dapat disimpan dalam kulkas (2-8°C) sampai 24 jam setelah dilarutkan. Untuk pembuangan yang aman, semua vial termasuk vial yang telah kadaluarsa atau peralatan yang langsung berhubungan dengan obat harus dibuang sebagai limbah medis. Jika tumpah maka gunakan larutan encer hipoklorit (0.5% atau 1%) sebelum dibuang sebagai limbah medis.

KEMASAN

Dus, 1 vial @ 200 Unit

Nomor Registrasi

HARUS DENGAN RESEP DOKTER

Pada proses pembuatannya bersinggungan dengan bahan bersumber babi

DISETUJUI OLEH BPOM: 03/03/26 ID EREG17228912500015

DIPRODUKSI OLEH

Daewoong Pharmaceutical Co., Ltd.,

35-14, Jeyakgongdan 4-gil, Hyangnam-Eup, Hwaseong-Si, Gyeonggi-Do

Korea

DIIMPOR OLEH

DAEWOONG PHARMACEUTICAL INDONESIA

PT Daewoong Pharmaceutical Indonesia

Cikarang, Indonesia

DISETUJUI OLEH BPOM: 03/03/26 ID EREG17228912500015

Contact	Design	QC	RA
	문동혁	-	염종선
Date	2025.08.18_1		

나보타 인쇄사양서
(Printing Specification for NABOTA)

변경관리 번호(Change Control Number)
PR-41281, PR-49338
주요 변경사항(Major changes)
허가 변경(C동 감압제형으로 변경) Change in Approval(Change to vacuum dried powder in building C)
한도견본의 색상 농도와 동일하게 색상 맞춤 Change the artwork to match the color concentration of the master sample
인쇄사양서 번호(Printing specification no.)
D-2300139-01
자재명(Component name)
나보타 Label(200U_인도네시아) Nabota Label(200U_ID)
인쇄자재 개정번호(Edition no. of printing material)
2300139ID-01
치수(Pitch)
64 x 25 mm
재질(Material)
ART - 60 g/m²
인쇄(Printing)
부분 홀로그램 콜드박 Partial Hologram cold stamping foil
코팅(Coating)
N/A
후가공(Post-processing)
홀로그램 은박 Hologram silver foil
접착 유형(Adhension type)
강접(Strong Adhesion)
바코드(Barcode)
N/A
비고(Remark)
라벨 풀림방향: 우출 Label roll direction: Right edge first
최대 롤 지름: 300 mm Maximum roll diameter: 300 mm
지관 사이즈: 75 mm Paper core tube size: 75 mm
로스 2 m 추가 Addition of loss 2 m
제조번호, 제조일자, 유효기한 인쇄소 착인 Lot no., Mfg. date, Exp. date will be printed by Printing company
인쇄 색상(Printing color)
CYAN
MAGENTA
YELLOW
BLACK
PANTONE Bright Red C
인쇄 도수(No. of Printing color)

전면 (Front Side)	원색 4도 + 별색 1도 CMYK 4 + PANTONE 1
후면 (Back Side)	N/A

Form info.: NQC01-019-F15 (Ver. 1.0)

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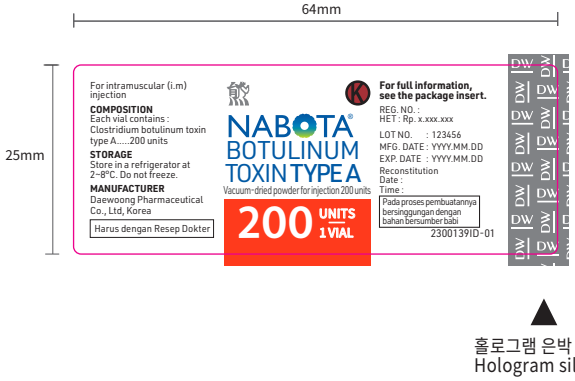
Roll Direction
풀림 방향

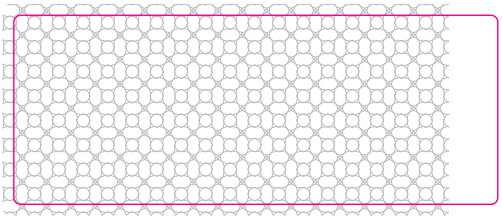
[Label / 라벨]

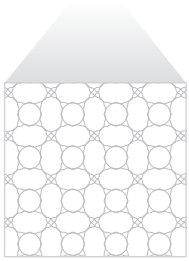


홀로그램 은박
Hologram silver foil

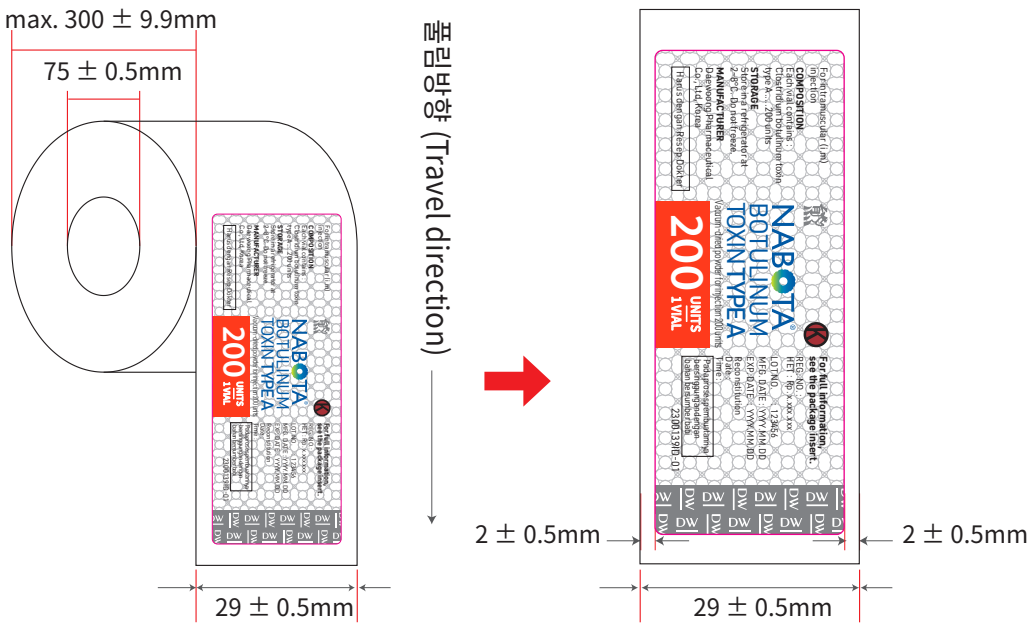
[Hologram Cold Stamping Foil / 홀로그램 콜드박]

Cold Stamping Foil Stroke: 0.2pt
콜드박 호일 스트로크: 0.2pt





[Detail of the pattern / 패턴 디테일]
Attention to detail of the pattern of a Cold Stamping Foil
콜드박 호일 패턴의 세부사항을 확인해주세요.



DISETUJUI OLEH BPOM: 03/03/26

ID EREG17228912500015

Contact	Design	QC	RA
	문동혁	-	염종선
Date	2025.08.18_1		

나보타 인쇄사양서
(Printing Specification for NABOTA)

변경관리 번호(Change Control Number)
PR-79282
주요 변경사항(Major changes)
후면 인쇄 삭제 Deletion of backside printing
인쇄사양서 번호(Printing specification no.)
D-2300140-03
자재명(Component name)
나보타 Case(200U_인도네시아) Nabota Case(200U_ID)
인쇄자재 개정번호(Edition no. of printing material)
2300140ID-02
치수(Pitch)
48 x 40 x 79mm
재질(Material)
CCP – 300 g/m²(종이 색상 편차 주의) (Paper color variation caution)
인쇄(Printing)
N/A
코팅(Coating)
무광 라미네이팅(전면), 무광 CR(후면) Matte laminating(Front), Matte CR(Back)
부분 실크 코팅(소량 필) Partial silk coating(little pearl)
후가공(Post-processing)
오시(Creasing)
절취선(Perforation line)
접착 유형(Adhension type)
자동 포장용 단면 접착 Regular slotted container
바코드(Barcode)
파마코드(Pharma code): 32002
비고(Remark)
제조번호, 제조일자, 유효기한 인쇄소 착인 Lot no., Mfg. date, Exp. date should be printed by printing company
인쇄 색상(Printing color)
CYAN
MAGENTA
YELLOW
BLACK
PANTONE 369 C
PANTONE Bright Red C
인쇄 도수(No. of Printing color)

전면 (Front Side)	원색 4도 + 별색 2도 CMYK 4 + PANTONE 2
후면 (Back Side)	N/A

Form info.: NQC01-019-F15 (Ver. 1.0)

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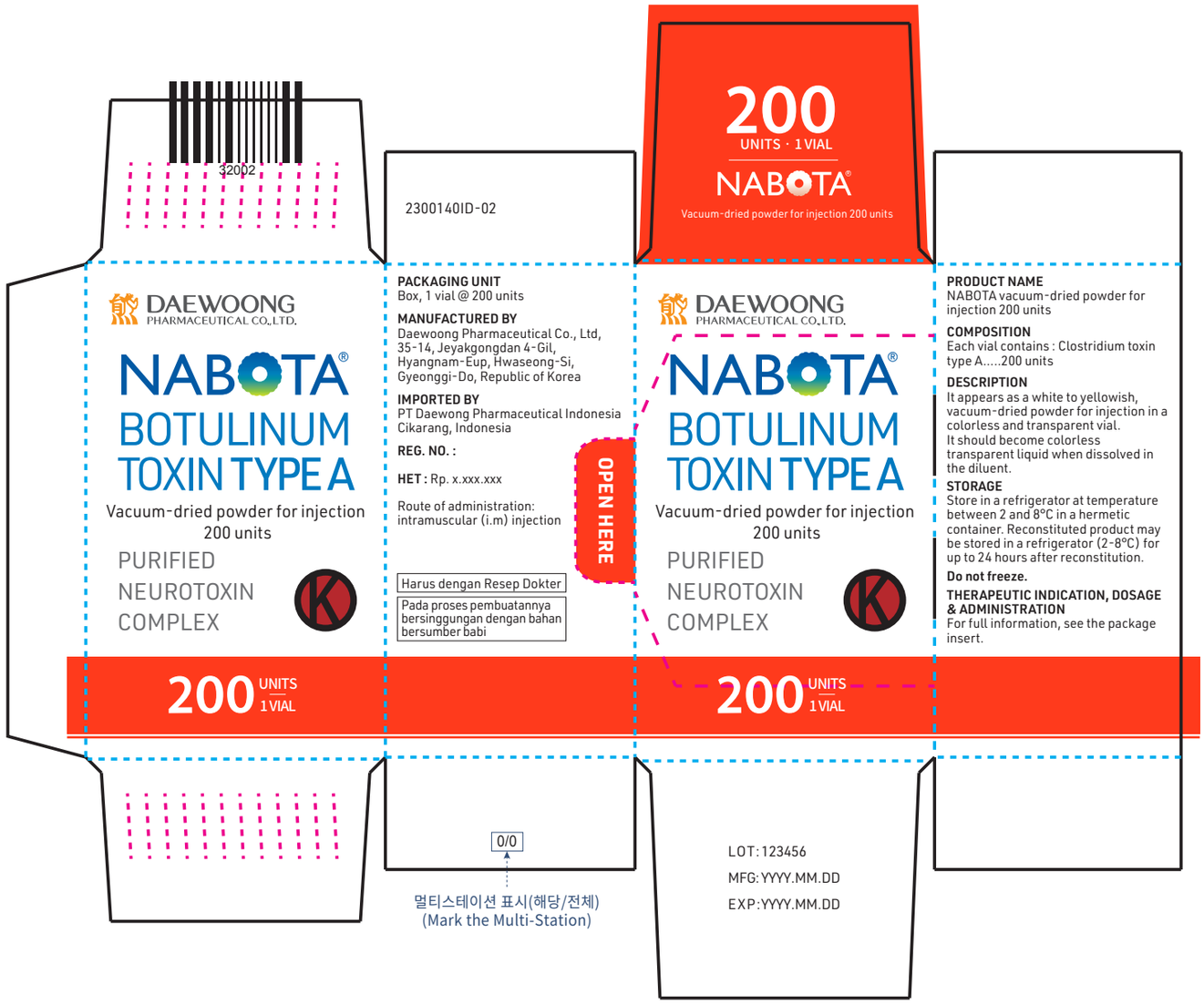
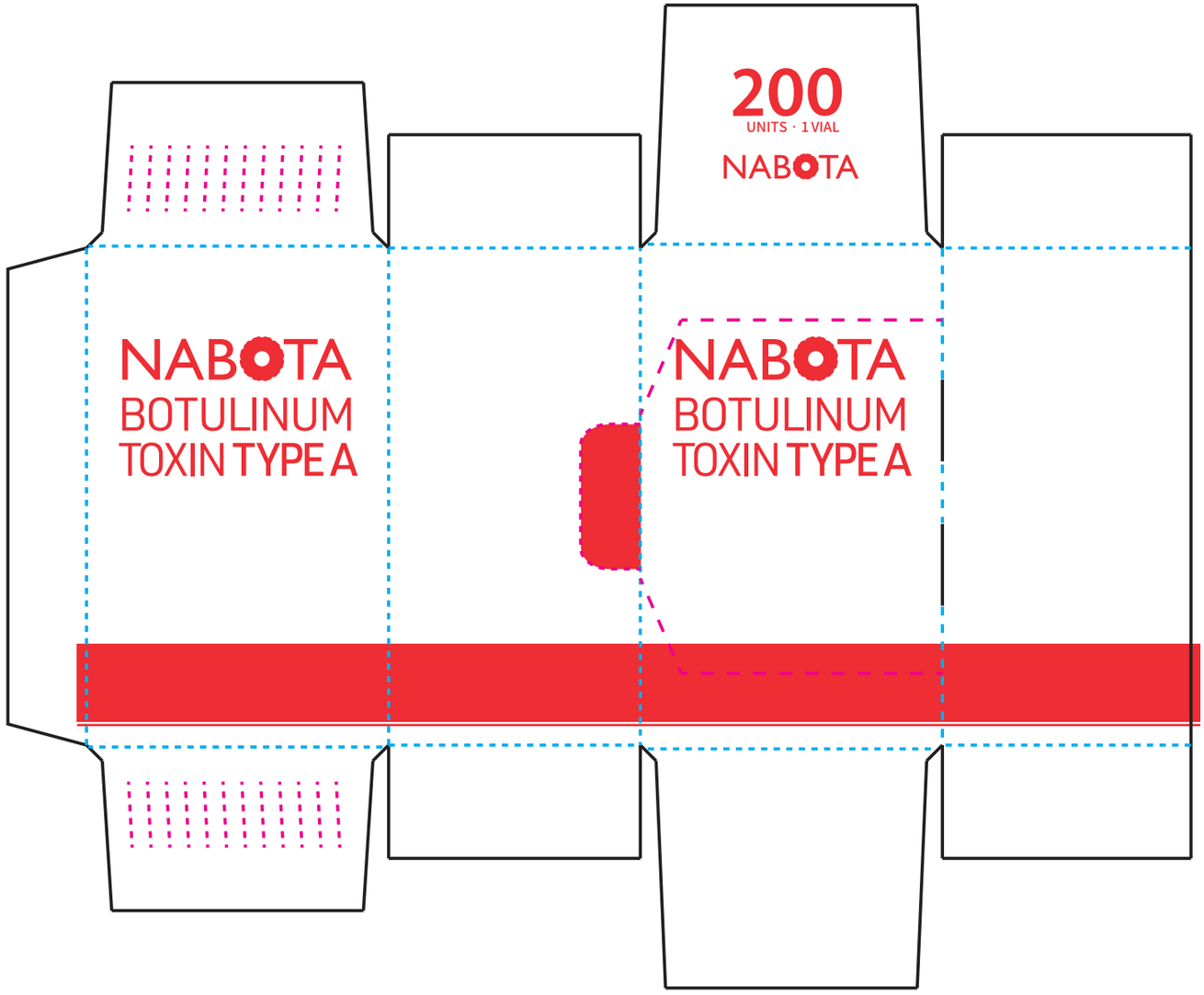


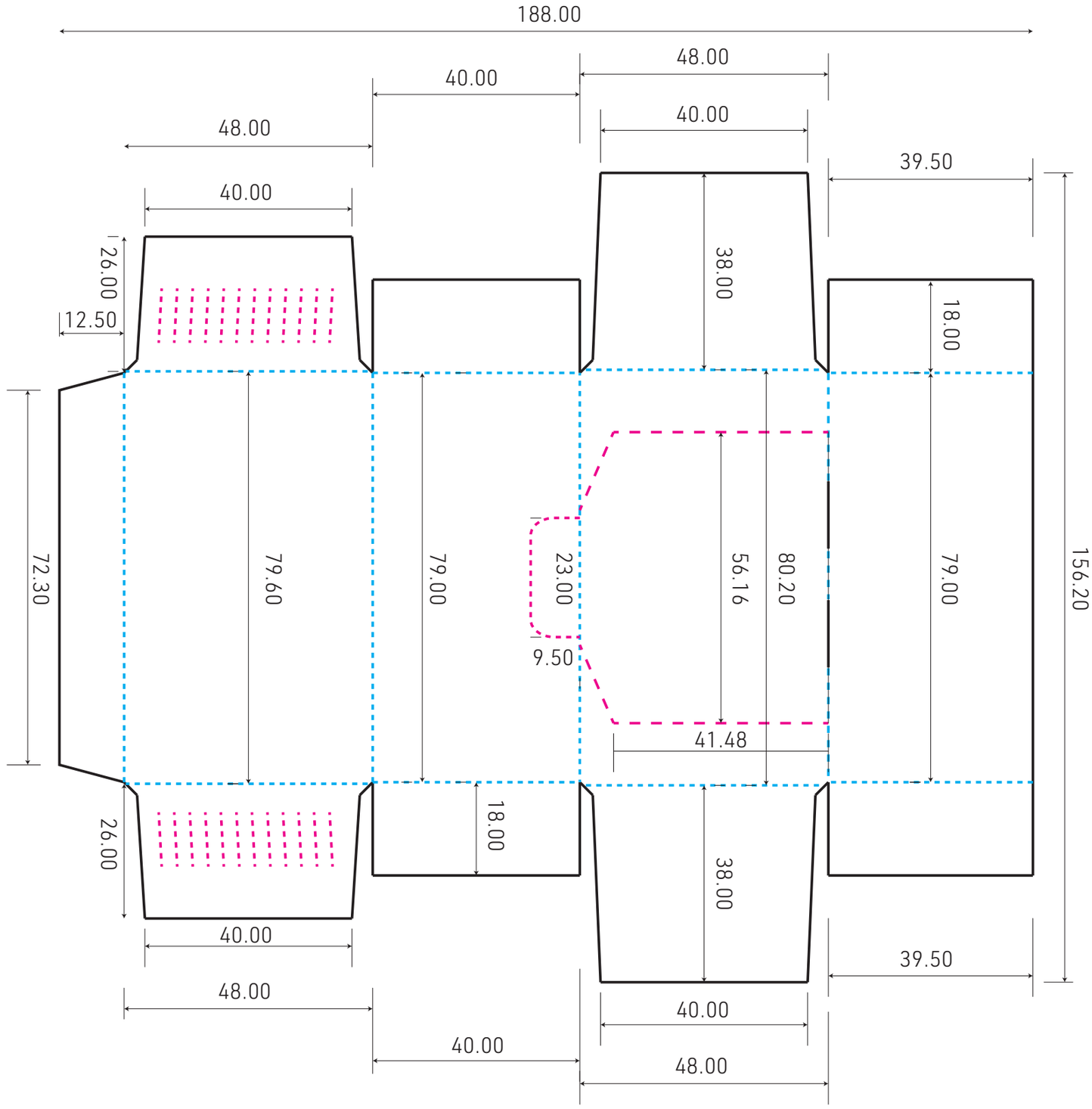
DISETUJUI OLEH BPOM: 03/03/26

ID EREG17228912500015



DISETUJUI OLEH BPOM: 03/03/26

ID EREG17228912500015



DISETUJUI OLEH BPOM: 03/03/26

ID EREG17228912500015