New Zealand Data Sheet

1. PRODUCT NAME

NABOTA® 100 units (U) Powder for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Prabotulinumtoxin A*, 100 Units/vial.
* from *Clostridium botulinum*

Botulinum toxin units are not interchangeable from one product to another.

Excipient(s) with known effect

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

It appears as a white to yellowish, vacuum dried powder for injection in a colourless and transparent vial.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

The temporary improvement in the appearance of moderate to severe glabellar lines in adult patients < 65 years of age.

4.2. Dose and method of administration

Dose

For Intramuscular Use Only

The potency Units of NABOTA are specific to the preparation and assay method utilized. They are not interchangeable with other preparations of botulinum toxin products and, therefore, Units of biological activity of NABOTA cannot be compared to or converted into Units of any other botulinum toxin products assessed with any other specific assay method.

Treatment should be administered at no more than the recommended dose and interval.

Injection intervals of NABOTA should be no more frequent than every three months.

Adults

Glabellar Lines

Four (4) Units should be injected intramuscularly at each of five injection sites, 2 in each corrugator muscle and 1 in the procerus muscle for a total dose of 20 Units (see Figure 1).

Typically, NABOTA indices chemical denervation of the injected muscles two days after injection, increasing in effect during the first two weeks.

Special populations

Elderly population

The clinical data for subjects ≥ 65 years of age are limited. No specific dose adjustment is required for use in the elderly.

Paediatric population

NABOTA is not recommended for use in children.

Method of Administration

Glabellar facial lines arise from the activity of the corrugator and orbicularis oculi muscles. These muscles move the brow medially, and the procerus and depressor supercilii pull the brow inferiorly. This creates a frown or "furrowed brow". The location, size, and use of the muscles can vary among individuals. Lines induced by facial expression occur perpendicular to the direction of action of contracting facial muscles.

Physicians administering NABOTA must understand the relevant neuromuscular and/or orbital anatomy of the area involved and any alterations to the anatomy due to prior surgical procedures.

In order to reduce the incidence of eyelid ptosis the following steps should be taken:

- Avoid injection near the levator palpebrae superioris, particularly in patients with larger brow depressor complexes.
- Lateral corrugator injections should be placed at least 1 cm above the bony supraorbital ridge.
- Do not inject toxin closer than 1 centimetre above the central eyebrow.
- Ensure the injected volume/dose is accurate and where feasible kept to a minimum.
- The use of one vial for more than one injection session or one patient is not recommended because the product and diluent do not contain a preservative.

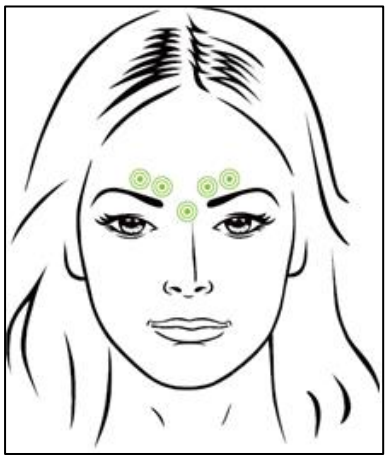
Following reconstitution (see below), the needle used could remain in the vial and the required amount of solution drawn up with a new sterile syringe suitable for injection, preferably a 1.0mL tuberculin syringe. Draw at least 0.5 mL of the properly reconstituted toxin into the syringe and expel any air bubbles seen in the barrel. Disconnect the syringe and attach a sterile 30 gauge needle.

Inject a dose of 0.1 mL (4 Units) intramuscularly into each of 5 sites, the inferomedial and superior middle of each corrugator and 1 in the mid-line of the procerus muscle for a total dose of 20 Units (see Figure 1).

NABOTA vials are for single-use only. Discard remaining solution.

For instructions on reconstitution of the medicine before administration, see section 6.6.

Figure 1. Injection Sites



4.3. Contraindications

- Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.
- Infection or inflammation at the proposed injection sites.

4.4. Special warnings and precautions for use

DISTANT SPREAD OF TOXIN EFFECT: The effects of NABOTA and all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. These symptoms have been reported hours to weeks after injection. Swallowing and breathing difficulties can be life-threatening and there have been reports of death. The risk of symptoms is probably greatest in children treated for spasticity but symptoms can occur in adults, particularly in those patients who have underlying conditions that would predispose them to these symptoms.

The term "Unit" upon which dosing is based, is a specific measurement of toxin activity that is unique to this formulation of Botulinum toxin Type A. Therefore, the Units used to describe NABOTA activity are different from those used to describe that of other botulinum toxin preparations and the Units representing NABOTA activity are not interchangeable with other products.

NABOTA should only be administered by physicians with the appropriate qualifications and experience in the use of botulinum toxins.

General

Use NABOTA only as directed. Injection intervals of NABOTA should be no more frequent than every three months. Indication-specific dosage and administration recommendations should be followed.

Do not use dosage recommendations and potency Units applied to other botulinum toxin products when using NABOTA. Do not exceed the recommended dosage and frequency of administration of NABOTA.

The safe and effective use of NABOTA depends upon proper storage of the product, selection of the correct dose, reconstitution, and injection technique.

Caution should be exercised when administering NABOTA to patients with neuromuscular junction disorders or when excessive weakness or atrophy is present in the target muscle, and in patients with prolonged bleeding times, surgical alterations to the facial anatomy, marked facial asymmetry, inflammation at the injection site(s), ptosis, excessive dermatochalasis, deep dermal scarring, or thick sebaceous skin.

Local muscle weakness represents the expected pharmacological action of botulinum toxin in muscle tissue. Muscle weakness remote to the site of injection and other serious adverse effects have been very rarely reported in the cosmetic applications. Progressive signs or symptoms of muscular weakness remote to the site of injection may include ptosis and diplopia, as well as other serious adverse effects including swallowing and speech disorders.

Patients with a history of underlying neurologic disorders, dysphagia and/or aspiration are at a greater risk of these effects and should be treated with extreme caution. The botulinum toxin product should be used under specialist supervision in these patients and should only be used if the benefit of treatment is considered to outweigh the risk.

Patients or caregivers should be advised to seek immediate medical care if swallowing, speech or respiratory disorders arise.

This product contains human serum albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases. The theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD) also is considered extremely remote. No known cases of transmission of viral diseases or CJD have been identified for human serum albumin.

Cardiovascular

There have been reports following administration of other botulinum toxin products of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. Some of these patients had risk factors including pre-existing cardiovascular disease. Use caution when administering to patients with pre-existing cardiovascular disease.

Immune

with all biologic products, an anaphylactic reaction may occur. Necessary precautions should be taken and epinephrine should be available. Serious and/or immediate hypersensitivity reactions such as anaphylaxis and serum sickness have been rarely reported, as well as other manifestations of hypersensitivity including urticaria, soft tissue edema, and dyspnea.

Treatment with botulinum toxins may result in the formation of antibodies that may reduce the effectiveness of subsequent treatments by inactivating biological activity of the toxin. The results from some studies suggest that botulinum toxin injections at more frequent intervals or at higher doses may lead to greater incidence of antibody formation.

The presence of antibotulinum antibodies in subjects receiving NABOTA was evaluated in two single dose Phase III studies (EV-001and EV-002) and one repeat dose Phase II study (EV006). There were no cases of seroconversion with NABOTA. One subject who had a history of exposure to botulinum toxin and tested positive at baseline did not respond to treatment.

The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to NABOTA with the incidence of antibodies to other products may be misleading.

Neurologic

Caution should be exercised when administering NABOTA to individuals with peripheral motor neuropathy (e.g. amyotrophic lateral sclerosis or other motor neuropathy), facial palsy or neuromuscular junctional disorders (e.g. myasthenia gravis or Lambert-Eaton syndrome). Patients with neuromuscular disorders may be at an increased risk of clinically significant systemic effects such as severe dysphagia and respiratory compromise. There have been rare cases of administration of a botulinum toxin to patients with known or unrecognized neuromuscular junction disorders where the patients have shown extreme sensitivity to the systemic effects of typical clinical doses. In some of these cases, dysphagia has lasted several months and required placement of a gastric feeding tube.

Ophthalmologic

Caution should be exercised when administering NABOTA to individuals with eye disorders, including dry eye and eyelid oedema.

Risk of ptosis can be mitigated by careful examination of the upper lid for separation or weakness of the levator palpebrae muscle (true ptosis) and evaluation of the range of lid excursion while manually depressing the frontalis to assess compensation. The potential risk of localized muscle weakness or visual disturbances linked with the use of NABOTA may temporarily impair the ability to drive or operate machinery.

Skin

Caution should be exercised when administering NABOTA to patients with inflammation at the injection site(s), deep dermal scarring, or thick sebaceous skin. As is expected for any injection procedure, localized pain, inflammation, paresthesia, hypoesthesia, tenderness, swelling/edema, erythema, localized infection, bleeding and/or bruising have been associated with injections.

Monitoring and Laboratory Tests

There are no specific requirements for laboratory test monitoring when patients are treated with NABOTA.

4.5. Interaction with other medicines and other forms of interaction

No formal drug interaction studies have been conducted with NABOTA.

Patients treated concomitantly with botulinum toxins and aminoglycosides or other agents interfering with neuromuscular transmission (e.g., curare-like agents) should be observed closely because the effect of the botulinum toxin may be potentiated. Use of anticholinergic drugs after administration of NABOTA may potentiate systemic anticholinergic effects such as blurred vision.

The effect of administering different botulinum toxin products at the same time or within several months of each other is unknown. Excessive weakness may be exacerbated by another administration of botulinum toxin prior to the resolution of the effects of a previously administered botulinum toxin.

Excessive weakness may also be exaggerated by administration of a muscle relaxant before or after administration of NABOTA.

Drug-Drug Interactions

Interactions with other drugs have not been established.

Table 1: Potential Drug-Drug Interactions

Proper/Common Name of Drug	Source of Evidence	Effect	Clinical Comment
aminoglycoside antibiotics or other medicinal products that interfere with neuromuscular transmission (e.g. curare-like agents, lincosamides, polymyxins, and anticholinesterases)	T	Theoretically, the effect of botulinum toxin may be potentiated	The effect of botulinum toxin may be potentiated by aminoglycoside antibiotics or other drugs that interfere with neuromuscular transmission. Caution should be exercised when NABOTA is used with aminoglycosides or any other drugs that interfere with neuromuscular transmission.
different botulinum neurotoxin serotypes	T	Unknown	The effect of administering different botulinum neurotoxin serotypes at the same time or within several months of each other is unknown. Excessive weakness may be exacerbated by administration of another botulinum toxin prior to the resolution of the

			effects of a previously administered botulinum toxin.

T = Theoretical

Drug-Food Interactions

Interactions with food have not been established

Drug-Herb Interactions

Interactions with herbal products have not been established

Drug-Laboratory Test Interactions

Interactions with laboratory test have not been established

Drug-Lifestyle Interactions

Lifestyle interactions have not been established

4.6. Fertility, pregnancy and lactation

Pregnancy

There is limited data from the use of Botulinum toxin Type A in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or postnatal development other than at high doses causing maternal toxicity. The potential risk to pregnant women is unknown. NABOTA should not be used during pregnancy. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be informed of the potential risks, including abortion or foetal malformations, which have been observed in rabbits.

Breast-feeding

It is unknown if the drug is excreted in human milk. The excretion of NABOTA in milk has not been studied in animals. Because many drugs are excreted in human milk precaution should be exercised. The use of NABOTA during lactation is not recommended.

Fertility

No studies have been conducted for NABOTA to evaluate the potential of fertility impairment.

4.7. Effects on ability to drive and use machines

NABOTA may cause loss of strength or general muscle weakness, blurred vision, or drooping eyelids within hours to weeks after injection. If this happens, patients should be advised not drive a car, operate machinery, or do other dangerous activities.

4.8. Undesirable effects

Adverse reaction overview

Adverse reactions may occur within the first few days following injection and while generally transient may have a duration of several months.

Local muscle weakness represents the expected pharmacological action of botulinum toxin in muscle tissue; however, weakness of adjacent muscles associated with local diffusion and/or injection technique has been reported. Muscle weakness remote to the site of injection and other serious adverse effects have been very rarely reported in the cosmetic application.

As is expected for any injection procedure, localized pain, inflammation, paresthesia, hypoesthesia, tenderness, swelling/oedema, erythema, localized infection, bleeding and/or bruising have been associated with injections. Needle-related pain and/or anxiety have resulted in vasovagal responses, including transient symptomatic hypotension and syncope.

Clinical Trial Adverse Reactions

Because clinical trials are conducted under very specific conditions, the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

Adverse events were evaluated in subjects receiving 20 U of NABOTA in the glabellar region in three single dose Phase III studies (EV-001, EV-002 and EVB-003; Table 2), and one repeat dose EV-006 study where 570 subjects could receive repeat treatments every 3 months up to a possible maximum total dose of 80 U. The demographics were similar in these studies: mean age was 50.3 years, 89.7% of the subjects were female, and commonly identified races were 83.6% White and 5.3% Black. Most treatment emergent adverse events (TEAEs) were mild to moderate in severity and none considered study drug related were serious.

Table 2. Treatment-emergent adverse events with > 1% incidence following a single dose of 20 Units in the glabellar region

System Organ Class and Preferred Term	Pooled Placebo (N=211) %	Pooled Single Dose (N=737) %
All AEs in ≥ 1% of subjects	21.8	22.7
Nervous System Disorders	**13.3**	**12.3**
Headache	13.3	12.3
Infections and Infestations	**7.6**	**8.8**
Gastroenteritis viral	1.4	0.4
Influenza	0.9	0.7
Nasopharyngitis	1.4	3.5
Sinusitis	2.4	0.9
Upper respiratory tract infection	1.4	1.8
Eye Disorders	**0.0**	**1.6**
Eyelid ptosis	0.0	1.6
Vascular Disorders	**0.9**	**0.5**
Hypertension	0.9	0.5

In the pooled single dose Phase III studies, all TEAEs with an incidence >1%, included headache, viral gastroenteritis, influenza, nasopharyngitis, sinusitis, upper respiratory tract infection, eyelid ptosis and hypertension. Common TEAEs that were considered study drug related included

headache, 7.6% in placebo and 9.4% in the NABOTA group, and eyelid ptosis with 0% in placebo and 1.2% in the NABOTA group.

Other TEAEs that were less frequent included dysphagia, dysphonia, paresthesia, pyrexia, urinary tract infection, urticaria and increased white blood cell count. Less frequent TEAEs considered study drug related included blepharospasm, blurred vision, diplopia, dry eye, eyebrow ptosis, eyelid edema, muscle twitching and injection site bruising.

In one year, open label, multi-dose Study EV-006, all TEAE's that occurred with an incidence of >1% included headache, bronchitis, nasopharyngitis, sinusitis, upper respiratory tract infection, urinary tract infection, contusion, contact dermatitis, pain in extremity, eyelid ptosis, cough, hypertension and injection site reactions (e.g. bruising/pain/swelling/pruritus). Headache and eyelid ptosis were the only study drug related TEAE's with an incidence of >1%.
The presence of antibotulinum antibodies in subjects receiving NABOTA was evaluated in two single dose Phase III studies (EV-001and EV-002) and one repeat dose Phase II study (EV-006). There were no cases of seroconversion with NABOTA. One subject who had a history of exposure to botulinum toxin and tested positive at baseline did not respond to treatment.

Post-Market Adverse Reactions

NABOTA contains the same active ingredient as other botulinum toxin containing products. Therefore, adverse events observed with these products also have the potential to be associated with the use of NABOTA.

Adverse reactions reported during post-marketing and not reflected elsewhere in the datasheet include the following:
Ear and labyrinth disorders: Vertigo
Eye disorders: Periorbital haematoma
Gastrointestinal disorders: Dry mouth, Nausea
General disorders: Asthenia, Malaise
Immune system disorders: Hypersensitivity
Investigations: Neutralizing antibodies
Nervous system disorders: Amyotrophy, Burning sensation, Dizziness, Dysarthria, Facial paresis, Hypoaesthesia
Renal and urinary disorders: Urinary incontinence
Respiratory, thoracic and mediastinal disorders: Dyspnea
Skin and subcutaneous tissue disorders: Erythema, Excessive granulation tissue.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected reactions https://nzphvc.otago.ac.nz/reporting/

4.9. Overdose

Excessive doses of NABOTA may be expected to produce neuromuscular weakness with a variety of symptoms. Respiratory support may be required when excessive doses cause paralysis of respiratory muscles. In the event of overdose, the patient should be medically monitored for

symptoms of excessive muscle weakness or muscle paralysis. Symptomatic treatment may be necessary.

Symptoms of overdose are not likely to be present immediately following injection. Should accidental injection or oral ingestion occur, the person should be medically supervised for several weeks for signs and symptoms of excessive muscle weakness or paralysis.
The antitoxin will not reverse any botulinum toxin-induced effects already apparent by the time of antitoxin administration.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Neuromuscular blocking agent; ATC code: M03AX01
NABOTA inhibits release of the neurotransmitter, acetylcholine, from peripheral cholinergic nerve endings, causing a flaccid paralysis of muscles. Toxin activity occurs in the following sequence: toxin heavy chain mediated binding to specific surface receptors on nerve endings, internalization of the toxin by receptor mediated endocytosis, pH-induced translocation of the toxin light chain to the cell cytosol and cleavage of SNAP25 leading to intracellular blockage of neurotransmitter (acetylcholine) exocytosis into the neuromuscular junction. This accounts for the therapeutic utility of the toxin in diseases characterized by excessive efferent activity in motor nerves.

Recovery of transmission occurs gradually as the neuromuscular junction recovers from SNAP25 cleavage and as new nerve endings are formed.

Pharmacodynamic effects

The primary pharmacodynamic effect of NABOTA is due to chemical denervation of the treated muscle resulting in a measurable decrease of the compound muscle action potential, causing a localized reduction of muscle activity.

Clinical Trials

Two identical multi-centre, randomized, double blind placebo-controlled Phase III clinical trials (EV-001 and EV-002) were conducted to evaluate NABOTA for the use in the temporary improvement of moderate to severe glabellar lines at maximum frown in healthy adults. The primary endpoint was based on the responder rate on Day 30 using a composite endpoint, where both the investigator and subject independently agreed that a ≥ 2 point improvement had occurred on a 4-point severity glabellar line scale (none, mild, moderate, severe) at maximum frown.

In a supportive Phase III trial (EVB-003), the efficacy of NABOTA was evaluated in a noninferiority design with a comparator product containing onabotulinumtoxinA. In this study, subject's satisfaction was evaluated as a secondary endpoint using a 5-point satisfaction scale on Day 30.

In these studies, exclusion criteria included the inability to substantially lessen glabellar frown lines by physically spreading them apart or any condition that might have affected neuromuscular function. Subjects received as single dose of 20U, divided into 5 injection sites (4U) in the corrugator and procerus muscles (see Figure 1).

Table 3. Summary of patient demographics for Studies EV-001, EV-002 and EV-003

Study #	Trial designs	Dosage, route of administration and duration	Study subjects (N)	Mean age (range)
EV-001	Phase III, multi-centre, double blind, placebo-controlled	Single dose (20U), administered on Day 0; and study duration of 150 days	Males 24 Females 306	Placebo 50.4 (23, 74) PrabotulinumtoxinA 50.2 (22, 81)
EV-002			Males 34 Females 290	Placebo 50.4 (18, 71) PrabotulinumtoxinA 51.5 (21, 81)
EV-003	Phase III, multi-centre, double blind, placebo and active controlled		Males 64 Females 476	Placebo 48.4 (26, 71) PrabotulinumtoxinA 48.8 (22,79) OnabotulinumtoxinA 49.7 (24, 75)

Based on the composite primary endpoint, the responder rates in the NABOTA (prabotulinumtoxinA) and placebo groups were, respectively, 67.5% and 1.2% in EV-001; and 70.4% and 1.3% in EV-002 (Table 4). The absolute differences between groups were 66.3% and 69.1% in EV-001 and EV-002, respectively (both $p<0.001$).

Table 4. Responder rates in Studies EV-001 and EV-002 based on ≥ 2 point improvement at maximum frown on Day 30 using a 4-point severity glabellar line scale

Study #	Responder rate (%)	NABOTA	PLACEBO
EV-001	**Composite endpoint** Absolute difference 95% CI for difference p-value (Exact Test) **Investigator's assessment** **Subject assessment**	**67.5** 66.3 59.0, 72.4 <0.001 77.5 76.7	**1.2** 1.2 3.6
EV-002	**Composite endpoint** Absolute difference 95% CI for difference p-value (Exact Test) **Investigator's assessment** **Subject assessment**	**70.4** 69.1 61.5, 75.1 <0.001 82.5 76.3	**1.3** 2.7 4.0

In the EVB-003 Study, the proportion of subjects reporting satisfied or very satisfied with NABOTA supported the results of the primary endpoint.

5.2. Pharmacokinetic properties

NABOTA is not expected to be present in the peripheral blood at measurable levels following intramuscular injection at the recommended doses. Using currently available analytical technology, it is not possible to detect NABOTA in the peripheral blood following intramuscular injection at the recommended doses.

5.3. Preclinical safety data

Carcinogenesis and Mutagenesis

Animal studies to evaluate the carcinogenic and genotoxic potential of NABOTA have not been conducted.

Reproductive toxicity

In an embryo-foetal developmental study, NABOTA was administered (0.5, 1, or 4 U/kg) intramuscularly to pregnant rats daily during the period of organogenesis (on gestation days 6 to 16). No significant test article-related toxicological effects were evident on embryo-development or in the maternal animals compared to the control group. Clinical signs in dams were consistent with pharmacologically mediated effects of botulinum toxin Type A (paralytic gait and curling of toes on the injected hind limb). No test substance-related toxicological changes on body weights, food consumption, organ weights and necropsy findings were evident in any dosing groups. The no observed adverse effect level (NOAEL) for developmental toxicity was ≤ 4 U/kg, approximately 2-fold the human dose of 20 U based on a body surface area for a 60 kg subject.

Animal Toxicity Studies

In two studies to evaluate the acute and repeat-dose toxicity of NABOTA, a single or onceweekly (for 4 weeks) intramuscular injection of 4, 8 or 32 U/kg was administered to rats in the hind limb. NABOTA produced similar pharmacologically mediated effects, including limb paralysis and correlated reductions in food consumption and body weight. At 32 U/kg/dose, these effects were statistically significant and were associated with additional clinical signs of toxicity. Decreased muscle weight and microscopic muscle atrophy of the injected limb as well as local inflammatory responses were observed at doses ≥ 4 U/kg. In male rats, unilateral seminiferous tubule degeneration and atrophy were also observed at doses ≥ 4 U/kg. The maximum tolerated dose for acute and repeat-dose toxicity was ≤ 8 U/kg.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

NABOTA contains human serum albumin and sodium chloride as excipients.

6.2. Incompatibilities

This medicine must not be mixed with other medicines except those mentioned in section 6.6.

6.3. Shelf life

36 months.
Reconstituted product may be stored at 2 to 8°C in a refrigerator for up to 24 hours.

6.4. Special precautions for storage

Store at 2 to 8°C in a refrigerator. Do not freeze.
Reconstituted product may be stored at 2 to 8°C in a refrigerator for up to 24 hours. Reconstituted NABOTA should be clear, colorless and free of particulate matter. Do not freeze after reconstitution.

6.5. Nature and contents of container

NABOTA is a sterile, preservative free, white to yellowish powder, composed of 100 units of Botulinum Toxin, Type A. It is supplied in a clear glass vial and a rubber stopper with aluminium flip-off crimp closure.

6.6. Special precautions for disposal and other handling

Each 100 Unit vial of NABOTA is to be reconstituted with 2.5 mL of 0.9% sterile, preservative-free, saline. As per the dilution table below, the 2.5 mL of sodium chloride 0.9% solution for injection is to be drawn into a sterile syringe and mixed in the vial in order to obtain a reconstituted solution at a concentration of 4 Units/0.1 mL.

Table 5. Reconstitution

Vial Size	Volume of Diluent to be Added to Vial	Nominal Concentration per mL
100 Unit Vial	2.50 mL	4 Units/0.1 mL

Inject the diluent into the vial gently. Discard the vial if a vacuum does not pull the diluent into the vial. Gently mix NABOTA with the saline by rotating the vial.

Once reconstituted, NABOTA should be stored in a refrigerator at 2 to 8°C and used within 24 hours. Do not freeze reconstituted NABOTA. Discard the vial and needle in accordance with local regulations.

All vials, including unused product remaining and expired vials, or equipment used with NABOTA should be disposed of carefully as is done with all medical waste. In cases when deactivation of the toxin is desired (e.g. spills), the use of dilute hypochlorite solution (0.5% or 1%) for five minutes is recommended prior to disposal as medical waste.

7. MEDICINE SCHEDULE

Prescription medicine

8. SPONSOR

Evolus New Zealand Limited
Suite 14485, Level 1
6 Johnsonville Road
Johnsonville, Wellington 6037
New Zealand
Phone: (04) 499 0772

9. DATE OF FIRST APPROVAL

16 March 2023

10.DATE OF REVISION OF THE TEXT

06 September 2024

Summary table of changes

Section Changed	**Summary of new information**
New	
8 Sponsor	New Sponsor information