Product Monograph

Including Patient Medication Information

PrBOEY™

TrenibotulinumtoxinE for Injection

Clostridium botulinum serotype E neurotoxin

Lyophilized powder for solution for injection

For Intramuscular use

1400 Units per single-use vial

Neuromuscular Paralytic Agent

AbbVie Corporation
8401 Trans-Canada Highway
St-Laurent, QC H4S 1Z1

Date of Authorization:
2026-06-22

Control Number: 300062

Recent Major Label Changes

None at time of the most recent authorization.

Table of Contents

Certain sections or subsections that are not applicable at the time of the preparation of the most recent authorized product monograph are not listed.

Part 1: Healthcare Professional Information

1. Indications

Boey™ (TrenibotulinumtoxinE for Injection) is indicated in adult patients for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity.

1.1. Pediatrics

Pediatrics (< 18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

1.2. Geriatrics

Geriatrics (≥ 65 years of age): No specific dose adjustment is required for use in the elderly. Clinical studies included 162 subjects aged 65 years or older; and no clinically meaningful differences in safety were observed between older and younger subjects in the study population.

2. Contraindications

Boey is contraindicated:

- In individuals with known hypersensitivity to any botulinum toxin preparation or to any of its excipients. For a complete listing, see 6 Dosage Forms, Strengths, Composition and Packaging.
- In the presence of infection at the proposed injection site(s).

3. Serious Warnings and Precautions Box

- DISTANT SPREAD OF TOXIN EFFECT: The effects of 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 those patients who have an underlying condition that would predispose them to these symptoms. See 7 Warnings and Precautions, Distant Spread of Toxin Effect.
- The potency Units of Boey for injection 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 Boey cannot be compared to nor converted into units of any other botulinum toxin products assessed with any other specific assay method.
- Boey should only be given by a physician or authorized prescriber with the appropriate qualifications and experience in the treatment and the use of required equipment.
- Follow the recommended dosage and frequency of administration for Boey (see 7 WARNINGS AND PRECAUTIONS, General and 4 DOSAGE AND ADMINISTRATION)

4. Dosage and Administration

4.1. Dosing Considerations

Boey should only be given by a physician or authorized prescriber with the appropriate qualifications and experience in the treatment of patients.

Dosage and administration recommendations should be followed.

The potency Units of Boey for injection 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 Boey cannot be compared to nor converted into units of any other botulinum toxin products assessed with any other specific assay method. See 7 Warnings and Precautions, Lack of Equivalency Between Botulinum Toxin Products.

The appropriate use of Boey depends upon proper storage of the product, selection of the correct dose, and proper aseptic reconstitution and administration techniques. See 4.3 Reconstitution and 4.4 Administration. A physician or authorized prescriber administering Boey must understand the relevant neuromuscular and structural anatomy of the area involved and any alterations to the anatomy due to prior surgical procedures and disease.

Do not use Boey and contact AbbVie (1-888-704-8271) if the carton perforations are broken.

Boey vials are for single-dose and for individual patients only.

The efficacy and safety of more than 3 consecutive injections of Boey beyond 18 weeks have not been evaluated.

4.2. Recommended Dose and Dosage Adjustment

The total dose is 700 Units per treatment session divided into five equal intramuscular injections of 140 Units for glabellar line treatment.

4.3. Reconstitution

Instruction for Preparation and Handling

It is good practice to perform vial reconstitution and syringe preparation over plastic-lined paper towels to catch any spillage. Reconstitute each vial of Boey as shown in **Table 1** to obtain a reconstituted solution at a concentration of 140 Units/0.1 mL and a total treatment dose of 700 Units in 0.5 mL.

Table 1 – Dilution Table

Vial Size	Diluent added (sterile, preservative-free 0.9% sodium chloride solution for injection)	Resulting Dose (Units/0.1 mL)
1400 Units	1 mL	140

Allow the vacuum to draw the saline from the syringe into the vial, letting it slowly and gently drip down the vial wall. DO NOT press/put force on the syringe plunger. Discard the vial if there is evidence of a loss of vacuum (i.e., if diluent is not pulled into the vial upon insertion of the needle). Gently mix Boey with the saline by slowly inverting the vial until completely dissolved.

Store reconstituted Boey in a refrigerator between 2 to 8°C and administer within 24 hours of reconstitution. Boey vials are for single-dose and for individual patients only. Discard any remaining solution after drug administration. Do not freeze reconstituted Boey.

Reconstituted Boey should be clear, colorless to slightly yellow. Do not inject reconstituted Boey if particulates are visible.

4.4. Administration

Glabellar 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 vary markedly among individuals. Lines induced by facial expression occur perpendicular to the direction of action of contracting facial muscles.

In order to reduce the complication of ptosis, the following steps should be taken:

- Avoid injection near the levator palpebrae superioris, particularly in patients with larger brow depressor complexes.
- Position lateral corrugator muscle injections at least one cm above the bony supraorbital ridge.
- Ensure the injected volume/dose is accurate.

Administration steps

NOTE: To achieve a 0.5 mL volume delivery, an adequate amount of reconstituted solution must be drawn into the syringe to account for volume loss from air bubble removal and needle priming.

- Draw more than 0.5 mL reconstituted solution into the sterile syringe barrel and expel any air bubbles.
- Remove the needle used to withdraw the product. Attach an appropriately sized needle for injection and prime the needle.
- Inject 140 Units (0.1 mL) of reconstituted Boey intramuscularly into each of five sites, two injections in each corrugator muscle and one injection in the procerus muscle for a total dose of 700 Units (see **Table 2** and **Figure 1 below**).

Figure 1. Injection Sites for Glabellar Lines

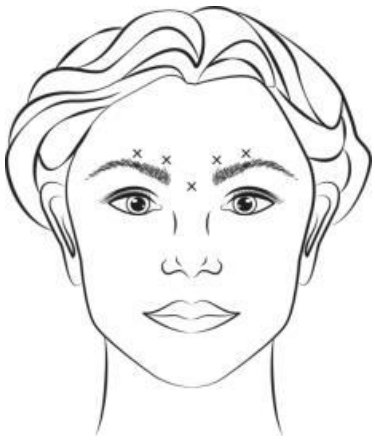


Table 2. Dosing for Glabellar Lines

Glabellar Lines	Injection sites	Total Dose (Number of Injection Sites)
140 Units (0.1 mL) per injection into each of five sites	1 injection in the procerus muscle 2 injections in each corrugator muscle	700 Units (5 sites)

Retreatment of Boey:

Boey was studied in up to two treatment cycles in pivotal clinical trials (see 14. Clinical Trials). Retreatment at more frequent intervals than every 6 weeks has not been evaluated. The timing of Boey retreatment should be determined by the physician or authorized prescriber assessment of wrinkle severity.

Transition to onabotulinumtoxinA:

After receiving Boey, patients may be treated with onabotulinumtoxinA after observation of moderate to severe glabellar lines as assessed by the physician or authorized prescriber.

4.5. Missed Dose

Not Applicable.

5. Overdose

Symptoms of overdose may not be apparent immediately post-injection. Excessive doses may produce local, or distant, generalized and profound neuromuscular paralysis.

Should accidental injection or oral ingestion occur, or overdose be suspected, medically monitor the patient for up to several weeks for progressive signs or symptoms of systemic muscular weakness which could be local to, or distant from, the site of injection, and may include ptosis, diplopia, dysphagia, dysarthria, generalized weakness or respiratory failure. Consider these patients for further

medical evaluation and immediately institute appropriate medical therapy, which may include hospitalization.

If the musculature 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 necessary 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.

For the most recent information in the management of a suspected drug overdose, contact your regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669).

6. Dosage Forms, Strengths, Composition, and Packaging

To help ensure the traceability of biologic products, physician or authorized prescriber should record both the brand name and the non-proprietary (active ingredient) name as well as other product-specific identifiers such as the Drug Identification Number (DIN) and the batch/lot number of the product supplied.

Table 3 – Dosage Forms, Strengths, and Composition

Route of Administration	Dosage Form/ Strength/Composition	Non-Medicinal Ingredients
Intramuscular	A sterile lyophilized preparation; Powder for solution for injection; 1400 Units per vial	L-Histidine, L-Histidine Hydrochloride Monohydrate, L-Methionine, Poloxamer 188, Sodium Chloride, Trehalose Dihydrate

Description

Boey powder for solution for injection is a white to off-white lyophilized powder, supplied in a single-use vial in the following size:

- 1400 Units of trenibotulinumtoxinE

The powder may appear as broken cake.

7. Warnings and Precautions

Please see the 3. Serious Warnings and Precautions Box.

General

Use Boey only as directed.

Do not use dosage recommendations and potency Units applied to other botulinum toxin products when using Boey.

The safe and effective use of Boey depends upon proper storage of the product, selection of the correct dose, and proper reconstitution and administration techniques.

A physician or authorized prescriber administering Boey should be familiar with the relevant anatomy of the area involved and any alterations to the anatomy due to prior surgical procedures. Care should be taken when injecting in or near vulnerable anatomic structures.

Caution should be used when Boey is used in the presence of inflammation at the proposed injection site(s) or when excessive weakness or atrophy is present in the target muscle.

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.

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, generalized weakness or respiratory failure. In addition, certain adverse effects (e.g., dysphagia, aspiration pneumonia) have been rarely reported with botulinum toxin Type A products, some of which have been associated with a fatal outcome.

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

Carcinogenesis and Mutagenesis

Studies have not been performed to evaluate the mutagenic and carcinogenic potential of Boey.

Cardiovascular

There have been reports following administration of botulinum toxin type A 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. The exact relationship of these events to botulinum toxin is unknown.

Distant Spread of Toxin Effect

Safety data from other approved botulinum toxins suggest that botulinum toxin effects may, in some cases, be observed beyond the site of local injection. The symptoms that are consistent with the mechanism of action of botulinum toxin may include muscular weakness, swallowing and speech disorders, aspiration pneumonia, difficulty breathing, and respiratory depression.

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

No definitive adverse event (serious or non-serious) reports of distant spread of toxin effect associated with dermatologic use of Boey for glabellar lines have been reported.

Hypersensitivity Reactions

Serious and/or immediate hypersensitivity reactions such as anaphylaxis and serum sickness, as well as other manifestations of hypersensitivity including urticaria, soft tissue edema, and dyspnea may occur. If such a reaction occurs, further injection should be discontinued and appropriate medical therapy immediately instituted. Necessary precautions should be taken, and epinephrine should be available.

Immune

Formation of neutralizing antibodies to botulinum toxin type E may reduce the effectiveness of Boey treatment by inactivating the biological activity of the toxin. The critical factors for neutralizing antibody formation have not been well characterized. 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. When appropriate, the potential for antibody formation may be minimized by injecting with the lowest effective dose given at the longest feasible intervals between injections. Among 2104 subjects treated with Boey, no subjects developed neutralizing antibodies. See 10.4 Immunogenicity.

Lack of Equivalency Between Botulinum Toxin Products

The potency Units of Boey are specific to the preparation and assay method utilized. Boey is not equivalent to other botulinum toxin products, and therefore, Units of biological activity of Boey cannot be compared to nor converted into units of any other botulinum toxin products assessed with any other specific assay method. See 13. Pharmaceutical Information.

Driving and Operating Machinery

Boey has negligible influence on the ability to drive and use machines. However, it may cause eyelid ptosis and visual disturbance. Patients should exercise caution before driving or using machinery until they are reasonably certain that Boey does not adversely affect performance.

Monitoring and Laboratory Tests

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

Pre-Existing Neuromuscular Disorders

Extreme caution, including close monitoring, should be exercised when administering Boey to individuals with peripheral motor neuropathic diseases (e.g., amyotrophic lateral sclerosis or motor neuropathy) or neuromuscular junctional disorders (e.g., myasthenia gravis or Lambert-Eaton syndrome). Patients with neuromuscular junction disorders may be at increased risk of clinically significant systemic effects including severe dysphagia and respiratory compromise.

Ophthalmologic

Ophthalmic Adverse Reactions in Patients Treated with Other Botulinum Toxin Products

Reduced blinking from injection with the use of other botulinum toxins has been reported which can lead to dry eye, corneal exposure, persistent epithelial defects and corneal ulceration, especially in patients with cranial nerve VII disorders. 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.

Skin

Injection Site Pre-existing Conditions and Reactions

The relevant anatomy, and any alterations to the anatomy due to prior surgical procedures, must be understood prior to administering Boey.

Caution should be exercised when Boey is used in the presence of inflammation at the proposed injection site(s), ptosis, or when excessive weakness or atrophy is present in the target muscle(s).

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

7.1. Special Populations

7.1.1. Pregnancy

There are no studies or adequate data on the developmental risk associated with use of trenibotulinumtoxinE in pregnant women.

The impairment of fertility and early embryonic development potential of Boey was studied in dose range-finding embryo-fetal development study in mice. Maternal death was observed at 75 Units/kg; there were no additional maternal or fetal effects up to 75 Units/kg. No further fertility and early embryonic development studies in animals have been conducted.

The use of Boey during pregnancy is not recommended.

During the clinical trials with Boey, there were two reported pregnancies. In addition, one pregnancy was reported after the end of the study. For the three pregnancies, time to onset from the last dose of Boey was the following: 12 days, 25 days, and >1 month. In two pregnancies, the outcome was live birth with no congenital anomalies or birth defects reported and in the remaining pregnancy, the outcome was unknown.

7.1.2. Breastfeeding

There are no data on the presence of Boey in human or animal milk, the effects on the breastfed infant, or the effects on milk production. Given the lack of data, the use of Boey during breastfeeding is not recommended.

7.1.3. Pediatrics

Pediatrics (< 18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4. Geriatrics

No specific dose adjustment is required for use in the elderly.

The clinical studies included 162 subjects aged 65 years or older. Although there was a limited number of subjects aged 65 years or older, no clinically meaningful differences in safety were observed between older and younger subjects.

8. Adverse Reactions

8.1. Adverse Reaction Overview

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.

As is expected for any injection procedure, localized pain, inflammation, paresthesia, hypoesthesia, tenderness, swelling/oedema, erythema, localized infection, bleeding and/or bruising may be associated with the injection.

8.2. Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. Therefore, the frequencies of adverse reactions observed in the clinical trials may not reflect frequencies observed in clinical practice and should not be compared to frequencies reported in clinical trials of another drug.

Glabellar Lines

Adverse drug reactions are adverse events reasonably associated with the use of a drug and thus imply a suspected causal relationship.

Adverse drug reactions from glabellar line clinical trials were all non-serious and mild in severity. Onset was generally within the first week. In most cases, the events resolved in 2 to 8 days rarely lasting longer

Safety was evaluated in two multicenter, double-blind, placebo-controlled studies of identical design for the treatment of glabellar lines (N = 947, 709 in the Boey-treated group and 238 in the placebo-treated group). The most frequently reported treatment-related adverse events were headache (3.4% in the Boey-treated group and 4.2% in the placebo-treated group), injection site pain (1.7% in the Boey-treated group and 2.9% in the placebo-treated group), and injection site erythema (0.6% in the Boey-treated group and 1.3% in the placebo-treated group) (see **Table 4**).

Table 4. Most Frequently Reported Treatment-Related Adverse Events

System organ class / preferred term	Boey N = 709 (%)	Placebo N= 238 (%)
General disorders and administration site conditions		
Injection site pain	1.7%	2.9%
Injection site erythema	0.6%	1.3%
Nervous System disorders		
Headache	3.4%	4.2%

Most adverse events were of mild severity. In a multicenter, open-label, repeat injection study, 846 patients received 3 treatment cycles. In this study, adverse events were comparable in type, incidence, severity, and causality to those reported in the two placebo-controlled, double-blind studies.

8.3. Less Common Clinical Trial Adverse Reactions

Overall, the safety of at least one treatment of Boey was evaluated across all completed studies involving eight clinical trials (seven double-blind, placebo-controlled clinical studies and an open-label safety study).

Adverse drug reactions are presented below by system organ class and frequency.

Eye Disorders: *Uncommon*: eyelid ptosis (0.17%)

Injury, Poisoning and Procedural Complications: *Rare*: Mephisto sign (0.04%)

Skin and Subcutaneous Tissue Disorders: *Uncommon*: brow ptosis (0.13%)

8.4. Abnormal Laboratory Findings: Hematologic, Clinical Chemistry, and Other Quantitative Data

Clinical Trial Findings

No specific trends in abnormal hematologic or clinical chemistry findings have been reported.

8.5. Post-Market Adverse Reactions

There is no post-market surveillance information available with the use of Boey.

9. Drug Interactions

9.2. Drug Interactions Overview

No formal drug interaction studies have been conducted with trenibotulinumtoxinE.

9.3. Drug-Behaviour Interactions

The interaction of trenibotulinumtoxinE with individual behavioural risks (e.g. cigarette smoking, cannabis use, and/or alcohol consumption) has not been studied.

9.4. Drug-Drug Interactions

Table 5 – Established or Potential Drug-Drug Interactions

[Non-proprietary name(s) of the drug product(s)]	Source of evidence	Effect	Clinical comment
Other Botulinum Neurotoxin Products	T	The effect of administering different botulinum neurotoxin serotypes at the same time is unknown.	Neuromuscular weakness may be exacerbated by administration of another botulinum toxin prior to the resolution of the effects of a previously administered botulinum toxin.

[Non-proprietary name(s) of the drug product(s)]	Source of evidence	Effect	Clinical comment
	CT	In a Phase 1 study, the sequential treatment of trenibotulinum toxinE or placebo on Day 1 followed by onabotulinumt oxinA administered at Day 30, identified no safety concerns (see 10. Clinical Pharmacology).	After receiving trenibotulinumtoxinE, patients may be treated with onabotulinumtoxinA after observation of moderate to severe glabellar lines as assessed by the physician or authorized prescriber.
Muscle Relaxants	T	Not studied	Excessive weakness may be exaggerated by administration of a muscle relaxant before or after administration of botulinum toxins, including trenibotulinumtoxinE.
Aminoglycosides and Other Agents Interfering with Neuromuscular Transmission	T	Not studied	The effect of botulinum toxins, including trenibotulinumtoxinE, may be potentiated by aminoglycoside antibiotics or other medicinal products that interfere with neuromuscular transmission (e.g. neuromuscular blocking agents)
Anticholinergic Drugs	T	Not studied	Use of anticholinergic drugs after administration of botulinum toxins, including trenibotulinumtoxinE, may potentiate systemic anticholinergic effects.
Legend: C = Case Study; CT = Clinical Trial; T = Theoretical;			

9.5. Drug-Food Interactions

Interactions with food have not been studied.

9.6. Drug-Herb Interactions

Interactions with herbal products have not been studied.

9.7. Drug-Laboratory Test Interactions

Interactions with laboratory test impacting the accuracy of test results have not been studied.

10. Clinical Pharmacology

10.1. Mechanism of Action

TrenibotulinumtoxinE blocks neuromuscular transmission by binding to acceptor sites on motor nerve terminals, entering the nerve terminals, and inhibiting the release of acetylcholine. This inhibition occurs as the neurotoxin cleaves SNAP-25, a pre-synaptic protein integral to the successful docking of vesicles situated within nerve terminals and subsequent release of acetylcholine from those vesicles. When injected intramuscularly at therapeutic doses, trenibotulinumtoxinE produces partial chemical denervation of the muscle resulting in a localized reduction in muscle activity within hours.

The early onset of effect may be due to rapid uptake and translocation of botulinum toxin type E into neuronal cells, and the short duration may be due to the short half-life of the light chain of botulinum toxin type E.

10.2. Pharmacodynamics

A Phase 1, double-blind study was conducted with sequential administration of trenibotulinumtoxinE 700 Units or placebo on Day 1 followed by onabotulinumtoxinA 20 Units (units are toxin-specific) on Day 30 in a total of 90 subjects with moderate to severe glabellar lines. Subjects were eligible for treatment with onabotulinumtoxinA if eligibility criteria were met, including moderate to severe glabellar line severity at maximum frown.

The overall incidence of treatment-emergent adverse events (TEAEs) was similar between treatment groups after onabotulinumtoxinA treatment, regardless of whether the subject initially received trenibotulinumtoxinE or placebo.

10.3. Pharmacokinetics

General characteristics of the active substance

Using currently available analytical technology, it is not possible to detect trenibotulinumtoxinE in peripheral blood after intramuscular injection at the recommended dose.

10.4. Immunogenicity

As with all proteins, there is a potential for immunogenicity. The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies, including those of other botulinum toxin products.

In five glabellar line studies, 2104 subjects treated with trenibotulinumtoxinE had samples analyzed for antibody formation. Among trenibotulinumtoxinE-treated subjects who received single or repeat treatments (up to three treatments), one subject (<0.1%) developed binding antibodies. This subject received three treatments of 700 Units trenibotulinumtoxinE at 6-week intervals and was negative for neutralizing antibodies. Across all studies, no subjects (0%) developed neutralizing antibodies. Overall, there was a low incidence of antibody formation and data were suggestive of no impact on safety or efficacy of trenibotulinumtoxinE.

In the Phase 1 study in which trenibotulinumtoxinE or placebo was administered at Day 1 followed by onabotulinumtoxinA at Day 30, no subject developed binding or neutralizing antibodies to trenibotulinumtoxinE or onabotulinumtoxinA.

11. Storage, Stability, and Disposal

- Unopened vial: Store at 2 to 8°C in a refrigerator. Do not use after the expiration date on the vial.
- Reconstituted vial: Store at 2 to 8°C in a refrigerator and administer within 24 hours of reconstitution.
- Keep the vial in the original carton in order to protect from light.
- Incompatibilities: In the absence of incompatibility studies, this medicinal product should not be mixed with other medicinal products.
- Boey vials are for single-dose and for individual patients only. Discard any remaining solution after drug administration.
- Medicine: keep out of reach of children.

All vials, including expired vials, or equipment used in direct contact with the drug should be disposed of as medical waste. In cases when deactivation of the toxin is desired (e.g., spills), the use of sodium hypochlorite (NaClO) at not less than 0.7% or household bleach solution at not less than 10% volume/volume for 10 minutes is recommended prior to disposal as medical waste.

Part 2: Scientific Information

13. Pharmaceutical Information

Drug Substance

Non-proprietary name of the drug substance(s): TrenibotulinumtoxinE

Chemical name: not applicable. TrenibotulinumtoxinE is a botulinum toxin serotype E

Molecular formula and molecular mass: Based on the amino acid sequence, the molecular formula of trenibotulinumtoxinE molecule is $C_{6438}H_{9972}N_{1696}O_{1971}S_{23}$, which corresponds to nicked (active) form. The predicted molecular weight of trenibotulinumtoxinE is approximately 150 kDa Structure: TrenibotulinumtoxinE protein is the 150 kDa subunit of the native 300 kDa complex expressed in Clostridium botulinum type E.

Physicochemical properties: TrenibotulinumtoxinE Drug Product (DP) is supplied as sterile lyophilized powder for solution for injection. It is reconstituted with 1 mL of 0.9% sodium chloride solution.

Product Characteristics:

Boey is a sterile, single use lyophilized powder for solution for injection. It is to be reconstituted with sterile, preservative free, normal saline prior to injection. See Dosage and Administration section for further details. The active ingredient is trenibotulinumtoxinE, a botulinum toxin type E, produced from Clostridium botulinum type E.

The primary release procedure for Boey uses a cell-based potency assay to determine the potency relative to a reference standard. The assay is specific to AbbVie's product Boey. One Unit corresponds to the calculated median intraperitoneal lethal dose (LD50) in mice. Units of Boey cannot be compared to nor converted into Units of any other botulinum toxin or any toxin.

14. Clinical Trials

14.1. Clinical Trials by Indication

Glabellar Lines

Two Phase 3 multicenter, randomized, double-blind, placebo-controlled studies (Study M21-500, Study M21-508) evaluated Boey (N=709 Boey and N=238 placebo) for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity.

The studies enrolled healthy adults with moderate to severe glabellar lines at maximum frown on baseline Day 1 (Hour 0). Subject assessment visits were at Day 1 (Hours 8 and 12), Day 2 (Hours 24 and 36), Day 3 (Hour 48), and Days 7, 14, 21, 28, 35, and 43.Subjects were eligible for treatment with Boey at the Day 43 Visit if retreatment criteria were met, including moderate to severe glabellar line severity at maximum frown.

Table 6. – Summary of Patient Demographics for Clinical Trials in [Glabellar Lines]

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Median Age (range), age subgroup	Sex
M21-500	Randomized, double-blind, placebo-controlled period, followed by open-label period	700 U Intramuscular 12 weeks Up to two treatments (one double-blind treatment, one open-label treatment)	Total: 638 Boey: 482 Placebo: 156	48 (21 to 81) years < 65 years: 92% ≥ 65 years: 8%	Female: 566 Male: 72
M21-508	Randomized, double-blind, placebo-controlled period, followed by open-label period	700 U Intramuscular 12 weeks Up to two treatments (one double-blind treatment, one open-label treatment)	Total: 309 Boey: 227 Placebo: 82	42 (20 to 76) years < 65 years: 94% ≥ 65 years: 6%	Female: 245 Male: 64

Efficacy was measured by the assessment of glabellar line severity at maximum frown using the 4-point Facial Wrinkle Scale (FWS) with Photonumeric Guide (0=none, 1=mild, 2=moderate, 3=severe) by both the investigator and subject. The investigator and subject assessments were performed independently.

The primary composite endpoint was defined as the achievement of Grade 0 or 1 (None or Mild) and ≥2-grade improvement from baseline in glabellar line severity at maximum frown based on both investigator and subject FWS assessments at Day 7. Key secondary endpoints included the achievement of Grade 0 or 1 (None or Mild) and ≥2-grade improvement from baseline in glabellar line severity at maximum frown based on both investigator and subject FWS assessments over time.

In Study M21-500, 89% were female, 90% were White, 3% were Asian, 4% were Black or African American, and 90% identified as not Hispanic or Latino. Subjects had a mean age of 47.2 years; 52 (8%) subjects were aged 65 years or older.

In Study M21-508, 79% were female, 83% were White, 6% were Asian, 6% were Black or African American, and 89% identified as not Hispanic or Latino. Subjects had a mean age of 43.1 years; 18 (6%) subjects were aged 65 years or older.

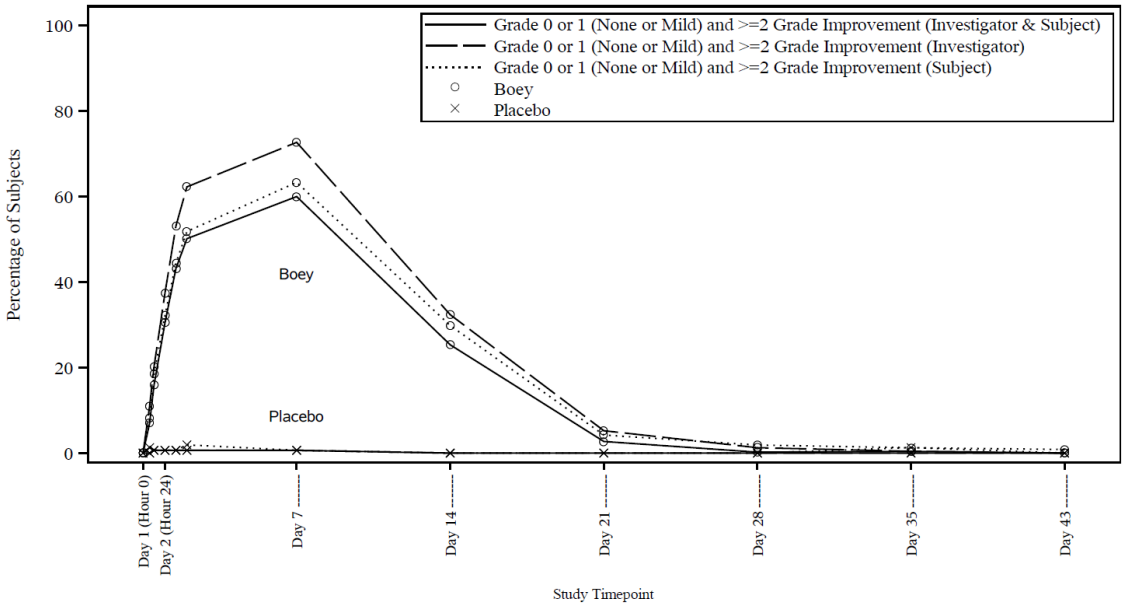
Efficacy results in Studies M21-500 and M21-508 are summarized in **Table 7**, **Figure 2**, and **Figure 3**.

Table 7. Responder Rate Results at Day 7 in Subjects with Moderate or Severe Glabellar Lines in Studies M21-500 and M21-508

	Study M21-500			Study M21-508		
	Boey 700 Units (N=482) n (%)	**Placebo (N=156) n (%)**	**Difference 95% CI**	**Boey 700 Units (N=227) n (%)**	**Placebo (N=82) n (%)**	**Difference 95% CI**
Composite[a]	289 (60.0%)	1 (0.6%)	59.3%[b] (54.7%, 63.9%)	149 (65.7%)	1 (1.2%)	64.5%[b] (57.9%, 71.1%)
Individual Components						
Investigator Assessment	350 (72.6%)	1 (0.6%)	72.0% (67.8%, 76.2%)	171 (75.5%)	2 (2.4%)	73.0% (66.5%, 79.6%)
Subject Assessment	305 (63.3%)	1 (0.6%)	62.6% (58.1%, 67.2%)	158 (69.4%)	1 (1.2%)	68.2% (61.7%, 74.7%)

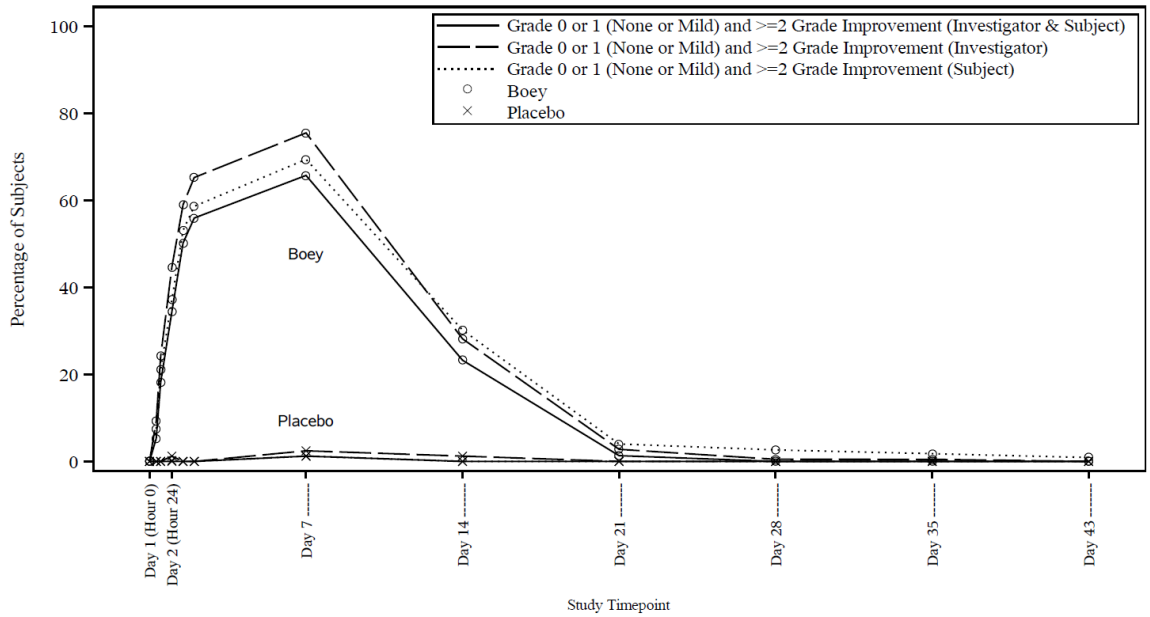
a. Achievement of Grade 0 or 1 (None or Mild) and ≥ 2-grade improvement from baseline based on both the investigator and subject FWS assessments at Day 7; responder rates are estimated after using multiple imputation for missing data.
b. $p < 0.0001$

Figure 2. **Percentages of Subjects Achieving None or Mild and ≥ 2-Grade Improvement from Baseline Based on the Investigator and Subject Assessments of Glabellar Line Severity at Maximum Frown Over Time (Study M21-500)**



Percentage of subjects is estimated after using multiple imputation for missing data

Figure 3. **Percentages of Subjects Achieving None or Mild and ≥ 2-Grade Improvement from Baseline Based on the Investigator and Subject Assessments of Glabellar Line Severity at Maximum Frown Over Time (Study M21-508)**



Percentage of subjects is estimated after using multiple imputation for missing data

In both studies, results for satisfaction with treatment and natural look were supportive of treatment benefit observed in the primary endpoints.

16. Non-Clinical Toxicology

General toxicology

Repeat administration of trenibotulinumtoxinE to mice resulted in limited usage, swelling and non-adverse minimal to mild myofiber regeneration in the injected hindlimb muscles. The established no-observed-adverse effect level doses of trenibotulinumtoxinE following repeat intramuscular administration in mice (once monthly for up to six months, seven total doses) of 75 Units/kg is approximately six times the human dose of 700 Units, based on a body weight (Units/kg).

Genotoxicity

Genotoxicity studies have not been conducted for trenibotulinumtoxinE.

Carcinogenicity

Studies in animals have not been performed to evaluate carcinogenic potential of trenibotulinumtoxinE.

Reproductive and developmental toxicology

Fertility and early embryonic development studies have not been conducted for trenibotulinumtoxinE.

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PRBOEY™

TrenibotulinumtoxinE for Injection

This Patient Medication Information is written for the person who will be taking **Boey**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This Patient Medication Information is a summary. It will not tell you everything about this medication. If you have more questions about this medication or want more information about **Boey,** talk to a healthcare professional.

Serious warnings and precautions box

- **Distant spread of toxin effects.** It is possible that the effect of botulinum toxin may affect areas of the body away from the injection site and cause symptoms of a serious condition called botulism. Trouble breathing and trouble swallowing can be life threatening.
- One unit (amount) of Boey is NOT the same as one unit of other botulinum products.
- Boey should only be given by a trained healthcare professional. They should have experience using Boey.
- Follow the dose and schedule of injection recommended by your healthcare provider.

What Boey is used for:

Boey is used in adults to temporarily improve the appearance of moderate to severe frown lines between the eyebrows (glabellar/frown lines).

How Boey works:

Boey is injected into muscles between the eyebrows. It works by blocking the signals that tell the muscles to move. This can reduce the appearance of wrinkles or lines where Boey is injected.

Boey begins working early once it is injected. This effect lasts for a short period of time.

The ingredients in Boey are:

Medicinal ingredient(s): TrenibotulinumtoxinE

Non-medicinal ingredients: L-Histidine, L-Histidine Hydrochloride Monohydrate, L-Methionine, Poloxamer 188, Sodium Chloride, Trehalose Dihydrate

Boey comes in the following dosage form(s):

Powder for solution for injection in a single-use vial; 1400 U / vial

Do not use Boey if:

- If you are allergic to botulinum toxin or any of the other ingredients (listed in "The ingredients in Boey are:")
- If you have a skin infection where you plan to get the injection

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Boey. Talk about any health conditions or problems you may have, including if you:

- You have allergies to any botulinum toxin product
- You had a side effect from any botulinum toxin product in the past
- You have had facial surgery or injured your face
- You are planning to have facial surgery soon
- You have any redness or swelling (inflammation) where you plan to get an injection
- Your muscles where the injection will be given are weak
- You have drooping of one or both eyelids (ptosis)
- You have any other change in the way your face normally looks
- You have certain diseases that affect your nervous system (such as amyotrophic lateral sclerosis or motor neuropathy)

Other warnings you should know about:

- **Injection site reactions:** Like with any injection procedure, injection site reactions may happen after receiving Boey. Symptoms at the injection site(s) may include:
  - Pain/discomfort
  - Swelling/inflammation
  - Redness
  - Bruising
  - Bleeding
  - Itching
  - Warmth
  - Hardness at the site where the needle entered your skin

- **Muscle weakness in areas next to or near the injection sites**: such as eyelid drooping and double vision (seeing two objects when there is only one).

Driving and using machines: If you have drooping eyelids or problems with your vision after using Boey, do not drive or use machinery until those symptoms go away.

After you get Boey, talk to your healthcare professional if you have the following:

- **Allergic reaction**: An allergic reaction is a reaction your body has to a medicine. This can cause symptoms such as hives, rash, or fever. Contact your healthcare professional right away if you have any of the symptoms listed below as they can be signs of a severe allergic reaction:
  - Trouble breathing, swallowing, or speaking
  - Swelling, including swelling of the face or throat
  - Wheezing (a whistling sound while breathing)
  - Feeling dizzy or light-headed

- Shortness of breath

- **Distant spread of toxin effect:** Sometimes, the effects of botulinum toxin may spread from the injection area to other parts of the body. Contact your healthcare provider right away if you have any of the symptoms listed below:
  - Muscle weakness
  - Trouble swallowing
  - Unwanted food or liquid going into the airways
- **Reduced blinking or experience dryness** in one or both eyes.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Boey:

- A different medicine that has botulinum toxin
- Muscle relaxants (medicines that reduce muscle tension)
- Antibiotics (medicines used to treat infections)
- Anticholinergics (medicines that reduce muscle strength)

Ask your healthcare provider for advice before you take any new medicines.

How to take Boey:

Boey should only be given by healthcare professionals with the right training and experience in the treatment of patients.

Boey is injected directly into the muscles (intramuscularly) at five injection sites between the eyebrows.

Boey is not recommended for patients younger than 18.

Usual dose:

The usual dose is 700 Units in total. You will be injected with 140 Units of Boey into each of the five injection sites.

Your healthcare professional will tell you when you should get another Boey treatment based on the appearance of your frown lines.

Overdose:

Contact your healthcare professional immediately if you notice symptoms that you might have received too much Boey. These symptoms may not happen for several days after the injection, and include:

- Muscle weakness. This can happen near or away from the injection site.
- Trouble breathing, swallowing, or speaking. This may happen because the muscle cannot move (muscle paralysis).
- Lung infection called aspiration pneumonia. This may be caused by food or liquid accidentally going into your lungs because the muscles cannot move (muscle paralysis).
- Drooping of the eyelids
- Double vision (seeing two objects when there is only one)

- Overall weakness in the body

If you swallow Boey or have it accidentally injected, see your healthcare provider. They may want to watch you closely for several days.

If you think you, or a person you are caring for, have taken too much Boey, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Possible side effects from using Boey:

Boey can have side effects, although not everybody gets them.

Side effects may include:

Uncommon: These may happen in up to 1 in 100 patients.

- Drooping eyelid
- Drooping eyebrow

Rare: These may happen in up to 1 in 1000 patients.

- Raising of the outer eyebrow

These are not all the possible side effects you may have when taking Boey. If you experience any side effects not listed here, tell your healthcare professional.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting side effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Keep out of reach and sight of children.

Your healthcare provider should not use this medicine after the expiry date.

Your healthcare provider will store this medicine in a refrigerator between 2 to 8°C. Your healthcare professional should keep the vial in the original carton in order to protect from light.

After mixing the powder with salt water, the medicine should be used immediately. It can be stored for up to 24 hours in a refrigerator between 2 to 8°C.

If you want more information about Boey:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes the Patient Medication Information by visiting the Health Canada Drug Product Database website (Drug Product Database: Access the database); the manufacturer's website www.abbvie.ca; or by calling 1-888-704-8271.

This leaflet was prepared by AbbVie Corporation

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