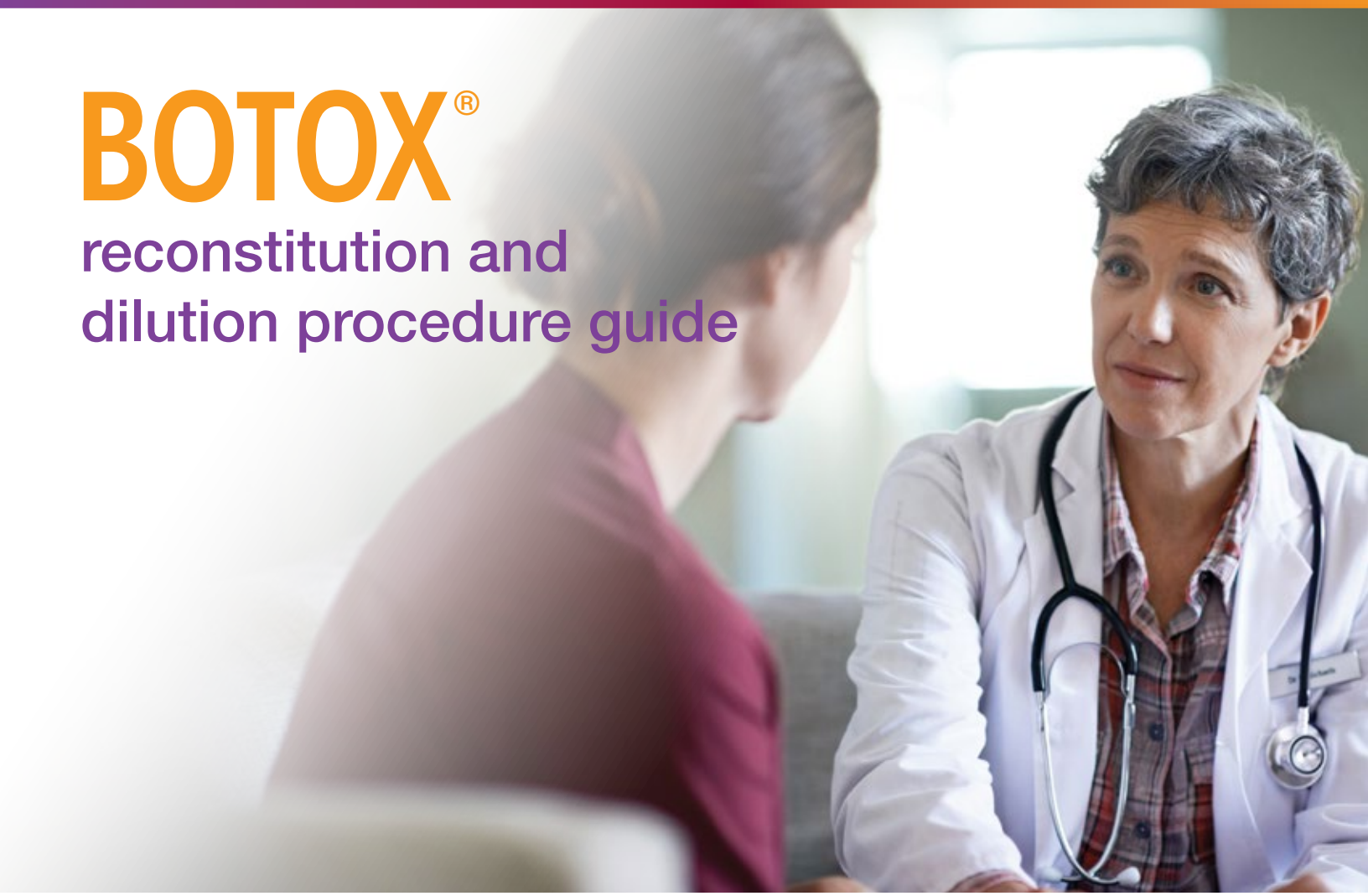
BOTOX®

reconstitution and dilution procedure guide



PrBOTOX® (onabotulinumtoxinA) is indicated for:

Focal spasticity

- In the management of focal spasticity, including the treatment of upper limb spasticity associated with stroke in adults
- For the symptomatic treatment of lower limb spasticity associated with stroke in adults
- For symptomatic treatment of upper and/or lower limb spasticity in pediatric patients 2 years of age or older

BOTOX is not intended as a replacement for usual standard of care regimens and is not likely to be effective in improving range of motion at a joint affected by a fixed contracture.

Blepharospasm

- For the treatment of blepharospasm associated with dystonia, including benign essential blepharospasm or VII nerve disorders in patients 12 years of age or older

Cervical dystonia

- To reduce the subjective symptoms and objective signs of cervical dystonia (spasmodic torticollis) in adults

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BOTOX® onabotulinumtoxinA

Preparing intramuscular injections for focal spasticity, blepharospasm and cervical dystonia

BOTOX should only be given by physicians with the appropriate qualifications and experience in the treatment and the use of required equipment

BOTOX dilution table

Resulting dose units per 0.1 mL

Quantity of diluent added (0.9% sodium chloride injection)	 50 U VIAL	 100 U VIAL	 200 U VIAL
1.0 mL	5.0 U	10.0 U	20.0 U
2.0 mL	2.5 U	5.0 U	10.0 U
4.0 mL	1.25 U	2.5 U	5.0 U

Note: These dilutions are calculated for an injection volume of 0.1 mL. A decrease or increase in the BOTOX dose is also possible by administering a smaller or larger injection volume (i.e., 0.05 mL [50% decrease in dose] to 0.15 mL [50% increase in dose]).

Storage

- The vacuum-dried product should be stored in a refrigerator at 2 to 8°C or in a freezer at or below -5°C
- BOTOX should be administered within 24 hours of reconstitution
- During the 24 hours, BOTOX should be stored in a refrigerator at 2 to 8°C. Do not freeze reconstituted BOTOX

Instructions for BOTOX reconstitution

1

Draw up the proper amount of diluent (see dilution table) in the appropriately sized syringe. A 21-gauge, 2-inch needle is recommended for reconstitution.

2

Using a 45-degree angle, insert the needle of the syringe containing saline into the BOTOX vial. Slowly inject the saline into the BOTOX vial. Vacuum is present in the vial, which demonstrates that the sterility of the vial is intact. Do not use the vial if the vacuum does not pull the saline into the vial.

3

Release the vacuum by disconnecting the syringe from the needle and allowing air to flow into the vial. Gently mix the BOTOX neurotoxin with the saline by rotating the vial.

4

Draw the fluid into the injection syringe by placing the needle into the bottom corner of the vial for full extraction. Do not invert the vial.

5

Disconnect the injection syringe from the vial and attach an appropriately sized needle for injection.

Visually inspect the reconstituted BOTOX to ensure it is clear, colourless and free of particulate matter. Record the date and time of reconstitution on the space on the label. Administer BOTOX within 24 hours after reconstitution.

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Note: At the time of use, confirm product acceptability relative to the expiration date indicated on the product vial and outer box.

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BOTOX dosing overview: Focal spasticity

Focal spasticity in adults

IN UPPER LIMB SPASTICITY:

- Dosing and number of injection sites must be tailored to the individual patient, based on the size, number and location of muscles involved, the severity of spasticity, presence of local muscle weakness, and their response to previous treatment(s)
- A 25-, 27- or 30-gauge needle may be used for superficial muscles while a 22-gauge needle may be used for deeper musculature

Dosing guidelines for patients with upper limb spasticity associated with stroke	
Muscle	**Total dosage; number of sites**
Biceps brachii	100–200 U; up to 4 sites
Flexor digitorum profundus	15–50 U; 1–2 sites
Flexor digitorum sublimis	15–50 U; 1–2 sites
Flexor carpi radialis	15–60 U; 1–2 sites
Flexor carpi ulnaris	10–50 U; 1–2 sites
Adductor pollicis	20 U; 1–2 sites
Flexor pollicis longus	20 U; 1–2 sites

Adapted from the BOTOX Product Monograph.

The degree and pattern of muscle spasticity may necessitate alterations in dose and muscles to be injected. The lowest effective dose should be used.

IN LOWER LIMB SPASTICITY:

- The recommended dose in adults with ankle and toe involvement is **300–400 U** divided among or up to 6 muscle groups

BOTOX dosing by muscle for adult lower limb spasticity	
Muscle	**Total dosage; number of sites**
Gastrocnemius	
Medial head	75 U; 3 sites
Lateral head	75 U; 3 sites
Soleus	75 U; 3 sites
Tibialis posterior	75 U; 3 sites
Flexor hallucis longus	50 U; 2 sites
Flexor digitorum longus	50 U; 2 sites
Flexor digitorum brevis	25 U; 1 site

Adapted from the BOTOX Product Monograph.

See Product Monograph for complete dosing and administration instructions.

If deemed appropriate by the treating physician, repeat BOTOX treatment may be administered no sooner than 12 weeks when the effect of a previous injection has diminished.

Focal spasticity in children (≥2 years of age)

IN UPPER LIMB SPASTICITY:

- Recommended dose is **3–6 U/kg** divided among the affected muscles
- Total dose of BOTOX in the first treatment session should not exceed 6 U/kg or 200 U, whichever is lower

Muscle	Total dosage; number of sites
Biceps brachii	1.5–3 U/kg; 4 sites
Brachialis	1–2 U/kg; 2 sites
Brachioradialis	0.5–1 U/kg; 2 sites
Flexor carpi radialis	1–2 U/kg; 2 sites
Flexor carpi ulnaris	1–2 U/kg; 2 sites
Flexor digitorum profundus	0.5–1 U/kg; 2 sites
Flexor digitorum sublimis	0.5–1 U/kg; 2 sites

Adapted from the BOTOX Product Monograph.

IN LOWER LIMB SPASTICITY:

- Recommended dose is **4–8 U/kg** body weight divided among the affected muscles
- Total dose of BOTOX in the first treatment session should not exceed 8 U/kg or 300 U, whichever is lower

Muscle	Total dosage; number of sites
Gastrocnemius medial head	1–2 U/kg; 2 sites
Gastrocnemius lateral head	1–2 U/kg; 2 sites
Soleus	1–2 U/kg; 2 sites
Tibialis posterior	1–2 U/kg; 2 sites

Adapted from the BOTOX Product Monograph.

When treating both upper and lower limbs in children:
Total dose of 10 U/kg or 340 U (whichever is lower) should **not** be exceeded in a 12-week interval

Patients may be considered for retreatment when the clinical effect of the previous injection has diminished. Reinjections should not occur before 12 weeks.

See Product Monograph for complete dosing and administration instructions.

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BOTOX dosing overview: Blepharospasm and cervical dystonia

Blepharospasm

1.25–2.25 U

- The initial recommended dose is 1.25–2.25 U (0.05–0.1 mL at each site) in the medial and lateral pretarsal orbicularis oculi of the upper lid and in the lateral pre-tarsal orbicularis oculi of the lower lid
- The initial dose should not exceed 25 U per eye
- Diluted BOTOX is injected using a sterile, 27–30-gauge needle with or without electromyographic guidance

~3 months

- Treatment effects last approximately 3 months, at which time the procedure can be repeated indefinitely
  - › Some tolerance may be found if treatments are given more frequently than every 3 months, and it is rare to have the effect be permanent
- At repeat treatment sessions, the dose may be increased up to 2-fold if the response from the initial treatment is considered insufficient, defined as an effect that lasts no longer than 2 months
  - › Injecting more than 5.0 U per site was found to be of little benefit
- The cumulative dose of BOTOX should not exceed 200 U in a 2-month period

Avoid injection near the levator palpebrae superioris to reduce the complication of ptosis. Avoid medial lower lid injections to help reduce diffusion into the inferior oblique, which may also reduce the complication of diplopia.

Cervical Dystonia (spasmodic torticollis)

200–360 U

- In initial controlled clinical trials, doses of diluted BOTOX ranged from 140 U to 280 U
- In clinical practice, a range of 200 U to 360 U has been used effectively
- Dosing must be tailored to the individual patient based on their head and neck position, localization of pain and muscle hypertrophy, body weight, and response
- A 25-, 27- or 30-gauge needle may be used for superficial muscles, and a 22-gauge needle may be used for deeper musculature
- The maximum cumulative dose should not generally exceed 360 U in a 3-month interval

~2 months

- Repeat doses should be administered when the clinical effect of a previous injection diminishes, but not more frequently than every 2 months

The extent of muscle hypertrophy and the muscle groups involved in the dystonic posture may change with time, necessitating alterations in the dose of toxin and muscles to be injected.

See Product Monograph for complete dosing and administration instructions.

Always be sure you've received actual BOTOX neurotoxin product

- To ensure product authenticity, look for the holographic film on the vial; "ALLERGAN" should appear within rainbow lines
- If you do not see the rainbow lines or if "ALLERGAN" does not appear, do not use the product, and please contact AbbVie directly

BOTOX is supplied in 200-, 100- and 50-unit sterile vials of *Clostridium botulinum* type A in a vacuum-dried form without a preservative.

Prior to intramuscular injection, reconstitute vacuum-dried BOTOX using sterile normal saline without a preservative; 0.9% sodium chloride injection is the only recommended diluent.

The term "Allergan unit" upon which dosing is based is a specific measurement of toxin activity that is unique to Allergan's formulation of botulinum toxin type A. Therefore, the "Allergan units" used to describe BOTOX activity are different from those used to describe that of other botulinum toxin preparations and the units representing BOTOX activity are not interchangeable with other products.

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Consult the Product Monograph at: abbv.ie/BotoxCanadaPMEN for contraindications, warnings, precautions, adverse reactions, interactions, dosing and conditions of clinical use.

The Product Monograph is also available by calling 1-888-704-8271.

REFERENCE: Current BOTOX Product Monograph, AbbVie Corporation.

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REVIEWED BY PAAB

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