

## **BOTULINUM A TOXIN vial:**

**Class:** Neuromuscular Blocker Agent

**Indications:** Bladder dysfunction, Blepharospasm, Cervical dystonia, Chronic migraine, Spasticity, Strabismus, Primary axillary hyperhidrosis, Cosmetic uses (Reduction of glabellar lines, Reduction of forehead lines, Reduction of lateral canthus lines).

**Available dosage form in the hospital:** VIAL (100 U, 500 U)

**Trade Names:**

**Dosage: Note:** The lowest recommended dose should be used when initiating treatment (regardless of indication). In adults treated for more than one indication, the maximum cumulative dose should be  $\leq 360$  units/3 months. Canadian labeling recommends a maximum cumulative dose of 6 units/kg (up to 360 units) over 3 months in adult patients receiving additional treatment for noncosmetic indications.

**-Bladder dysfunction:** Intradetrusor: **Note:** Prophylactic antimicrobial therapy (excluding aminoglycosides) should be administered 1-3 days prior to, on the day of, and for 1-3 days following onabotulinumtoxinA administration to decrease risk of urinary tract infection (UTI). Discontinue antiplatelet therapy at least 3 days prior to administration.

*-Detrusor overactivity associated with neurologic condition:* 30 injections of 1 mL (recommended concentration:  $\sim 6.7$  units/mL) for a total dose of 200 units/30 mL (maximum: 200 units); for the final injection,  $\sim 1$  mL of sterile NS should be injected to ensure that the remaining medication in the needle is delivered to the bladder; may consider retreatment with diminishing effect but no sooner than 12 weeks from previous administration (median time until second treatment in studies: 42-48 weeks).

*-Overactive bladder:* 20 injections of 0.5 mL (recommended concentration: 10 units/mL) for a total dose of 100 units/10 mL (maximum: 100 units); for the final injection,  $\sim 1$  mL of sterile NS should be injected to ensure that the remaining medication in the needle is delivered to the bladder; may consider retreatment with diminishing effect but no sooner than 12 weeks from the previous administration (median time until second treatment in studies:  $\sim 24$  weeks)

**-Blepharospasm: I.M.:**

Botox®: Initial dose: 1.25-2.5 units injected into the medial and lateral pretarsal orbicularis oculi of the upper lid and lateral pretarsal orbicularis oculi of lower lid

Dose may be increased up to twice the previous dose if the response from the initial dose lasted  $\leq 2$  months; maximum dose per site: 5 units. Tolerance may occur if treatments are given more often than every 3 months, but the effect is not usually permanent.

Cumulative dose:

*-U.S. labeling:*  $\leq 200$  units in 30-day period

*-Canadian labeling (not in U.S. labeling):* Botox®:  $\leq 200$  units in 2-month period

**-Cervical dystonia: I.M.:** For dosing guidance, the mean dose is 236 units (25th to 75th percentile range 198-300 units) divided among the affected muscles in patients previously treated with botulinum toxin (maximum:  $\leq 50$  units/site). Initial dose in previously untreated patients should be lower. Sequential dosing should be based on the patient's head and neck position, localization of pain, muscle hypertrophy, patient response, and previous adverse reactions. The total dose injected into the sternocleidomastoid muscles should be  $\leq 100$  units to decrease the occurrence of dysphagia.

*-Canadian labeling (not in U.S. labeling):* I.M.: Botox®: Effective range of 200-360 units has been used in clinical practice; administer no more frequently than every 2 months

**-Chronic migraine: I.M.:** Administer 5 units/0.1 mL per site. Recommended total dose is 155 units once every 12 weeks. Each 155 unit dose should be equally divided and administered bilaterally, into 31 total sites as described below (refer to prescribing information for specific diagrams of recommended injection sites):

*-Corrugator:* 5 units to each side (2 sites)

*-Procerus:* 5 units (1 site only)

*-Frontalis:* 10 units to each side (divided into 2 sites/site)

*-Temporalis:* 20 units to each side (divided into 4 sites/site)

- Occipitalis: 15 units to each side (divided into 3 sites/site)
- Cervical paraspinal: 10 units to each side (divided into 2 sites/site)
- Trapezius: 15 units to each side (divided into 3 sites/site)

**-Spasticity (focal): I.M.:** Individualize dose based on patient size, extent, and location of muscle involvement, degree of spasticity, local muscle weakness, and response to prior treatment. In clinical trials, total doses up to 360 units (Botox®) were administered as separate injections typically divided among selected muscles; may repeat therapy at  $\geq 3$  months with appropriate dosage based upon the clinical condition of patient at time of retreatment.

Suggested guidelines for the treatment of upper limb spasticity. The lowest recommended starting dose should be used and  $\leq 50$  units/site should be administered. **Note:** Dose listed is total dose administered as individual or separate intramuscular injection(s):

- Biceps brachii: 100-200 units (divided into 4 sites)
- Flexor digitorum profundus: 30-50 units (1 site)
- Flexor digitorum sublimis: 30-50 units (1 site)
- Flexor carpi radialis: 12.5-50 units (1 site)
- Flexor carpi ulnaris: 12.5-50 units (1 site)

Suggested guidelines for the treatment of stroke-related upper limb spasticity:

**Canadian labeling: Note:** Dose listed is total dose administered as individual or separate intramuscular injection(s):

- Biceps brachii: 100-200 units (up to 4 sites)
- Flexor digitorum profundus: 15-50 units (1-2 sites)
- Flexor digitorum sublimis: 15-50 units (1-2 sites)
- Flexor carpi radialis: 15-60 units (1-2 sites)
- Flexor carpi ulnaris: 10-50 units (1-2 sites)
- Adductor pollicis: 20 units (1-2 sites)
- Flexor pollicis longus: 20 units (1-2 sites)

**-Strabismus: I.M.: Note:** Several minutes prior to injection, administration of local anesthetic and ocular decongestant drops are recommended.

Initial dose:

- Vertical muscles and for horizontal strabismus  $< 20$  prism diopters: 1.25-2.5 units in any one muscle.
- Horizontal strabismus of 20-50 prism diopters: 2.5-5 units in any one muscle.
- Persistent VI nerve palsy  $\geq 1$  month: 1.25-2.5 units in the medial rectus muscle.

Re-examine patients 7-14 days after each injection to assess the effect of that dose. Subsequent doses for patients experiencing incomplete paralysis of the target may be increased up to twice the previous administered dose. The maximum recommended dose as a single injection for any one muscle is 25 units. Do not administer subsequent injections until the effects of the previous dose are gone.

**-Primary axillary hyperhidrosis:** Intradermal: 50 units/axilla. Injection area should be defined by standard staining techniques. Injections should be evenly distributed into multiple sites (10-15), administered in 0.1-0.2 mL aliquots, ~1-2 cm apart. May repeat when clinical effect diminishes.

**-Cosmetic uses:**

**-Reduction of glabellar lines:** Adults  $\leq 65$  years: I.M.: An effective dose is determined by gross observation of the patient's ability to activate the superficial muscles injected. The location, size, and use of muscles may vary markedly among individuals. Inject 0.1 mL (4 units) dose into each of five sites, two in each corrugator muscle and one in the procerus muscle for a total dose 0.5 mL (20 units) administered no more frequently than every 3-4 months. **Note:** Treatment of adults  $> 65$  years is approved in the Canadian labeling.

**-Reduction of forehead lines** (*Canadian labeling; not in U.S. labeling*): I.M.: Inject 2-6 units into each of four sites in the frontalis muscle every 1-2 cm along either side of forehead crease and 2-3 cm above eyebrows for total dose of 24 units.

**-Reduction of lateral canthus lines;** (*Canadian labeling; not in U.S. labeling*): I.M.: Inject 2-6 units into each of 1-3 injection sites, lateral to the lateral orbital rim.

## **Geriatric**

Initiate therapy at lowest recommended dose. Refer to adult dosing.

### **Renal Impairment :**

No dosage adjustment provided in manufacturer's labeling.

### **Hepatic Impairment :**

No dosage adjustment provided in manufacturer's labeling.

### **Common side effect:**

Bladder dysfunction:

Genitourinary: Urinary tract infection (18% to 49%), urinary retention (17%)

Cervical dystonia:

Central nervous system: Pain (32%), headache ( $\leq 11\%$ )

Gastrointestinal: Dysphagia (19%)

Neuromuscular & skeletal: Focal weakness (17%), neck pain (11%)

Respiratory: Upper respiratory infection (12%)

Other indications (blepharospasm, primary axillary hyperhidrosis, strabismus):

Ocular: Ptosis (blepharospasm 21%; strabismus 1% to 38%), vertical deviation (strabismus 17%)

**Pregnancy Risk Factor: C**