

Series Editor: William W. Huang, MD, MPH

Neurotoxins

Sarah L. Taylor, MD, MPH

Dr. Taylor is Assistant Professor of Dermatology, Wake Forest University School of Medicine, Winston-Salem, North Carolina. The author reports no conflict of interest.

Table 1.

Injectable Botulinum Neurotoxin Products^{a-c}

Trade Name (Manufacturer)	Generic Name	Type	Relative Per Unit Strength ^d	FDA-Approved Indications (Year Approved)	How Supplied, U
Botox (Allergan, Inc)	OnabotulinumtoxinA	A	1:1	Strabismus, blepharospasm (1989); cervical dystonia (2000); severe axillary hyperhidrosis (2004); chronic migraine headaches (2010); overactive bladder (2013)	100 and 200
Botox Cosmetic (Allergan, Inc)	OnabotulinumtoxinA	A	1:1	Glabellar rhytides (2002); lateral canthal lines (2013)	50 and 100
Dysport (Medicis Aesthetics Inc/Ipsen Pharmaceuticals, Inc)	AbobotulinumtoxinA	A	3:1	Glabellar rhytides (2009); cervical dystonia (2009)	300 and 500
Xeomin ^e (Merz Pharmaceuticals, LLC)	IncobotulinumtoxinA	A	1:1	Glabellar rhytides, blepharospasm, cervical dystonia (2010)	50 and 100
Myobloc (Solstice Neurosciences, Inc)	RimabotulinumtoxinB	B	40:1	Cervical dystonia (2000)	2500, 5000, and 10,000

Abbreviation: FDA, US Food and Drug Administration.

^aThere are 7 serologically distinct botulinum neurotoxins designated A through G; they are fermented from various strains of *Clostridium botulinum*. All share a common structural organization consisting of a heavy chain and a light chain polypeptide linked by a single disulfide bond. Serotypes A and B have clinical applications, with serotype A derived from the Hall strain and serotype B from the Bean strain.

^bMechanism of action for botulinum neurotoxin is inhibition of acetylcholine (ACh) release at the neuromuscular junction, thus inhibiting muscle contraction. The heavy chain binds to the cell membrane receptors of the nerve terminal to allow endocytosis of the neurotoxin complex. The light chain cleaves proteins in the soluble N-ethylmaleimide sensitive factor attachment protein receptors (SNARE) complex, preventing the ability of ACh-containing vesicles to fuse with the cell membrane to transmit ACh into the neuromuscular junction. Serotype A neurotoxins cleave synaptosomal associated protein of 25 kDa (SNAP-25), whereas serotype B neurotoxins cleave vesicle-associated membrane protein (VAMP).

^cAll of the above neurotoxins are sterile, vacuum-dried, purified botulinum toxin type A, which must be reconstituted with sterile 0.9% sodium chloride (with preservative or preservative free) prior to injection, except for rimabotulinumtoxin B, which is a sterile liquid with purified toxin that is ready to inject directly from the vial.

^dSuggested bioequivalence ratio compared to botulinum toxin type A (Botox). Different botulinum toxin products of the same serotype are not bioequivalent; therefore, the doses of different products are not interchangeable.

^eXeomin is unique because it is produced free of complexing proteins, which may prevent formation of antibodies to the neurotoxin.

Table 2.

Sites and Target Muscles^a

Site ^b	Target Muscle(s)	No. of Injections	Total Dose, U ^c	Treatment Target	Injection Tips	Potential Complications ^{d-f}
Forehead	Frontalis	4–12 total	10–30	Horizontal forehead lines	At least 1 cm above orbital rim	Brow ptosis
Glabella	Corrugator supercillii, procerus, depressor supercillii, orbicularis oculi, frontalis	5–7 total	20–40	“Elevens” or “worry or frown lines” in between the eyebrows, which are primarily due to hyperfunctioning corrugators; nasal root wrinkles are primarily from hyperfunctioning of the procerus	V-shaped pattern directed away from orbit, avoiding injection into the levator palpebrae superioris, which can result in eyelid ptosis	Eyelid ptosis (can treat with α_2 -adrenergic agonist apraclonidine ophthalmic drops, which give 2–3 mm temporary eyelid elevation due to contraction of Müller muscle)
Lateral eyelid	Lateral orbicularis oculi	2–5 per side	10–25	Crow’s-feet	At least 1 cm outside orbital rim	Eyelid ptosis, diplopia
Nasal dorsum	Nasalis (superior portion)	2–6 total	2–5	“Bunny lines”	Nasal dorsum, inject superficial to angular vein	Diplopia due to medial rectus muscle palsy
Lower eyelid	Orbicularis oculi	2–3 per side	2–8	Lower eyelid “roll”	Infraorbital rhytides	Lower eyelid weakness
Mouth	Levator labii superioris alaeque nasi	1 per side	8–10	“Gummy smile”	Very superficial and narrow muscle along each side of nose	Asymmetric smile
Perioral	Orbicularis oris	2–6 total	1–4	Short vertical lip lines (“smoker’s lines”)	“White roll,” inject between vermilion border and white portion of upper and lower lip	Lip incompetence, difficult phonation, cheek droop
Oral commissures	Depressor anguli oris	2 per side	2–6	Downturning of mouth at corners	Pinch muscle while frowning	Smile asymmetry
Chin	Mentalis	1–2 total	2–8	Pebbly, dimpled chin	Pinch muscle low on chin	Lip incompetence
Anterior neck	Platysma	1–2 per band	10–40	“Neck cords”	Pinch cord to inject	Dysphagia, dysphonia

^aInitial muscle paralysis usually occurs within 7 days after injection with peak effect at 14 days; paralysis lasts about 3–4 months.

^bWith the exception of the glabellar treatment, all others mentioned are off-label use.

^cTotal dose is expressed relative to onabotulinumtoxinA (Botox Cosmetic).

^dTemporary reactions: pain, bruising, or swelling at injection site; headache; asthenia; and localized infection.

^eSpread of neurotoxin effects: ptosis, dry eyes, diplopia, blurred vision, and asymmetry.

^fContraindications to treatment: pregnancy (category C), breastfeeding, neuromuscular disorders (eg, amyotrophic lateral sclerosis, Eaton-Lambert syndrome, myasthenia gravis), history of hypersensitivity to albumin or botulinum toxin as well as certain medications (eg, aminoglycosides, penicillamine, quinine, calcium channel blockers, cyclosporine, muscle relaxants).

Practice Questions

- 1. Activation of the procerus muscle causes:**
 - a. forehead wrinkling
 - b. infraorbital wrinkling
 - c. nasal root wrinkling
 - d. periocular wrinkling
 - e. suprabrow wrinkling

- 2. Botulinum toxin type A cleaves which of the following presynaptic proteins?**
 - a. acetylcholine
 - b. serotonin
 - c. synaptobrevin
 - d. synaptosomal associated protein of 25 kDa (SNAP-25)
 - e. syntaxin

- 3. Which of the following muscles is the most responsible for creating deep vertical lines in the glabellar area?**
 - a. corrugator supercilii
 - b. depressor supercilii
 - c. levator palpebrae superioris
 - d. orbicularis oculi
 - e. procerus

- 4. Eyelid ptosis is a common side effect due to inadvertent migration of botulinum toxin to which muscle?**
 - a. depressor superciliaris
 - b. frontalis
 - c. levator palpebrae superioris
 - d. nasalis
 - e. orbicularis oculi

- 5. Apraclonidine ophthalmic drops can give a 2- to 3-mm elevation in a ptotic eyelid by which mechanism?**
 - a. activation of the lateral orbicularis oculi
 - b. activation of the upper orbicularis oculi
 - c. contraction of Müller muscle
 - d. weakening of the levator palpebrae superioris
 - e. weakening of the lower frontalis

Fact sheets and practice questions will be posted monthly. Answers are posted separately on www.cutis.com.