

Marketed BTX Brands

Serotypes A and B of botulinum toxin (BTX) have been developed for human use. Neurotoxin type A preparations are the most widely used worldwide and the only ones approved for esthetic use by the US Food and Drug Administration.¹ There are currently three leading BTX-A products on the market in the Western hemisphere: onabotulinumtoxinA (ONA; Botox, Allergan), abobotulinumtoxinA (ABO; Dysport/Azzalure, Ipsen), and incobotulinumtoxinA (INCO; Xeomin/Bocouture, Merz).

All three preparations of BTX-A have a similar mechanism of action.^{2,3} BTX consists of the 150-kDa neurotoxin itself and a set of neurotoxin-associated complexing proteins (NAPs), which together form high-molecular weight progenitor complexes. Commercially available BTX-A formulations contain different complements of NAPs and therefore have different molecular weights and 3D structures.^{4,5} INCO differs from ONA and ABO in that it is free from complexing proteins and consists of only the 150-kDa neurotoxin responsible for the therapeutic effect.⁶ Importantly, it has been argued that the molecular weight or protein complex size does not affect the biologic activity or pharmacologic properties, as the BTX-A rapidly dissociates from the complexing proteins (if present) after dilution, drying, and reconstitution of the preparation, with 85% of the neurotoxin present in the 150-kDa free form prior to injection into target tissues.⁷

Stability

The commercial formulations evaluated by Frevert¹ showed that human serum albumin (HSA) is required to stabilize the BTX-A products, with ABO having the lowest content of all. The low amount of HSA in ABO could at least partly explain why not all the neurotoxin in ABO is bioavailable depending on the concentration of the HSA in the injected volume.⁸

Shelf life

According to respective product labels, ABO has a shelf life of 2 years at 2°C to 8°C. ONA can be stored for 2 or 3 years at 2°C to 8°C (depending on the number of units) or in the freezer, and INCO has a shelf life of 3 or 4 years at room temperature. After reconstitution, ONA and INCO are stable for 24 hours at 2°C to 8°C, and ABO is stable for 4 hours at this temperature.¹ The prolonged shelf life and less stringent temperature restrictions displayed by INCO suggest that complexing proteins are not required for BTX-A stability.⁹ Among the three leading available BTX-A products, INCO is the only botulinum product that is stable in lyophilized form for up to 4 years at room temperature, whereas ONA and ABO products must be refrigerated.¹⁰ Xeomin is free from complexing proteins. In a stress stability study, INCO survived storage at temperatures as high as 60°C for 1 month without loss of potency.⁹

BTX-B

RimabotulinumtoxinB, marketed as Myobloc (Solstice Neuroscience) in the United States and NeuroBloc (Eisai) in the United Kingdom, is primarily indicated for cervical dystonia.¹¹ BTX-B might also be indicated as an off-label drug for patients who have become resistant to BTX-A. Various factors impact the immunogenicity of botulinum neurotoxins, including product-related factors such as the manufacturing process, the antigenic protein load, and the presence of accessory proteins, as well as treatment-related factors such as the overall toxin dose, booster injections, and prior vaccination or exposure.¹² The development of neutralizing antibodies to BTX¹³ is also related to sequential high doses for long periods of time, being the most common cause of negative response to clinical treatment.

BTX-B has a mechanism of action similar to type A, but it cleaves VAMP (vesicle-associated membrane protein) instead of SNAP-25 (synaptosomal-associated protein 25). A disadvantage of BTX-B is that it is more expensive than BTX-A.

Table 1 lists all of the commercial brands of BTX-A and BTX-B available in the market.

Table 1 Commercial brands of BTX-A and BTX-B available in the market¹⁴

| COMMERCIAL NAME | TYPE | MANUFACTURER | MECHANISM OF ACTION | UNITS | INDICATIONS |
|--------------------------------|------|--|---------------------|--------------------|--|
| Botox (Onabotulinum-toxinA) | A | Allergan | SNAP-25 | 50U, 100U, or 200U | <ul style="list-style-type: none"> • Blepharospasm (repetitive and involuntary closure of the eyelid caused by contraction of the orbicularis oculi muscle) • Hemifacial spasm (involuntary and repetitive contraction of one half of the face) • Strabismus (crossed eyes) • Cervical dystonia (involuntary contraction of the neck muscles) • Pediatric cerebral palsy • Focal spasticity (muscle stiffness that limits or prevents movement, associated with stroke) • Hyperhidrosis (excessive sweating) • Hyperactive bladder (urinary incontinence) • Hyperkinetic facial lines (expression wrinkles on the forehead, glabella, around the eyes, mouth, and platysma) • Chronic migraine |
| Dysport (Abobotulinum-toxinA) | A | Ipsen | SNAP-25 | 300U or 500U | <ul style="list-style-type: none"> • Blepharospasm/hemifacial spasm • Strabismus • Cervical dystonia • Pediatric cerebral palsy • Dynamic equinus deformity • Cervical dystonia • Muscle spasticity • Hyperhidrosis |
| Xeomin (Incobotulinum-toxinA) | A | Merz | SNAP-25 | 100U | <ul style="list-style-type: none"> • Blepharospasm • Spasmodic torticollis (involuntary and repetitive contraction of the neck muscles) • Spasticity of upper limbs in adults (increased muscle tension/uncontrolled muscle stiffness) • Temporary improvement in the appearance of hyperkinetic facial lines (expression lines or wrinkles) |
| Botulift | A | Medytox | SNAP-25 | 100U | <ul style="list-style-type: none"> • Blepharospasm • Hemifacial spasm • Pediatric cerebral palsy • Dynamic equinus deformity • Hyperkinetic facial lines |
| Prosigne | A | Lanzhou Institute of Biological Products | SNAP-25 | 50U or 100U | <ul style="list-style-type: none"> • Strabismus • Blepharospasm • Hemifacial spasm • Spasmodic torticollis • Cervical dystonia • Spasticity • Cerebral palsy • Muscle rehabilitation • Hyperkinetic facial lines • Hyperhidrosis |
| Myobloc (Rimabotulinum-toxinB) | B | Solstice Neuroscience | VAMP | 5,000U | Cervical dystonia |
| NeuroBloc | B | Eisai | VAMP | 5,000U | Cervical dystonia |

*SNAP-25 is an intracellular protein fundamental for synaptic vesicle transmission; it was identified as the BTX-A target molecule. The formula contains complexes with sizes ranging from 500 kDa to 900 kDa.

References

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