Botox (onabotulinumtoxinA) - Drug Summary

Allergan, Inc.

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Related Drug Information

Botox (onabotulinumtoxinA)

BOXED WARNING

Effects may spread from the area of inj to produce symptoms consistent w/ botulinum toxin effects (eg, asthenia, generalized muscle weakness, diplopia, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence, breathing difficulties). Symptoms have been reported hrs to weeks after inj. Swallowing and breathing difficulties can be life threatening and there have been reports of death. Risk of symptoms is probably greatest in children treated for spasticity but can also occur in adults treated for spasticity and other conditions, particularly in patients who have an underlying condition that would predispose them to these symptoms. In unapproved uses and approved indications, cases of spread of effect have been reported at doses comparable to those used to treat cervical dystonia and spasticity and at lower doses.

THERAPEUTIC CLASS

Acetylcholine release inhibitor

DEA CLASS

RX

ADULT DOSAGE & INDICATIONS

Bladder Dysfunction

Overactive Bladder (OAB):
W/ symptoms of urge urinary incontinence, urgency, and frequency, in patients who have an inadequate response to or are intolerant of an anticholinergic medication

100 U; recommended dilution is 100 U/10mL w/ preservative-free 0.9% NaCl inj
Max: 100 U

Detrusor Overactivity:
Treatment of urinary incontinence due to detrusor overactivity associated w/ a neurologic condition in patients who have an inadequate response to or are intolerant of an anticholinergic medication

200 U per treatment; do not exceed

Consider for reinjection when the clinical effect of the previous inj has diminished, but no sooner than 12 weeks from the prior bladder inj

Refer to PI for further dosing and administration instructions

Migraine

Prophylaxis of headaches in patients w/ chronic migraine (≥15 days per month w/ headache lasting ≥4 hrs/day)

155 U IM using a sterile 30-gauge, 0.5-inch needle as 0.1mL (5 U) inj per each site; recommended dilution is 200 U/4mL or 100 U/2mL, w/ a final concentration of 5 U/0.1mL

Inj should be divided across 7 specific head/neck muscle areas as follows:
Frontalis: 20 U divided in 4 sites
Corrugator: 10 U divided in 2 sites
Procerus: 5 U in 1 site
Occipitalis: 30 U divided in 6 sites
Temporalis: 40 U divided in 8 sites
Trapezius: 30 U divided in 6 sites
Cervical Paraspinal: 20 U divided in 4 sites

Recommended re-treatment schedule is every 12 weeks

Refer to PI for further dosing and administration instructions

Spasticity

Recommended Dilution: 200 U/4mL or 100 U/2mL w/ preservative-free 0.9% NaCl inj

Tailor dosing based on individual size, number, and location of muscles involved, severity of spasticity, presence of local muscle weakness, patient's previous response, or adverse event history w/ therapy. Repeat treatment may be administered when the effect of a previous inj has diminished, but generally no sooner than 12 weeks after the previous inj

Upper Limb:
To decrease the severity of increased muscle tone in elbow flexors (biceps), wrist flexors (flexor carpi radialis and flexor carpi ulnaris), finger flexors (flexor digitorum profundus and flexor digitorum sublimis), and thumb flexors (adductor pollicis and flexor pollicis longus)

Dosing by Muscle for Upper Limb:
Biceps Brachii: 100-200 U divided in 4 sites
Flexor Carpi Radialis: 12.5-50 U in 1 site
Flexor Carpi Ulnaris: 12.5-50 U in 1 site
Flexor Digitorum Profundus: 30-50 U in 1 site
Flexor Digitorum Sublimis: 30-50 U in 1 site
Adductor Pollicis: 20 U in 1 site
Flexor Pollicis Longus: 20 U in 1 site

Max: 50 U/site

Lower Limb:
To decrease the severity of increased muscle tone in ankle and toe flexors (gastrocnemius, soleus, tibialis posterior, flexor hallucis longus, and flexor digitorum longus)

Dosing by Muscle for Lower Limb:
Gastrocnemius Medial Head: 75 U divided in 3 sites
Gastrocnemius Lateral Head: 75 U divided in 3 sites
Soleus: 75 U divided in 3 sites
Tibialis Posterior: 75 U divided in 3 sites
Flexor Hallucis Longus: 50 U divided in 2 sites
Flexor Digitorum Longus: 50 U divided in 2 sites

Refer to PI for further dosing and administration instructions

Cervical Dystonia

To reduce the severity of abnormal head position and neck pain associated w/ cervical dystonia

≥16 Years:
Tailor dose based on patient's head and neck position, localization of pain, muscle hypertrophy, patient response, and adverse event history
Initial: Start at a lower dose for a patient w/o prior use of Botox
Recommended Dilution: 200 U/2mL, 200 U/4mL, 100 U/1mL, or 100 U/2mL w/ preservative-free 0.9% NaCl inj, depending on volume and number of inj sites desired to achieve treatment objectives; refer to PI for dilution instructions for Botox vials
Max: 50 U/site

Refer to PI for further dosing and administration instructions

Hyperhidrosis

Severe Primary Axillary Hyperhidrosis Inadequately Managed w/ Topical Agents:
50 U/axilla; recommended dilution is 100 U/4mL w/ 0.9% preservative-free sterile saline

Administer repeat inj when the clinical effect of previous inj diminishes

Refer to PI for further dosing and administration instructions

Blepharospasm and Strabismus

Associated w/ dystonia, including benign essential blepharospasm or VII nerve disorders

Blepharospasm:
Initial: 1.25-2.5 U (0.05-0.1mL at each site)
Dose may be increased up to 2-fold if response from initial treatment does not last longer than 2 months; little benefit obtainable from injecting >5 U/site
Max: 200 U in a 30-day period

Recommended Dilution:
For 1.25 U: 100 U/8mL
For 2.5 U: 100 U/4mL

Strabismus:
Inject between 0.05-0.15mL/muscle

Initial Doses in Units:
Use the lower listed doses for treatment of small deviations. Use the larger doses only for large deviations
Vertical Muscles and Horizontal Strabismus <20 Prism Diopters: 1.25-2.5 U in any 1 muscle
Horizontal Strabismus of 20-50 Prism Diopters: 2.5-5 U in any 1 muscle
Persistent VI Nerve Palsy of ≥1 Month Duration: 1.25-2.5 U in the medial rectus muscle

Subsequent Doses for Residual/Recurrent Strabismus:
1. Reexamine patients 7-14 days after each inj to assess the effect of that dose
2. Patients experiencing adequate paralysis of the target muscle that require subsequent inj should receive a

dose comparable to the initial dose
3. Subsequent doses for patients experiencing incomplete paralysis of the target muscle may be increased up to 2-fold compared to the previously administered dose
4. Do not administer subsequent inj until effects of the previous dose have dissipated as evidenced by substantial function in the injected and adjacent muscles

Max: 25 U single inj for any 1 muscle

Refer to PI for further dosing and administration instructions

PEDIATRIC DOSAGE & INDICATIONS

Blepharospasm and Strabismus

Associated w/ dystonia, including benign essential blepharospasm or VII nerve disorders

≥12 Years:
Blepharospasm:
Initial: 1.25-2.5 U (0.05-0.1mL at each site)
Dose may be increased up to 2-fold if response from initial treatment does not last longer than 2 months; little benefit obtainable from injecting >5 U/site
Max: 200 U in a 30-day period

Recommended Dilution:
For 1.25 U: 100 U/8mL
For 2.5 U: 100 U/4mL

Strabismus:
Inject between 0.05-0.15mL/muscle

Initial Doses in Units:
Use the lower listed doses for treatment of small deviations. Use the larger doses only for large deviations
Vertical Muscles and Horizontal Strabismus <20 Prism Diopters: 1.25-2.5 U in any 1 muscle
Horizontal Strabismus of 20-50 Prism Diopters: 2.5-5 U in any 1 muscle
Persistent VI Nerve Palsy of ≥1 Month Duration: 1.25-2.5 U in the medial rectus muscle

Subsequent Doses for Residual/Recurrent Strabismus:
1. Reexamine patients 7-14 days after each inj to assess the effect of that dose
2. Patients experiencing adequate paralysis of the target muscle that require subsequent inj should receive a dose comparable to the initial dose
3. Subsequent doses for patients experiencing incomplete paralysis of the target muscle may be increased up to 2-fold compared to the previously administered dose
4. Do not administer subsequent inj until effects of the previous dose have dissipated as evidenced by substantial function in the injected and adjacent muscles

Max: 25 U single inj for any 1 muscle

Refer to PI for further dosing and administration instructions

DOSING CONSIDERATIONS

Elderly
Start at lower end of dosing range

Other Important Considerations
In treating adult patients for ≥1 indication, the max cumulative dose should not exceed 400 U in a 3-month interval

ADMINISTRATION

Intradermal/IM/Intradetrusor route

Refer to PI for further administration instructions.

Preparation/Dilution
1. Prior to inj, reconstitute each vial w/ only sterile, preservative-free 0.9% NaCl inj.
2. Draw up the proper amount of diluent in the appropriate size syringe; refer to PI for dilution instructions for Botox vials.
3. Slowly inject the diluent into the vial.
4. Discard the vial if a vacuum does not pull the diluent into the vial.
5. Gently mix w/ the saline by rotating the vial.
6. Draw into an appropriately sized sterile syringe an amount of the reconstituted toxin slightly greater than the intended dose.
7. Expel air bubbles in the syringe barrel.
8. Attach the syringe to an appropriate inj needle; confirm patency of the needle.
9. A new, sterile needle and syringe should be used to enter the vial on each occasion for removal.
10. Reconstituted Botox should be stored at 2-8°C (36-46°F) and should be administered w/in 24 hrs.

Overactive Bladder
Administration Instructions:
1. Fill (prime) inj needle w/ approx 1mL of reconstituted Botox prior to the start of inj (depending on the needle length) to remove any air.
2. Insert the needle approx 2mm into the detrusor, and space 20 inj of 0.5mL each (total volume of 10mL) approx 1cm apart.
3. For the final inj, inject approx 1mL of sterile normal saline so that the remaining Botox in the needle is delivered to the bladder.
4. After the inj are given, patients should demonstrate their ability to void prior to leaving the clinic; observe patient for at least 30 min post-inj and until a spontaneous void has occurred.

Detrusor Overactivity
200 U Vial of Botox:

1. Reconstitute a 200 U vial w/ 6mL of preservative-free 0.9% NaCl inj and mix vial gently.
2. Draw 2mL from the vial into each of three 10mL syringes.
3. Complete reconstitution by adding 8mL of preservative-free 0.9% NaCl inj into each of 10mL syringes, and mix gently; this will result in three 10mL syringes each containing 10mL (approx 67 U in each), for a total of 200 U of reconstituted Botox.
4. Use immediately after reconstitution in the syringe; dispose of any unused saline.

100 U Vial of Botox:
1. Reconstitute two 100 U vials, each w/ 6mL of preservative-free 0.9% NaCl inj and mix vials gently.
2. Draw 4mL from each vial into each of two 10mL syringes; draw the remaining 2mL from each vial into a third 10mL syringe for a total of 4mL in each syringe.
3. Complete reconstitution by adding 6mL of preservative-free 0.9% NaCl inj into each of the 10mL syringes, and mix gently; this will result in three 10mL syringes each containing 10mL (approx 67 U in each), for a total of 200 U of reconstituted Botox.
4. Use immediately after reconstitution in the syringe; dispose of any unused saline.

Administration Instructions:
1. Fill (prime) inj needle w/ approx 1mL of reconstituted Botox prior to the start of inj (depending on the needle length) to remove any air.
2. Insert the needle approx 2mm into the detrusor, and space 30 inj of 1mL each (total volume of 30mL) approx 1cm apart.
3. For the final inj, inject approx 1mL of sterile normal saline so that the remaining Botox in the needle is delivered to the bladder.
4. After the inj are given, the saline used for bladder wall visualization should be drained; observe patient for at least 30 min post-inj.

Migraine
A 1-inch needle may be needed in the neck region for patients w/thick neck muscles.
W/ the exception of the procerus muscle, which should be injected at 1 site (midline), all muscles should be injected bilaterally w/ half the number of inj sites administered to the left, and half to the right side of the head and neck.

Spasticity
An appropriately sized needle (eg, 25-30 gauge) may be used for superficial muscles, and a longer 22-gauge needle may be used for deeper musculature; localization of the involved muscles w/ techniques such as needle electromyographic guidance or nerve stimulation is recommended.

Cervical Dystonia
Use a sterile needle (eg, 25-30 gauge) of an appropriate length; localization of the involved muscles w/ electromyographic guidance may be useful.

Primary Axillary Hyperhidrosis
Define the hyperhidrotic area to be injected using standard staining techniques (eg, Minor's Iodine-Starch Test); refer to PI for instructions.
Using a 30-gauge needle, inject 50 U (2mL) intradermally in 0.1-0.2mL aliquots to each axilla evenly distributed in multiple sites (10-15) approx 1-2cm apart.
Each inj site has a ring of effect of up to approx 2cm in diameter; evenly space inj sites to minimize the area of no effect.
Inject each dose to a depth of approx 2mm and at a 45° angle to the skin surface, w/ the bevel side up to minimize leakage and to ensure the inj remain intradermal; if inj sites are marked in ink, do not inject Botox directly through the ink mark to avoid a permanent tattoo effect.

Blepharospasm
Use a sterile, 27- to 30-gauge needle w/o electromyographic guidance to inject into the medial and lateral pre-tarsal orbicularis oculi of upper lid and into the lateral pre-tarsal orbicularis oculi of the lower lid.
Avoiding inj near levator palpebrae superioris may reduce complication of ptosis.
Avoiding medial lower lid inj, and thereby reducing diffusion into inferior oblique, may reduce the complication of diplopia.
Ecchymosis occurs easily in soft eyelid tissues; prevent by applying pressure at inj site immediately after inj.

Strabismus
Inject into extraocular muscles utilizing electrical activity recorded from tip of inj needle as a guide to placement w/in the target muscle; inj w/o surgical exposure or electromyographic guidance should not be attempted.
To prepare the eye for inj, it is recommended that several drops of a local anesthetic and an ocular decongestant be given several min prior to inj.

HOW SUPPLIED

Inj: 100 U, 200 U

CONTRAINDICATIONS

Infection at the proposed inj site(s). Intradetrusor inj is contraindicated in patients w/ OAB or detrusor overactivity associated w/ a neurologic condition who have a UTI, in patients w/ urinary retention, and in patients w/ post-void residual (PVR) urine volume >200mL who are not routinely performing clean intermittent self-catheterization (CIC). Hypersensitivity to any botulinum toxin preparation or to any of the components in the medication.

WARNINGS/PRECAUTIONS

Not interchangeable w/ other botulinum toxin products; cannot be compared to nor converted into U of any other botulinum toxin products. Serious adverse reactions reported w/ unapproved uses. Serious and/or immediate hypersensitivity reactions reported; d/c and institute appropriate medical therapy immediately. Patients w/ neuromuscular disorders may be at increased risk of clinically significant effects; monitor patients w/ peripheral motor neuropathic diseases, amyotrophic lateral sclerosis, or neuromuscular junction disorders. May cause swallowing or breathing difficulties; increased risk of dysphagia in patients w/ smaller neck muscle mass and in those who require bilateral inj into the sternocleidomastoid muscle for treatment of cervical dystonia. Inj into levator scapulae may increase risk of URI and dysphagia. Closely monitor patients w/ compromised respiratory status being treated for spasticity. Reduced blinking from inj of orbicularis muscle may lead to corneal exposure, persistent epithelial defect, and corneal ulceration, especially in patients w/ VII nerve disorders; employ vigorous treatment for any epithelial defect. Retrobulbar hemorrhages sufficient to compromise retinal circulation reported

in patients being treated for strabismus; appropriate instruments to decompress the orbit should be accessible. Bronchitis was reported more frequently in patients being treated for upper limb spasticity and URTIs were reported more frequently in patients being treated for upper/lower limb spasticity. Autonomic dysreflexia associated w/ intradetrusor inj may occur in patients treated for detrusor overactivity associated w/ a neurological condition. Increases the incidence of UTI in patients w/ OAB. In patients who are not catheterizing, assess PVR urine volume w/in 2 weeks post-treatment and periodically as medically appropriate up to 12 weeks, particularly in patients w/ multiple sclerosis (MS) or diabetes mellitus (DM). Depending on patient symptoms, institute catheterization if PVR urine volume exceeds 200mL and continue until PVR falls to <200mL. Contains albumin; carries an extremely remote risk for transmission of viral diseases and Creutzfeldt-Jakob disease.

ADVERSE REACTIONS

OAB: UTI, dysuria, urinary retention, bacteriuria, residual urine volume.
Detrusor Overactivity Associated w/ a Neurologic Condition: UTI, urinary retention, hematuria, constipation, muscular weakness, dysuria, gait disturbance.
Chronic Migraine: Neck pain, headache, migraine, eyelid ptosis, musculoskeletal stiffness, muscular weakness, myalgia, inj-site pain, bronchitis, musculoskeletal pain.
Upper Limb Spasticity: Nausea, fatigue, bronchitis, pain in extremity, muscular weakness.
Lower Limb Spasticity: Arthralgia, back pain.
Cervical Dystonia: Dysphagia, URI, neck pain, headache.
Primary Axillary Hyperhidrosis: Inj-site pain/hemorrhage, non-axillary sweating, infection, pharyngitis, flu syndrome, headache, fever, neck/back pain, pruritus, anxiety.

DRUG INTERACTIONS

Potentiation of toxin effect may occur w/ aminoglycosides or other agents interfering w/ neuromuscular transmission (eg, curare-like compounds). Use of anticholinergic drugs after administration may potentiate systemic anticholinergic effects. Excessive neuromuscular weakness may be exacerbated by administration of another botulinum toxin prior to the resolution of the effects of a previously administered botulinum toxin. Use of a muscle relaxant before/after administration may exaggerate excessive weakness.

PREGNANCY AND LACTATION

Pregnancy: Category C.
Lactation: Caution in nursing.

MECHANISM OF ACTION

Purified neurotoxin complex; blocks neuromuscular transmission by binding to acceptor sites on motor or sympathetic nerve terminals, entering the nerve terminals, and inhibiting release of acetylcholine.

ASSESSMENT

Assess for infection at proposed inj site(s), muscle weakness/hypertrophy, neuromuscular disorders, compromised swallowing or respiratory function, increased risk for dysphagia, VII nerve disorders, MS, DM, potential causes of secondary hyperhidrosis (eg, hyperthyroidism), hypersensitivity, pregnancy/nursing status, and possible drug interactions. In patients undergoing intradetrusor inj, assess for UTI, urinary retention, and if PVR urine volume is >200mL and not routinely performing CIC.

MONITORING

Monitor for spread of toxin effects, hypersensitivity reactions, weakening of neck muscles, swallowing/speech/respiratory disorders, UTI, and other adverse reactions. Monitor patients w/ peripheral motor neuropathic diseases, amyotrophic lateral sclerosis, neuromuscular junction disorders, or compromised respiratory status. In patients w/ strabismus, monitor for retrobulbar hemorrhages. Monitor for bronchitis and URTIs in patients w/ spasticity. Monitor PVR urine volume (in patients who are not catheterizing) w/in 2 weeks post-treatment and periodically as medically appropriate up to 12 weeks, particularly in patients w/ MS or DM.

PATIENT COUNSELING

Advise to inform physician if unusual symptoms (eg, swallowing, speaking, breathing difficulty) develop, or if any existing symptom worsens. Instruct to avoid driving or engaging in other potentially hazardous activities if loss of strength, muscle weakness, blurred vision, or drooping eyelids occur. Advise to contact physician if experiencing difficulties in voiding or burning sensation upon voiding after bladder inj for urinary incontinence.

STORAGE

Unopened Vials: 2-8°C (36-46°F) for up to 36 months. Administer w/in 24 hrs of reconstitution; during this time period, store reconstituted sol at 2-8°C (36-46°F).

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