There are four neurotoxins on the market with aesthetic indications and others due to the market soon. Off-label use is common, as physicians experiment with dosing and dilution, placement of injection, and more in order to get the best results for each individual patient. Ahead is a guide to the available toxins with insights on market trends and future developments. Be sure to read on for expert tips on use of toxins and practice growth.

**BOTOX COSMETIC ONABOTULINUMTOXINA**
Allergan Aesthetics
Approved: 2002
Molecular Weight: 900kDa

**Indications**
Indicated in adult patients for the temporary improvement in the appearance of:
- Moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity
- Moderate to severe lateral canthal lines associated with orbicularis oculi activity
- Moderate to severe forehead lines associated with frontalis activity

**Dosage and Administration**
- Glabellar Lines: 0.1mL (4 Units) into each of five sites, for a total dose of 20 Units
- Lateral Canthal Lines: 0.1mL (4 Units) into each of three sites per side (6 total injection points), for a total of 24 Units
- Forehead Lines: 0.1mL (4 Units) into each of five forehead line sites (20 Units) with 0.1mL (4 Units) into each of five glabellar line sites (20 Units), for a recommended total of 40 Units
- In treating adults for more than one approved indications with Botox and Botox Cosmetic, do not exceed a total dose of 400 Units administered in a three-month interval

**Contraindications**
- Hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation
- Infection at the injection site

**VIRAL DISEASE NOTICE**
All available neuromodulators in the US contain human serum albumin and therefore a warning about associated risks:
“…contains human serum albumin. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases and Creutzfeldt-Jakob disease (CJD). No cases of transmission of viral diseases or CJD have ever been reported for albumin.”
INTERCHANGEABILITY NOTICE

All available Neuromodulators in the US have a similar warning in the PI, advising that potency units are not interchangeable.

The potency Units of [BoNT Neuromodulator Formulation] are specific to the preparation and assay method utilized. They are not interchangeable with other preparations of botulinum toxin products and, therefore, units of biological activity of [BoNT Neuromodulator Formulation] cannot be compared to nor converted into units of any other botulinum toxin products assessed with any other specific assay method.

DISTANT SPREAD OF TOXIN EFFECT

Postmarketing reports indicate that the effects of all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. These may include asthenia, generalized muscle weakness, diplopia, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence, and breathing difficulties. These symptoms have been reported hours to weeks after injection. Swallowing and breathing difficulties can be life threatening and there have been reports of death. The risk of symptoms is probably greatest in children treated for spasticity but symptoms can also occur in adults treated for spasticity and other conditions, particularly in those patients who have an underlying condition that would predispose them to these symptoms. In unapproved uses and in 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.

The warnings also state that there are no definitive serious adverse event reports of distant spread of toxin effect associated with dermatologic use of any of the approved neuromodulators for aesthetic indications at the approved doses.

How Supplied

Botox Cosmetic is supplied in single-dose 50 Units and 100 Units per vial. Prior to intramuscular injection, reconstitute each vacuum-dried vial of Botox Cosmetic with sterile, preservative-free 0.9% Sodium Chloride Injection USP. Store at 2-8°C before/after reconstitution.

Adverse Events

The most common adverse reactions are:

- Glabellar Lines: eyelid ptosis (3%)
- Lateral Canthal Lines: eyelid edema (1%)
- Forehead Lines: headache (9%) and brow ptosis (2%)

Immunogenicity

Among 916 Botox Cosmetic treated subjects, 14 subjects (1.5%) developed binding antibodies and no subjects (0%) developed the presence of neutralizing antibodies.

DYSPORT

Abobotulinumtoxina

Galderma

Approved: 2009

Molecular Weight: 500-900kDa

TOXIN TALK: MICRO-TOX

Also known as mesotox, this approach involves the relatively superficial placement of small aliquots of neuromodulator for an effect on skin texture, “brightness,” and sebum production. To learn more, read Dr. Gold’s article on page 26.

Indications

- The treatment of cervical dystonia in adults
- The temporary improvement in the appearance of moderate to severe glabellar lines associated with procerus and corrugator muscle activity in adults < 65 years of age
- The treatment of spasticity in patients 2 years of age and older

Dosage and Administration

- Administer a total dose of 50 Units, divided in five equal aliquots of 10 Units each, intramuscularly to affected muscles to achieve clinical effect
- Re-treatment should be administered no more frequently than every three months

Contraindications:

Hypersensitivity to:
- Any botulinumtoxin product or excipients
- Cow’s milk protein
- Infection at the proposed injection site(s)

How Supplied

Dysport is supplied as a dry powder, in single-dose 300 Unit and 500 Unit vials, which must be reconstituted with preservative-free 0.9% Sodium Chloride Injection, USP. Store at 2-8°C Before/after reconstitution.

Adverse Events

Nasopharyngitis, headache, injec-
Sheila Barbarino, MD shares insights on current trends with neuromodulators, from the areas being treated to the use of different dilutions, to combination treatments.

“The trend in the last five years with neuromodulators, instead of freezing the area, is relaxing the area...I really think that in the past, the target goal for the doctor was to freeze that area. And now it’s not so much anymore. I think that’s a good trend because I don’t think anybody looks completely natural or normal when their expressions are completely frozen. I think it’s very exciting that the consumers have caught up to this trend...

“What I like about the higher dilutions is I think that it achieves that natural result with less units and I think in my hands for certain neuromodulators it tends to last longer...I think patients also appreciate that they don’t have to spend as much every time they see you.”

Watch now: ModernAesthetics.com/series/aesthetics-dispatches/

Immunogenicity

Among 1,554 subjects who received up to nine cycles of treatment with Dysport for glabellar lines, two subjects (0.013%) tested positive for binding antibodies at baseline. Three additional subjects tested positive for binding antibodies after receiving treatment with Dysport. None of these subjects tested positive for neutralizing antibodies.

Ethnic Groups

Dysport has a label entry specific to ethnic groups: “Exploratory analysis in trials for glabellar lines in African-American subjects with Fitzpatrick skin types IV, V, or VI and in Hispanic subjects suggested that response rates at Day 30 were comparable to and no worse than the overall population.”

XEOMIN INCOBOTULINUMTOXINA

Merz Aesthetics
Approved: 2011
Molecular Weight: 150kDa

Indications

• Chronic sialorrhea
• Upper limb spasticity
• Cervical dystonia
• Blepharospasm
• Temporary improvement in the appearance of moderate to severe glabellar lines with corrugator and/or procerus muscle activity

Dosage and Administration

Glabellar Lines: the recommended dose is 20 Units per treatment session divided into five equal intramuscular injections of 4 Units each (two injections in each corrugator muscle and one injection in the procerus muscle); wait a minimum of three months before retreatment.

Contraindications

• Known hypersensitivity to the active substance botulinum neurotoxin type A or to any of the excipients
• Infection at the proposed injection sites

How Supplied

50 Units, 100 Units, or 200 Units lyophilized powder in a single-dose vial; Prior to injection, reconstitute each vial of Xeomin with sterile, preservative-free 0.9% Sodium Chloride Injection, USP
Store at <25°C Before/2-8°C after reconstitution

Adverse Events

Glabellar Lines: (>1% of patients) headache

Immunogenicity

Of the 1,490 patients treated with Xeomin in placebo-controlled clinical trials supporting approved indications, five (0.3%) patients were positive for...
neutralizing antibodies after treatment whose antibody status at baseline was unknown and four (0.2%) additional patients developed neutralizing antibodies after treatment. No patients demonstrated a secondary lack of treatment response due to neutralizing antibodies.

"Currently, there is much excitement and anticipation for a fifth botulinum toxin on the US market from Revance therapeutics called daxibotulumtoxinA. What makes this botulinum toxin unique is that it has been evaluated in clinical trials for a longer duration than the currently available botulinum toxins. It has demonstrated efficacy for a duration of 24 weeks or six months. Only time will tell if this botulinum toxin will really offer duration for six months in a real life setting but myself and my colleagues are very excited to see how this new botulinum toxin will play out in our practices, potentially offering a better duration, higher patient satisfaction...

The limited duration of botulinum toxins of only three to four months from the currently available botulinum toxins on the market has been one of the biggest complaints about this treatment modality, as many of our patients would enjoy a longer duration and have complained about the limited duration of their previous treatments. We hope that a longer duration and a new botulinum toxin will help expand the market."

Watch Now: ModernAesthetics.com/series/aesthetics-dispatches

TOXIN TALK: MYOMODULATION

Popularized by Mauricio de Maio, MD, the concept of myomodulation has taken two angles: Chemical myomodulation uses neurotoxins to affect muscles contraction; Mechanical myomodulation involves the use of HA fillers to either increase or reduce muscle action. (Aesthetic Plast Surg. 2018 Jun;42(3):798-814)

JEUVEAU PRABOTULINUMTOXINA
Evolum
Approved: 2019
Molecular Weight: 900kDa

Indications
Indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients

Dosage and Administration:
Glabellar Lines Administration: 0.1mL (4 Units) by intramuscular injection into each of five sites, for a total dose of 20 Units

Contraindications
Hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation
Infection at the injection site

How Supplied
Jeuveau is supplied in a single-dose 100Unit vial. Prior to intramuscular injection, reconstitute each vacuum-dried vial of Jeuveau with only sterile, preservative-free 0.9% Sodium Chloride Injection, USP.
Store at 2-8°C Before/after reconstitution

Adverse Events
The most common adverse reactions are headache (12%), eyelid ptosis (2%), upper respiratory tract infection (3%), increase white blood cell count (1%).

Immunogenicity
Among 1,414 subjects treated with prabotulinumtoxinA-xvfs, two subjects were found to have pre-existing antibodies and two subjects had treatment-emergent antibodies.

2. Prescribing information of the respective agents.