POLICY: Botulinum Toxin – Xeomin® (incobotulinumtoxinA for injection – Merz)

DATE REVIEWED: 06/03/2020

OVERVIEW

Xeomin® (incobotulinumtoxinA) is indicated in adult patients for the following:

- blepharospasm;
- cervical dystonia;
- chronic sialorrhea; AND
- upper limb spasticity.[1]

Xeomin is also indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugators and/or procerus muscle activity in adult patients.

The labels for the botulinum toxin type A products (Botox® [onabotulinumtoxinA], Dysport® [abobotulinumtoxinA], and Xeomin) state that there is a lack of interchangeability between the products for various reasons, including differences in the units of biological activity.[1-3] However, studies have demonstrated that identical units of Xeomin and Botox were equally effective.[4-7] Based on published literature, it has been established that Xeomin and Botox have identical therapeutic effects and adverse event (AE) profiles with a 1:1 conversion ratio.[7]

Other Uses with Supportive Evidence

Botulinum toxins, including Xeomin, have been studied in a variety of indications outside of FDA-approved uses. Literature is available to support use of Xeomin in the following conditions:

- **Hyperhidrosis, Primary Axillary, Palmar/Plantar, and Facial:** Overall, topical antiperspirants (e.g., aluminum chloride) are the recommended first-line therapy for the treatment of primary axillary hyperhidrosis and focal hyperhidrosis.[8-11] In the setting of primary axillary hyperhidrosis, Qbrexza, a topical anticholinergic, may also be used first-line.[12] The efficacy of Xeomin in the treatment of palmar/plantar hyperhidrosis and cranial hyperhidrosis was demonstrated in patients (n = 20) previously treated with Botox.[13] In a double-blind clinical trial, patients (n = 25) with moderate or severe palmar hyperhidrosis received in the same session intradermal injections of Botox on one hand and Xeomin on the other; the two products appeared to be comparable.[14] The efficacy of Xeomin for axillary hyperhidrosis was demonstrated in a prospective, double-blind, head-to-head intra-individual comparison trial vs. Botox.[15] A total of 46 patients received 50 units of botulinum toxin type A treatment (Xeomin in one axilla, and Botox in the other axilla). Efficacy and tolerability were similar between Botox and Xeomin. In addition, the efficacy of Xeomin in the treatment of axillary hyperhidrosis was demonstrated in patients (n = 41) previously treated with Botox.[13] AAN guidelines state that botulinum toxins are probably safe and effective and should be considered for palmar hyperhidrosis (plantar and facial hyperhidrosis are not addressed in the AAN guideline).[16]
- **Spasticity, Other Than Upper Limb (i.e., spasticity or hypertonia due to cerebral palsy, stroke, brain injury, spinal cord injury, multiple sclerosis, hemifacial spasm):** Oral medications have a long history in spasticity treatment (e.g., baclofen, benzodiazepines, phenytoin, or gabapentin) yet they have dose-limiting side effects and limited diffusion across the blood brain barrier.[17] In a prospective, randomized study in patients (n = 192) with upper limb spasticity due to stroke, brain injury, multiple sclerosis, or cerebral palsy, the majority of Xeomin-treated patients had improvement in functional disability and in muscle tone.[18] In a Phase III randomized study in patients (n = 148) with post-stroke upper limb spasticity, Xeomin was significantly more effective than placebo at Week 4 and at Week 12.[19] In addition, the efficacy of Xeomin in the treatment of

hemispasticity, arm spasticity, generalized spasticity, paraspasticity, leg spasticity, and hemifacial spasm was demonstrated in patients (n = 95) previously treated with Botox for at least 1 year under stable conditions and crossed over in a blinded fashion to Xeomin for 3 years.[13] Per the AAN, botulinum toxin is established effective in upper and lower limb spasticity and in cerebral palsy (Level A), and it may be considered in hemifacial spasm (Level C).[20,21]

Dosing Considerations

Definitive dosing has not been established for off-label uses of botulinum toxins, including Xeomin. Recommendations for maximum dosing and frequency for Xeomin are based on a suggested relative conversion of 1:1 between Xeomin and Botox units.[7] Specific dosing considerations by indication are noted below. For other indications addressed in this policy, specific dosing guidance is not available. In these cases, dosing is based on the Botox prescribing information, which states not to exceed a total dose of 400 units in a 3-month interval.[2]

- **Hyperhidrosis, Primary Axillary, Palmar/Plantar, and Facial**: Botox is indicated for axillary hyperhidrosis at a dose of 50 units per axilla.[2] For other forms of hyperhidrosis, definitive dosing has not been established.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Xeomin. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Requests for doses outside the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for 1 year in duration. In cases where the dosing interval is provided in months, 1 month is equal to 30 days.

Medical benefit coverage is not recommended for cosmetic conditions.

RECOMMENDED AUTHORIZATION CRITERIA

FDA-Approved Indications

1. Blepharospasm. Approve for 1 year.

Dosing. Approve up to a maximum dose of 100 units (50 units per eye), administered not more frequently than once every 12 weeks.

2. Cervical Dystonia (spasmodic torticollis). Approve for 1 year.

Dosing. Approve up to a maximum dose of 120 units, administered not more frequently than once every 12 weeks.

3. Sialorrhea, Chronic. Approve for 1 year.

Dosing. Approve up to a maximum dose of 100 units (50 units per side), administered not more frequently than once every 16 weeks.

4. Spasticity, Upper Limb. Approve for 1 year.

Dosing. Approve up to a maximum dose of 400 units, administered not more frequently than once every 12 weeks.

Other Uses with Supportive Evidence

5. Hyperhidrosis, Primary Axillary, Palmar/Plantar, and Facial. Approve for 1 year if the patient has tried at least one topical agent (e.g., aluminum chloride, Qbrexza™ [glycopyrronium cloth 2.4% for topical use]).

Dosing. Approve one of the following regimens (A or B):

A) For primary axillary hyperhidrosis: Approve a maximum dose of 50 units per axilla, administered not more frequently than once every 3 months.

B) For palmar/plantar or facial hyperhidrosis: Approve a maximum dose of 400 units, administered not more frequently than once every 3 months.

6. Spasticity, Other Than Upper Limb (i.e., spasticity or hypertonia due to cerebral palsy, stroke, brain injury, spinal cord injury, multiple sclerosis, hemifacial spasm). Approve for 1 year. (Note: For upper limb spasticity, see FDA-Approved Indication criterion #4 [above].)

Dosing.[1,2] Approve up to a maximum dose of 400 units, administered not more frequently than once every 3 months.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Xeomin has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. Cosmetic Uses (e.g., facial rhytides, frown lines, glabellar wrinkling, horizontal neck rhytides, mid and lower face and neck rejuvenation, platsymal bands, rejuvenation of the periorbital region). Cosmetic use is not recommended for coverage as this indication is excluded from coverage in a typical medical benefit.

2. Fibromyalgia. Limited data are available with Botox. No data are available with Xeomin at this time.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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HISTORY

Type of Revision	Summary of Changes	Date Reviewed
New policy	--	8/08/2018
Selected revision	Dosing updated throughout policy to simplify maximum approved dosing regimens.	12/05/2018
Early annual revision	**Spasticity, Other Than Upper Limb (i.e., spasticity or hypertonia due to cerebral palsy, stroke, brain injury, spinal cord injury, multiple sclerosis, hemifacial spasm):** "Other than upper limb" added to clarify this covers uses other than the FDA-approved indications, and "e.g." was changed to "i.e.".	05/08/2019
Selected revision	**Blepharospasm:** Removed requirement for previous trial of Botox, and increased maximum allowable dosing to 100 units (50 units per eye), in alignment with revised labeling.	05/22/2019
Annual revision	**FDA-Approved Indications:** • "Cervical Dystonia" updated to "Cervical Dystonia (spasmodic torticollis)".	06/03/2020