BOTOX®
onabotulinumtoxinA injection

Companion *iPad®/ iPhone® App*

3D Cervical Dystonia

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Injection Workbook for **Movement Disorders**

Patient Assessment, Advanced Anatomy, and Injection Considerations for Cervical Dystonia

Treatment Considerations for Blepharospasm

INDICATIONS

Cervical Dystonia

BOTOX® (onabotulinumtoxinA) for injection is indicated for the treatment of adults with cervical dystonia to reduce the severity of abnormal head position and neck pain associated with cervical dystonia.

Blepharospasm and Strabismus

BOTOX is indicated for the treatment of strabismus and blepharospasm associated with dystonia, including benign essential blepharospasm or VII nerve disorders in patients 12 years of age and older.

IMPORTANT SAFETY INFORMATION, INCLUDING BOXED WARNING

WARNING: DISTANT SPREAD OF TOXIN EFFECT

Postmarketing reports indicate that the effects of BOTOX and 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 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.

Please see additional Important Safety Information throughout.

Please see full Prescribing Information, including Boxed Warning and Medication Guide, or visit https://www.rxabbvie.com/pdf/botox_pi.pdf

BOTOX®
onabotulinumtoxinA injection

Introduction

This workbook contains essential information regarding the use of BOTOX® for Cervical Dystonia (CD). It is designed to help hone your skills and understanding of the following areas:

- Patient identification and assessment
- Safety and efficacy data
- Muscle/dose selection strategies
- Dilution and reconstitution guidelines

Additionally, you'll find information about resources and services provided by AbbVie, as part of our commitment to support your practice.

Table of contents

IMPORTANT SAFETY INFORMATION (continued)

CONTRAINDICATIONS

BOTOX is contraindicated in the presence of infection at the proposed injection site(s) and in patients who are hypersensitive to any botulinum toxin product or to any of the components in the formulation.

WARNINGS AND PRECAUTIONS

Spread of Toxin Effect

See *Boxed Warning*.

No definitive serious adverse event reports of distant spread of toxin effect associated with BOTOX for blepharospasm at the recommended dose (30 Units and below) or strabismus at the labeled dose have been reported.

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Common postures involved in Cervical Dystonia

According to a study of 300 patients[1]:

82% of patients

Torticollis *(rotated)*

42% of patients

Laterocollis *(to the side)*

25% of patients

Anterocollis *(forward)*

29% of patients

Retrocollis *(backward)*

66% of **Cervical Dystonia** patients present with a **combination of postures**[1]

Complex clinical features may lead to delayed diagnosis and treatment[2,3]

Cervical Dystonia can be difficult to identify

- Patients can linger outside of specialists' care (eg, diagnosis by PCP as muscle strain)[4]
  - Misdiagnosed as other conditions, such as cervical spondylosis, myofascial pain syndrome, or Parkinson's disease[5]
- Symptoms may still persist when treated with oral medications (eg, antispasmodic, pain) and physical therapy

According to the largest observational study of Cervical Dystonia patients (N = 1037)[3]:

5 years

Time from Cervical Dystonia onset to diagnosis (mean)[3]

1.2 years

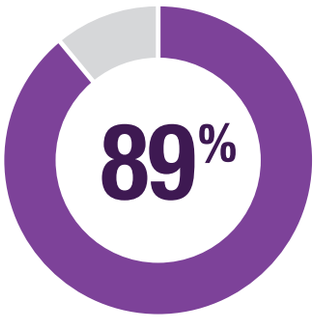
Time from Cervical Dystonia diagnosis to any treatment (mean)[3]

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Lack of Interchangeability Between Botulinum Toxin Products
The potency Units of BOTOX 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 BOTOX cannot be compared to nor converted into Units of any other botulinum toxin products assessed with any other specific assay method.

Please see additional Important Safety Information throughout.

Look for subtle features of Cervical Dystonia

Neck Pain[3]



of patients with Cervical Dystonia (N = 1037)

Head Tremor[1]

of patients with Cervical Dystonia (N = 300)

Distinguishing between dystonic and essential tremor

- Cervical Dystonia may first manifest as tremor before clear abnormal head posture, thus potentially leading to misdiagnosis of essential tremor (ET)[6]
- Consider evaluating all patients presenting with tremor for dystonic head position
- ET often has a regular oscillation while the movement in CD is usually irregular[7,8]
- When a patient lies down, ET may stop whereas head tremor in CD usually persists[8]
- Sensory tricks can reduce or stop tremor in CD, but not ET[8]

Consider symptoms beyond neck pain and tremor

- Sensory tricks[9,10]
- Morning benefit (symptoms are milder in the morning)[9]
- Tenderness on palpation[9]
- Exacerbating factors—may be frequent and prominent[9]
  - Fatigue, stress, motor tasks (eg, driving, walking, or writing)

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Serious Adverse Reactions With Unapproved Use
Serious adverse reactions, including excessive weakness, dysphagia, and aspiration pneumonia, with some adverse reactions associated with fatal outcomes, have been reported in patients who received BOTOX injections for unapproved uses. In these cases, the adverse reactions were not necessarily related to distant spread of toxin, but may have resulted from the administration of BOTOX to the site of injection and/or adjacent structures. In several of the cases, patients had preexisting dysphagia or other significant disabilities. There is insufficient information to identify factors associated with an increased risk for adverse reactions associated with the unapproved uses of BOTOX. The safety and effectiveness of BOTOX for unapproved uses have not been established.

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Use screening techniques to help identify Cervical Dystonia

- Ask the patient if they've been experiencing neck pain[9]
  Look for patient's use of sensory tricks, or *gestes antagonistes*[9]
- Distinguish between Cervical Dystonia tremor and other tremors, such as essential or Parkinson's disease[6,8]
- Instruct patient to move upper extremities in a repetitive and alternating pattern (or other exacerbating maneuver) and observe the full expression of the abnormal movement and posture[9]
- Observe head position during patient's gait[9]
- Consult TWSTRS* to help establish baseline postures/head position, assess neck pain, and identify the impact of CD

*TWSTRS = Toronto Western Spasmodic Torticollis Rating Scale.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

Hypersensitivity Reactions

Serious and/or immediate hypersensitivity reactions have been reported. These reactions include anaphylaxis, serum sickness, urticaria, soft-tissue edema, and dyspnea. If such a reaction occurs, further injection of BOTOX should be discontinued and appropriate medical therapy immediately instituted. One fatal case of anaphylaxis has been reported in which lidocaine was used as the diluent, and consequently, the causal agent cannot be reliably determined.

Please see additional Important Safety Information throughout.

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Cervical Dystonia screening guide*

Patient's name _____

In addition to traditional methods of patient assessment, these 5 pivotal questions can aid in Cervical Dystonia screening[11]

1. Does your patient find his/her head turning, tilting, or shifting in any direction?
2. Does your patient's head shake or jerk?
3. Do your patient's shoulders lift or pull up or down without his/her control?
4. Have other people told your patient that he/she has head tremor?
5. Does your patient have any pain or stiffness in his/her neck most of the time?

Further screening may proceed as follows[9]

Does the patient have…

1. Clinical features of Cervical Dystonia in addition to head deviations:

- ☐ Sensory tricks
- ☐ Morning benefit
- ☐ Common exacerbating factors
  - – Fatigue; stress; motor tasks such as driving, walking, or writing
- ☐ Neck pain
- ☐ Tremor
- ☐ Tenderness on palpation

2. Other neurological deficits:

- ☐ Dysphagia
  - – Delayed swallowing reflex and/or residue at the back of the tongue
- ☐ Cervical vertebral degeneration impinging on neural structures

3. A disability:

- ☐ Mild ☐ Moderate ☐ Severe
- ☐ Compensatory strategies _____

_____

Patient's perception of disability associated with Cervical Dystonia

☐ Mild ☐ Moderate ☐ Severe

Perform differential diagnosis[9]

1. Etiology:

- ☐ Idiopathic
- ☐ Other _____
- ☐ Neck or head trauma

2. Rule out nondystonic causes such as:

- ☐ Orthopedic
- ☐ Neurological
- ☐ Congenital abnormalities
- ☐ Neuro-ophthalmologic
- ☐ Infectious

3. Rule out other hyperkinetic movement disorders such as:

- ☐ Motor tics
- ☐ Myoclonic dystonia vs myoclonic jerks
- ☐ Choreic movements
- ☐ Postural (vs dystonic) head tremor

*Does not constitute all of the screening criteria or clinical observations required for appropriate diagnosis of Cervical Dystonia.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Increased Risk of Clinically Significant Effects With Preexisting Neuromuscular Disorders
Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis (ALS), or neuromuscular junction disorders (eg, myasthenia gravis or Lambert-Eaton syndrome) should be monitored when given botulinum toxin.

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

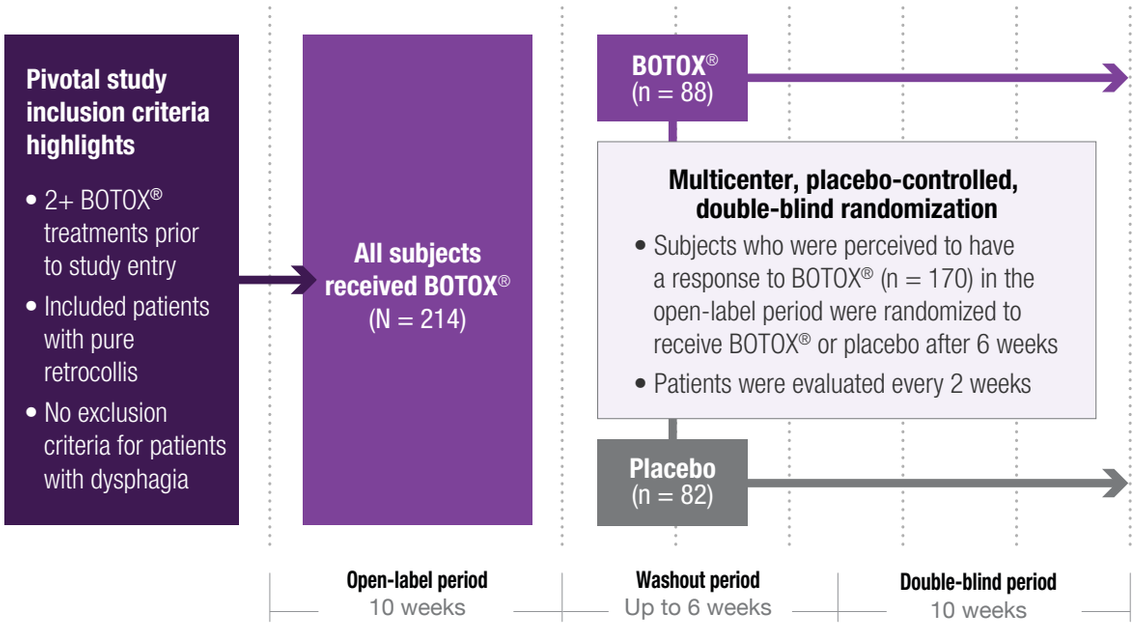
BOTOX®: A proven treatment for Cervical Dystonia for 20+ years

Most studied neurotoxin in the world

23K+	3.3K+	155+	84%
PATIENTS STUDIED[12,*]	**PUBLISHED PAPERS**[13,†]	**SPONSORED STUDIES**[12,*]	**OF TOXIN-TREATED CD PATIENTS RECEIVE BOTOX®**[14,15,‡] (N = 11,107)

*Across all indications.
†Across therapeutic indications.
‡According to claims data.

The first pivotal study in Cervical Dystonia[16-18]



Patients received 4+ BOTOX® treatments by end of study

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Increased Risk of Clinically Significant Effects With Preexisting Neuromuscular Disorders (continued)
Patients with known or unrecognized neuromuscular disorders or neuromuscular junction disorders may be at increased risk of clinically significant effects, including generalized muscle weakness, diplopia, ptosis, dysphonia, dysarthria, severe dysphagia, and respiratory compromise from therapeutic doses of BOTOX (see *Warnings and Precautions*).

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Pivotal study design[16-18]

DUAL PRIMARY ENDPOINTS

Change in CDSS* at Week 6

Percentage of patients with any improvement on Physician Global Assessment Scale at Week 6

*CDSS = Cervical Dystonia Severity Scale.

SECONDARY ENDPOINTS

Change in pain intensity at Week 6

Change in pain frequency at Week 6

Baseline characteristics of subjects in the double-blind period[17,18]

	BOTOX® (n = 88)	Placebo (n = 82)
Gender, Female	71%	81%
Age (mean)	55 years	55 years
Duration of CD (mean)	11.2 years	9.1 years
Posture†	**BOTOX® (n = 88)**	**Placebo (n = 82)**
Torticollis	98%	99%
Laterocollis	88%	89%
Anterocollis	34%	37%
Retrocollis	38%	32%
Shift	38%	29%
Shoulder elevation	59%	62%

†Patients indicated 1 or more postures prior to initiation of open-label treatment. Patients with pure anterocollis or pure shift were not enrolled.

INCLUSION CRITERIA[18]

- Male or female, ≥ 21 to ≤ 75 years of age
- Clinical diagnosis of Cervical Dystonia
- Stable clinical course for at least 1 month prior to study
- A minimum severity score of 4 or greater on the CDSS at Visit 1 and at Visit 7
- Documented history of treatment with BOTOX® for a minimum of 2 consecutive injections administered at 12- to 16-week intervals prior to entry into the study
- Documented dose at the 2 previous injections prior to enrollment of ≤ 360 Units per treatment
- Females of childbearing potential must have had a negative urine pregnancy test at the time of study entry

EXCLUSION CRITERIA[18]

- Concurrent or previous BOTOX® treatment for any other indication (eg, blepharospasm)
- Current or previous surgery, peripheral denervation, and/or spinal cord stimulation for Cervical Dystonia
- Profound atrophy of the muscles to be injected
- Presence of pure anterocollis or pure head shift as the sole component of Cervical Dystonia
- Known sensitivity to any of the components of the study medication, which are *Clostridium botulinum*, albumin (human), and sodium chloride
- Uncontrolled systemic disease (eg, hypertension, diabetes, severe cardiovascular disease) that might interfere with the ability to complete this study
- Current infection at the injection site or symptoms of a systemic infection
- Diagnosis of myasthenia gravis, Eaton-Lambert syndrome, amyotrophic lateral sclerosis, or any other significant neuromuscular disease that might interfere with the study
- Concurrent use of aminoglycoside antibiotics or agents that interfere with neuromuscular transmission
- Females only: pregnant, nursing, or planning pregnancy during the course of the study or a woman of childbearing potential not using a reliable means of contraception

IMPORTANT SAFETY INFORMATION (continued)

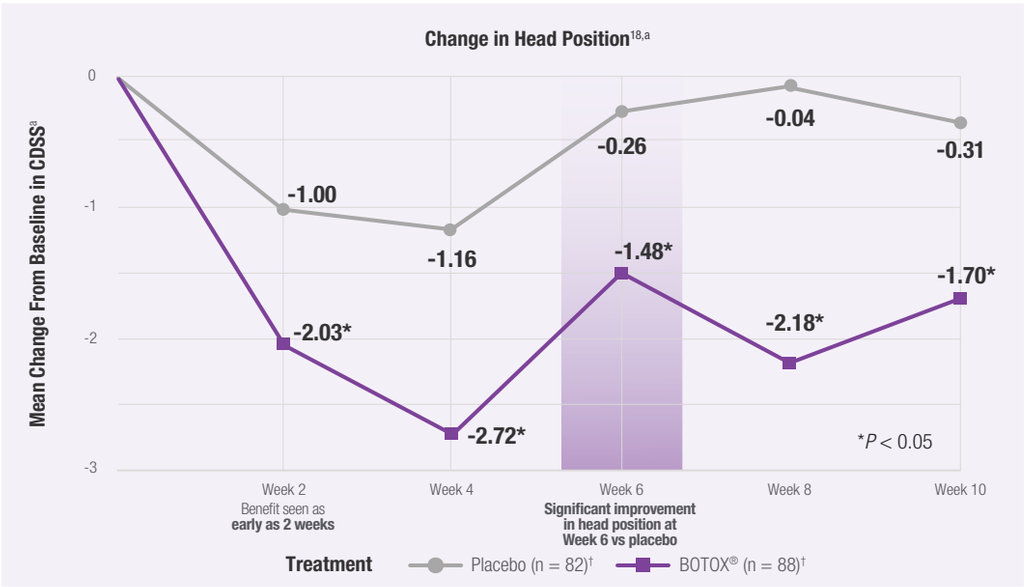
WARNINGS AND PRECAUTIONS (continued)

Dysphagia and Breathing Difficulties

Treatment with BOTOX and other botulinum toxin products can result in swallowing or breathing difficulties.

Please see additional Important Safety Information throughout.

BOTOX® significantly improved head position at Week 6 (primary endpoint)[16,18]

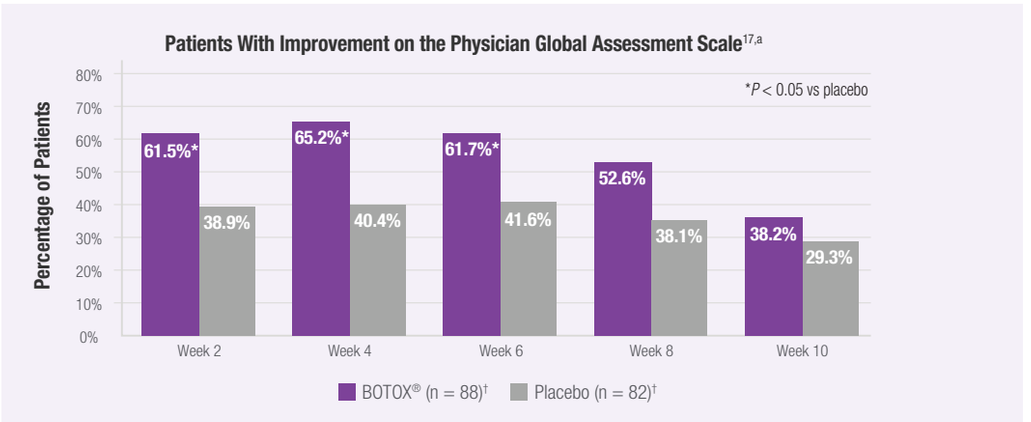


NOTES:

- Week 2 was the first prespecified efficacy evaluation time point; primary endpoint was measured at 6 weeks
- The adjusted mean change in CDSS score from the double-blind period baseline showed a significant, greater reduction in the BOTOX® group than in the placebo group at weeks 2, 4, 8, and 10[18]

[a]CDSS quantifies the severity of abnormal head positioning and was devised for this study. CDSS allots 1 point for each 5 degrees (or part thereof) of head deviation in each of the 3 planes of head movement (range of scores up to theoretical maximum of 54).[16]
†Represents total patients randomized for each treatment group. At different follow-up time points, n-values range from 72 to 88 for BOTOX® and 58 to 82 for placebo.[17,18]

Significant increase in the percentage of patients who showed improvement on the Physician Global Assessment Scale at Week 6 (primary endpoint)[16,17]



Physicians noted overall improvements as early as 2 weeks with BOTOX®

NOTE:

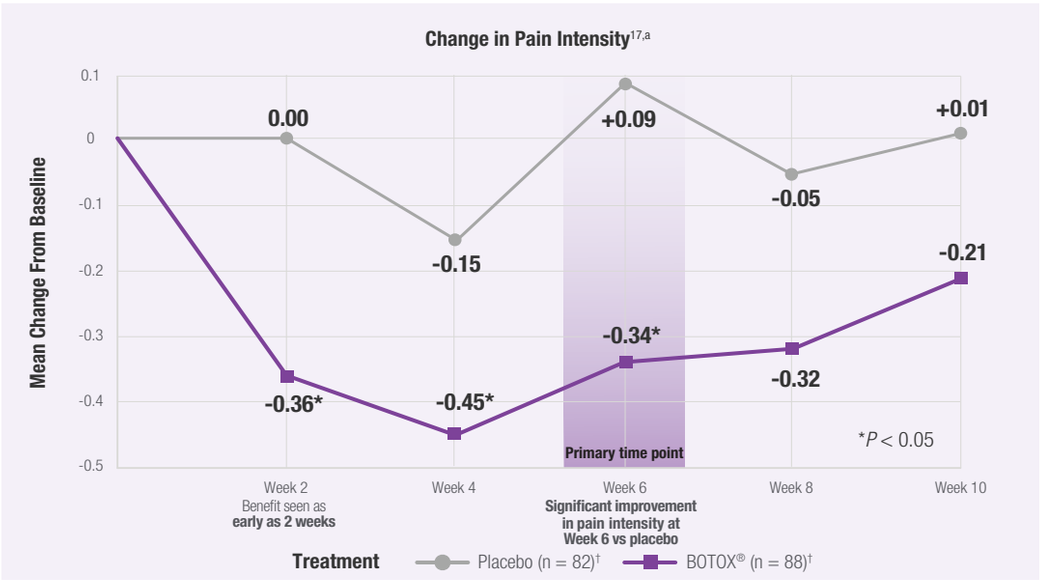
- Week 2 was the first prespecified efficacy evaluation time point; primary endpoint was measured at 6 weeks

[a]The Physician Global Assessment Scale is a 9-category scale scoring the physician's evaluation of the patient's status compared with baseline, ranging from -4 to +4 (very marked worsening to complete improvement), with 0 indicating no change from baseline and +1 indicating slight improvement.[16]
†Represents total patients randomized for each treatment group. Sample size varied for each observed data point depending on the number of subjects available for follow-up.[17]

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Dysphagia and Breathing Difficulties (continued)
Patients with preexisting swallowing or breathing difficulties may be more susceptible to these complications. In most cases, this is a consequence of weakening of muscles in the area of injection that are involved in breathing or oropharyngeal muscles that control swallowing or breathing (see *Boxed Warning*).

Please see additional Important Safety Information throughout.

BOTOX® significantly improved pain intensity associated with Cervical Dystonia at Week 6 (secondary endpoint)[16,17]

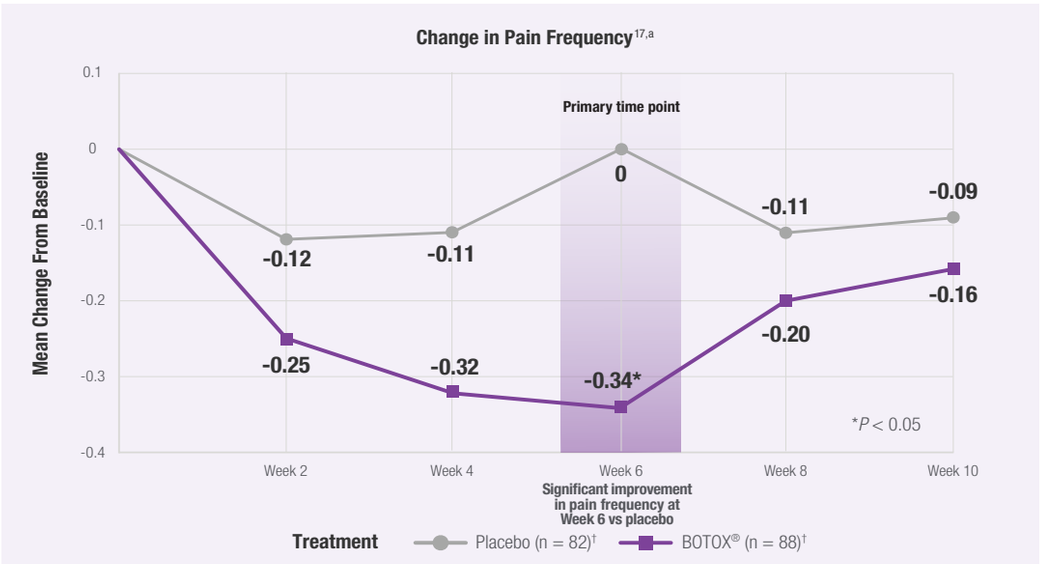


NOTE:

- Week 2 was the first prespecified efficacy evaluation time point; primary endpoint was measured at 6 weeks

[a]Pain intensity was evaluated on a scale of 0 (no pain) to 4 (very severe in intensity).[16]
†Represents total patients randomized for each treatment group. Sample size varied for each observed data point depending on the number of subjects available for follow-up.[17]

BOTOX® significantly improved pain frequency associated with Cervical Dystonia at Week 6 (secondary endpoint)[16,17]



NOTE:

- Week 2 was the first prespecified efficacy evaluation time point; primary endpoint was measured at 6 weeks

[a]Pain frequency was evaluated on a scale of 0 (no pain) to 4 (constant in frequency).[16]
†Represents total patients randomized for each treatment group. Sample size varied for each observed data point depending on the number of subjects available for follow-up.[17]

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

Corneal Exposure and Ulceration in Patients Treated With BOTOX for Blepharospasm

Reduced blinking from BOTOX injection of the orbicularis muscle can lead to corneal exposure, persistent epithelial defect, and corneal ulceration, especially in patients with VII nerve disorders.

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Established and well-characterized safety profile with 20+ years of clinical use

Most frequently reported adverse reactions in patients with Cervical Dystonia evaluated for safety in double-blind and open-label studies following injection of BOTOX®[16]

Adverse Reactions	BOTOX®
Dysphagia	19%
Upper respiratory infection	12%
Neck pain	11%
Headache	11%

0% **Discontinuation rate due to adverse events in a pivotal trial up to 10 weeks (n = 214)**[17]

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

Retrobulbar Hemorrhages in Patients Treated With BOTOX for Strabismus

During the administration of BOTOX for the treatment of strabismus, retrobulbar hemorrhages sufficient to compromise retinal circulation have occurred. It is recommended that appropriate instruments to decompress the orbit be accessible.

Please see additional Important Safety Information throughout.

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236 Units Mean Dose in Pivotal Trial[16]

Muscle[16]	Low BOTOX® dose[19]	Mean dose in pivotal study[18]	High BOTOX® dose[19]
Levator scapulae	20 Units	49 Units	100 Units
Scalene complex	15 Units	42 Units	50 Units
Sternocleidomastoid	15 Units	55 Units	100 Units
Trapezius (upper)	20 Units	70 Units	100 Units
Longissimus	30 Units	71 Units*	100 Units
Semispinalis capitis	30 Units		100 Units
Splenius capitis	15 Units	87 Units†	100 Units
Splenius cervicis	20 Units		60 Units

236 Units = mean BOTOX® dose in CD pivotal study
(25th to 75th percentile range was 198 Units to 300 Units)[16]

- In treating adult patients for 1 or more indications, the maximum cumulative dose should not exceed 400 Units in a 3-month interval

*Mean dose administered in 1+ of these 2 muscles.
†Mean dose administered in both muscles together.

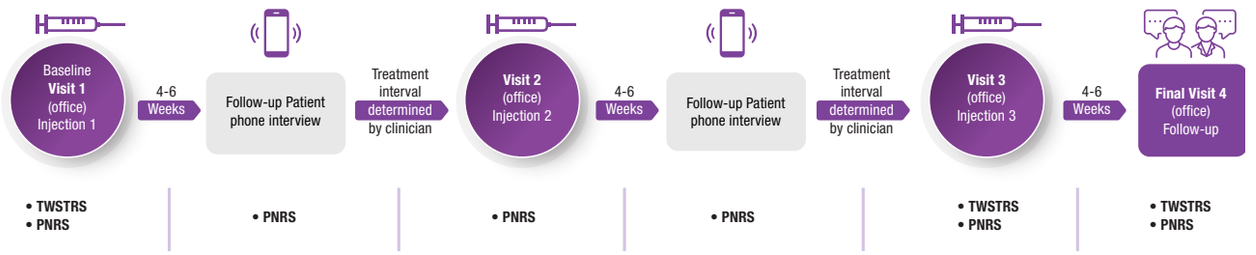
IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Human Albumin and Transmission of Viral Diseases
This product contains albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases and variant Creutzfeldt-Jakob disease (vCJD). There is a theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD), but if that risk actually exists, the risk of transmission would also be considered extremely remote. No cases of transmission of viral diseases, CJD, or vCJD have ever been identified for licensed albumin or albumin contained in other licensed products.

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Observational Study in Cervical Dystonia: CD PROBE Post Hoc Analysis

CD PROBE Study Design[20, 21]	
Objective	To describe real-world, clinical practices of neurologists, physiatrists, and other physicians who regularly treat CD patients
Study Design	Prospective, multicenter, observational, clinical registry study
Study participants	Diagnosis of Cervical Dystonia • Candidates for BOTOX® (based on investigator's clinical judgement), and/or: – New to the physician's practice or new to botulinum toxin therapy* – Previous participants in a clinical trial of botulinum toxin could be included if > 16 weeks since last dose



*Dosing and injection pattern were those customary for practice of the physician.
CD PROBE, Cervical Dystonia Patient Registry for Observation of OnabotulinumtoxinA Efficacy; PNRS, Pain Numeric Rating Scale, TWSTRS, Toronto Western Spasmodic Torticollis Rating Scale.

Baseline Characteristics of Post Hoc Analysis[22]	N = 319
Female, n (%)	236 (74.0)
Age (years); mean (SD)	58.8 (14.1)
White; n (%)	294 (92.2)
Age at Symptom Onset (years); mean (SD)	49.3 (16.6)
Time from CD Onset to CD Diagnosis (years); (SD)	5.2 (7.4)
Time from CD Diagnosis to First Treatment (years); mean (SD)	1.1 (3.4)
Baseline Posture; n (%)	
Torticollis	165 (51.7)
Laterocolis	135 (42.3)
Retrocolis	12 (3.8)
Anterocolis	7 (2.2)

Patients enrolled in the CD PROBE registry were included in this analysis if:

1. They recieved treatment in a manner consistent with product labeling through all scheduled sessions.[a]
2. Treatment was administered exclusively to one (or more) of the following treatment sites within the dose ranges indicated[b] (maximum total dose treatment session = 400 Units): Levator scapulae: 20-100 Units; Scalene complex: 15-50 Units; Splenius capitis: 15-100 Units; Sternocleidomastoid: 15-100 Units; Longissimus: 30-100 Units; Semispinalis capitis[c]: 30-100 Units; Splenius cervicis: 20-60 Units; Trapius (Upper): 20-100 Units

[a]Patients were excluded from this cohort analysis if any single treatment did not conform to the stated criteria.
[b]If bilateral treatments of the same muscle were administered during a single treatment session, the dose administered to each side must have been within the dose ranges.
[c]Not differentiated in the study from Semispinalis.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
ADVERSE REACTIONS

Adverse reactions to BOTOX for injection are discussed in greater detail in the following sections: *Boxed Warning*, *Contraindications*, and *Warnings and Precautions*.

Please see additional Important Safety Information throughout.

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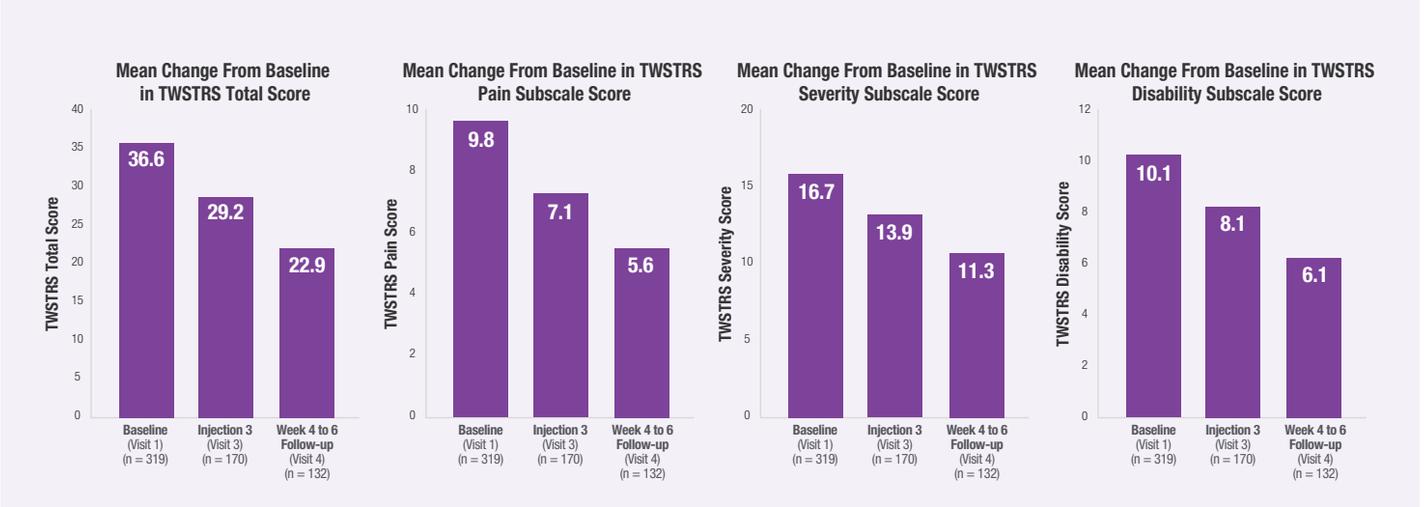
According to a Post Hoc Analysis (N = 319) of CD PROBE Study:

Changes in TWSTRS Scores[21, 22*]



*Patients with all available data at each visit (no data collected at visit 2).
TWSTRS, Toronto Western Spasmodic Torticollis Rating Scale.

Limitations:

Because CD PROBE was exploratory in nature, no formal sample size calculations were carried out. Descriptive statistics were utilized. As CD PROBE was designed as an observational registry, there were no prospectively defined primary or secondary endpoints.[23]

CDSS[16, 23]

- In the pivotal study for BOTOX for Cervical Dystonia, CDSS was developed by AbbVie and used as a co-primary efficacy measure.
- It measures head deviation with 1 point for each 5 degrees of head deviation in each of the three planes of head movement, providing a more specific measure to assess head deviation.

TWSTRS[22, 23]

- In clinical practice as well as in the vast majority of Cervical Dystonia clinical trials, TWSTRS is frequently used as opposed to CDSS.
- TWSTRS is a composite, validated rating scale used to assess patients with CD on 3 subscales — severity (range 0-35), disability (range 0-30), and pain (range 0-20) — and a total score (range 0-85).
- Higher scores indicate greater impairment.
- Within the severity subscale, degree of head deviation was included, similar to CDSS used in the CD pivotal trial.
- TWSTRS was used in this large, observational registry to assess efficacy of BOTOX for the treatment of Cervical Dystonia.

CDSS, Cervical Dystonia Severity Scale; TWSTRS, Toronto Western Spasmodic Torticollis Rating Scale.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
ADVERSE REACTIONS (continued)

Cervical Dystonia

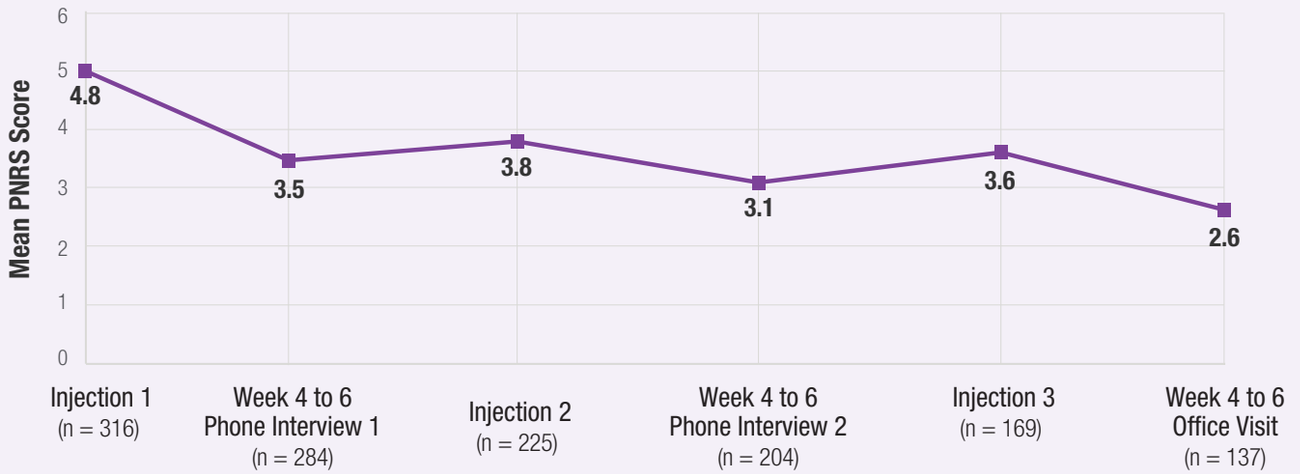
The most frequently reported adverse reactions following injection of BOTOX for cervical dystonia include dysphagia (19%), upper respiratory infection (12%), neck pain (11%), and headache (11%).

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

According to a Post Hoc Analysis (N = 319) of CD PROBE Study:

Changes on the Pain Numeric Rating Scale[21, 22]



Limitations:

Becasue CD PROBE was exploratory in nature, no formal sample size calculations were carried out. Descriptive statistics were utilized. As CD PROBE was designed as an observational registry, there were no prospectively defined primary or secondary endpoints.[23]

NOTE: Patients were asked "Please rate the pain you have experienced during the last 24 hours on a scale from 0 to 10 where 0 indicates 'no pain' and 10 indicates 'pain as bad as you can imagine.' " This is consistent with pain intensity measured in the BOTOX® CD pivotal trial.

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)

Blepharospasm

The most frequently reported adverse reactions following injection of BOTOX for blepharospasm include ptosis (21%), superficial punctate keratitis (6%), and eye dryness (6%).

Strabismus

The most frequently reported adverse events following injection of BOTOX for strabismus include ptosis (1% after inferior rectus injections, 16% after horizontal rectus injections, and 38% after superior rectus injections) and vertical deviation (17%).

Postmarketing Experience

Adverse reactions that have been identified during postapproval use of BOTOX are discussed in greater detail in *Postmarketing Experience* (Section 6.3 of the Prescribing Information).

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

CD PROBE Post Hoc Analysis: Adverse Events[22]

All Adverse Events*

Frequency	Patients, n (%) N = 319	Events, n
Overall	**76 (23.8%)**	**139**
Muscular weakness	25 (7.8%)	30
Dysphagia†	18 (5.6%)	19
Neck pain	8 (2.5%)	8
Headache	4 (1.3%)	6
Injection site pain	4 (1.3%)	4

*Adverse events (regardless of relationship to treatment and including serious adverse events) with frequency ≥ 1.0%
†One patient had 1 dysphagia event that was considered related to treatment.

Treatment-Related Adverse Events (including Serious Adverse Events)‡

Frequency	Patients, n (%) N = 319	Events, n
Overall	**50 (15.7%)**	**85**
Muscular weakness	24 (7.5%)	29
Dysphagia	16 (5.0%)	17
Neck pain	6 (1.9%)	6
Headache	4 (1.3%)	6
Injection site pain	3 (0.9%)	3
Dry mouth	2 (0.6%)	2
Musculoskeletal pain	2 (0.6%)	2
Myalgia	2 (0.6%)	2
Hypokinesia	2 (0.6%)	2
Dyspnea	2 (0.6%)	2

‡Treatment-related adverse events (including serious adverse events) with frequency ≥ 0.6%

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Postmarketing Experience (continued)
There have been spontaneous reports of death, sometimes associated with dysphagia, pneumonia, and/or other significant debility or anaphylaxis, after treatment with botulinum toxin. There have also been reports of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. Some of these patients had risk factors, including cardiovascular disease. The exact relationship of these events to the botulinum toxin injection has not been established.

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Key guiding principles for BOTOX® treatment

OPTIMIZING MUSCLE/DOSE SELECTION

Use patient goals and presenting postures/symptoms to help optimize muscle selection and appropriate BOTOX® dose

- Identify muscles contributing to the posture(s) and symptoms
- Select muscles that might yield a noticeable improvement after the first treatment
- Starting at dose(s) below those proven to provide clinical benefit may not result in an adequate response, leading to treatment discontinuation

SETTING PROPER GOALS AND TREATMENT EXPECTATIONS

Establish specific and realistic goals to help guide the course of care, considering:

- Primary symptom/complaint (eg, head deviation, neck pain)
- Impact of condition on patient (eg, discomfort while driving) and exacerbating factors
- Time frame within which the patient hopes to achieve his/her goals

Set the right expectations with patients to help them follow the treatment plan:

- BOTOX® is not a cure; it helps reduce the severity of abnormal head position and neck pain associated with Cervical Dystonia
- Multiple injection sessions may be needed
- It's important to return for a 4- to 6-week follow-up evaluation

IMPORTANT SAFETY INFORMATION (continued)
DRUG INTERACTIONS
Co-administration of BOTOX and other agents interfering with neuromuscular transmission (eg, aminoglycosides, curare-like compounds) should only be performed with caution as the effect of the toxin may be potentiated. Use of anticholinergic drugs after administration of BOTOX may potentiate systemic anticholinergic effects. The effect of administering different botulinum neurotoxin products at the same time or within several months of each other is unknown. 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. Excessive weakness may also be exaggerated by administration of a muscle relaxant before or after administration of BOTOX.

Please see full Prescribing Information, including Boxed Warning and Medication Guide, or visit https://www.rxabbvie.com/pdf/botox_pi.pdf

BOTOX®
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ESTABLISHING AN EFFECTIVE TREATMENT PLAN

Reevaluate the performance of BOTOX® over initial and subsequent treatment sessions

- Goals as well as muscle/dose selections should be evaluated at each treatment, since the patient's condition may change over time
- Based on goal progress and treatment response, an adjustment in muscle/dose selections may be needed
- Patients can return for BOTOX® retreatment no sooner than 12 weeks, as soon as the clinical effect of the previous treatment has lessened[16]

IMPORTANT SAFETY INFORMATION (continued)

CONTRAINDICATIONS

BOTOX is contraindicated in the presence of infection at the proposed injection site(s) and in patients who are hypersensitive to any botulinum toxin product or to any of the components in the formulation.

WARNINGS AND PRECAUTIONS

Spread of Toxin Effect

See *Boxed Warning*.

No definitive serious adverse event reports of distant spread of toxin effect associated with BOTOX for blepharospasm at the recommended dose (30 Units and below) or strabismus at the labeled dose have been reported.

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Notes

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Lack of Interchangeability Between Botulinum Toxin Products
The potency Units of BOTOX 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 BOTOX cannot be compared to nor converted into Units of any other botulinum toxin products assessed with any other specific assay method.

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Cervical Dystonia dosing information

- BOTOX® dosing in initial and sequential treatment sessions should be tailored to each individual patient based on his or her head and neck position, localization of pain, muscle hypertrophy, patient response, and adverse event history. The initial dose for a patient without prior use of BOTOX® should be at a lower dose, with subsequent dosing adjusted based on individual response[16]
- The recommended dilution is 200 Units/2 mL, 200 Units/4 mL, 100 Units/1 mL, or 100 Units/2 mL with preservative-free 0.9% sodium chloride injection, USP. Limiting the total dose injected into the sternocleidomastoid muscle to 100 Units or less may decrease the occurrence of dysphagia. In general, no more than 50 Units per site should be administered. Localization of the involved muscles with electromyographic guidance may be useful[16]
- In treating adult patients for 1 or more indications, the maximum cumulative dose should not exceed 400 Units in a 3-month interval[16]
- An understanding of standard electromyographic techniques may be useful for the treatment of Cervical Dystonia. Physicians administering BOTOX® must understand the relevant neuromuscular and structural anatomy of the area involved and any alterations to the anatomy due to prior surgical procedures and disease, especially when injecting near the lungs[16]
- Clinical improvement generally begins within the first 2 weeks after injection, with maximum clinical benefit at approximately 6 weeks postinjection. In clinical studies, most subjects were observed to have returned to pretreatment status by 3 months posttreatment[16]

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Serious Adverse Reactions With Unapproved Use
Serious adverse reactions, including excessive weakness, dysphagia, and aspiration pneumonia, with some adverse reactions associated with fatal outcomes, have been reported in patients who received BOTOX injections for unapproved uses. In these cases, the adverse reactions were not necessarily related to distant spread of toxin, but may have resulted from the administration of BOTOX to the site of injection and/or adjacent structures. In several of the cases, patients had preexisting dysphagia or other significant disabilities. There is insufficient information to identify factors associated with an increased risk for adverse reactions associated with the unapproved uses of BOTOX. The safety and effectiveness of BOTOX for unapproved uses have not been established.

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Injection insights and considerations

GENERAL CONSIDERATIONS

- The recommended dilution rate is 2:1 or 1:1:
  - For 2:1, put 4 mL of saline into a 200-Unit vial or 2 mL into a 100-Unit vial
  - For 1:1, put 2 mL of saline into a 200-Unit vial or 1 mL into a 100-Unit vial
- Evaluate the anatomy, including relevant function and the effects of treatment on these muscles, when considering muscle and dose selection
- Recognize the impact of dystonia on the anatomy, as no 2 patients are alike; muscles may be hypertrophied or atrophied, so thorough assessment of the impacted muscles is critical at each injection cycle
- Utilize EMG and/or E-Stim guidance to help ensure proper needle placement
  - Accurate needle guidance is necessary to ensure proper muscle selection
- Talk patients through the injection session step-by-step, explaining what they may experience (see, hear, and/or feel)
  - For example: "You are going to feel pressure," "Now a stick and a little burning," "Okay, now we are going to move on to the next injection site," etc

BEFORE INJECTION

- Examine the patient to identify the muscles contributing to the posture(s) (ie, head and neck position) and neck pain
  - Isolate the involved muscles using a clinical exam as well as EMG and/or E-Stim guidance
- Verify the needle is securely fastened to the injection syringe
- Consider the type of needle/syringe to minimize the chance of the needle popping out during the injection
- Consider using *Luer-Lok*™ syringes to prevent the leakage of BOTOX® during the injection
- Consider lining up the bevel of the needle with the gradations on the syringe so the bevel is facing upward; this will help you read the syringe when injecting
- Consider discussing the option of cold spray to numb the injection site(s)
- Explain that some injection sites may be more sensitive than others so the pain level can vary with each injection

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

Hypersensitivity Reactions

Serious and/or immediate hypersensitivity reactions have been reported. These reactions include anaphylaxis, serum sickness, urticaria, soft-tissue edema, and dyspnea. If such a reaction occurs, further injection of BOTOX should be discontinued and appropriate medical therapy immediately instituted. One fatal case of anaphylaxis has been reported in which lidocaine was used as the diluent, and consequently, the causal agent cannot be reliably determined.

Please see additional Important Safety Information throughout.

DURING INJECTION

- An assistant may be helpful to position the patient's head/neck and maintain stability during the injection
- Hold the skin at the injection site taut, if possible. Loose skin is more difficult to puncture
- It may be helpful to hold the hub of the needle with one hand like a pencil to ensure better control of the syringe
- Aspirate to ensure no blood return
- Consider the angulation of the injection needle and the patient's head/neck position
- Insert the needle into the targeted muscle with consistent pressure to reduce pain at the injection site

This information provides suggestions and considerations for injection training but does not constitute professional medical advice.

BOTOX®
onabotulinumtoxinA injection

Ensure your office is ready for your first BOTOX® injections

- Set up an account for BOTOX® ordering (1-800-811-4148)
- Ensure there is a refrigerator to store BOTOX® vials
- Make sure materials have been ordered:
  - 100- and/or 200-Unit BOTOX® vials
  - 25- to 30-gauge needles for superficial muscles
  - 22-gauge needles for deeper muscles
  - 21-gauge, 2-inch needles for reconstitution
  - 1-mL syringes for injections
  - Appropriately sized syringes for reconstitution
  - Single-use vials of preservative-free, 0.9% sodium chloride, USP (saline)
  - Alcohol swabs for cleaning the rubber stoppers on the saline and BOTOX® vials
  - Adhesive bandages
  - Electromyographic (EMG) or nerve stimulation equipment, if needed
- Review the BOTOX® reconstitution process
- Confirm insurance plan requirements for scheduled patients to ensure appropriate chart-documentation and prior-authorization steps are met (if required)
- Call to remind patients of their scheduled injections

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Dysphagia and Breathing Difficulties
Treatment with BOTOX and other botulinum toxin products can result in swallowing or breathing difficulties. Patients with preexisting swallowing or breathing difficulties may be more susceptible to these complications. In most cases, this is a consequence of weakening of muscles in the area of injection that are involved in breathing or oropharyngeal muscles that control swallowing or breathing (see *Boxed Warning*).

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Consider using EMG/E-Stim for BOTOX® injections

- Can be used to help identify individual muscles contributing to the patient's condition[24]
- Assists in localizing approved muscles and ensuring accurate placement of BOTOX®[24]
- Allows the injector to direct BOTOX® into more susceptible parts of the fascicle[24]

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Corneal Exposure and Ulceration in Patients Treated With BOTOX for Blepharospasm
Reduced blinking from BOTOX injection of the orbicularis muscle can lead to corneal exposure, persistent epithelial defect, and corneal ulceration, especially in patients with VII nerve disorders.

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Notes

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

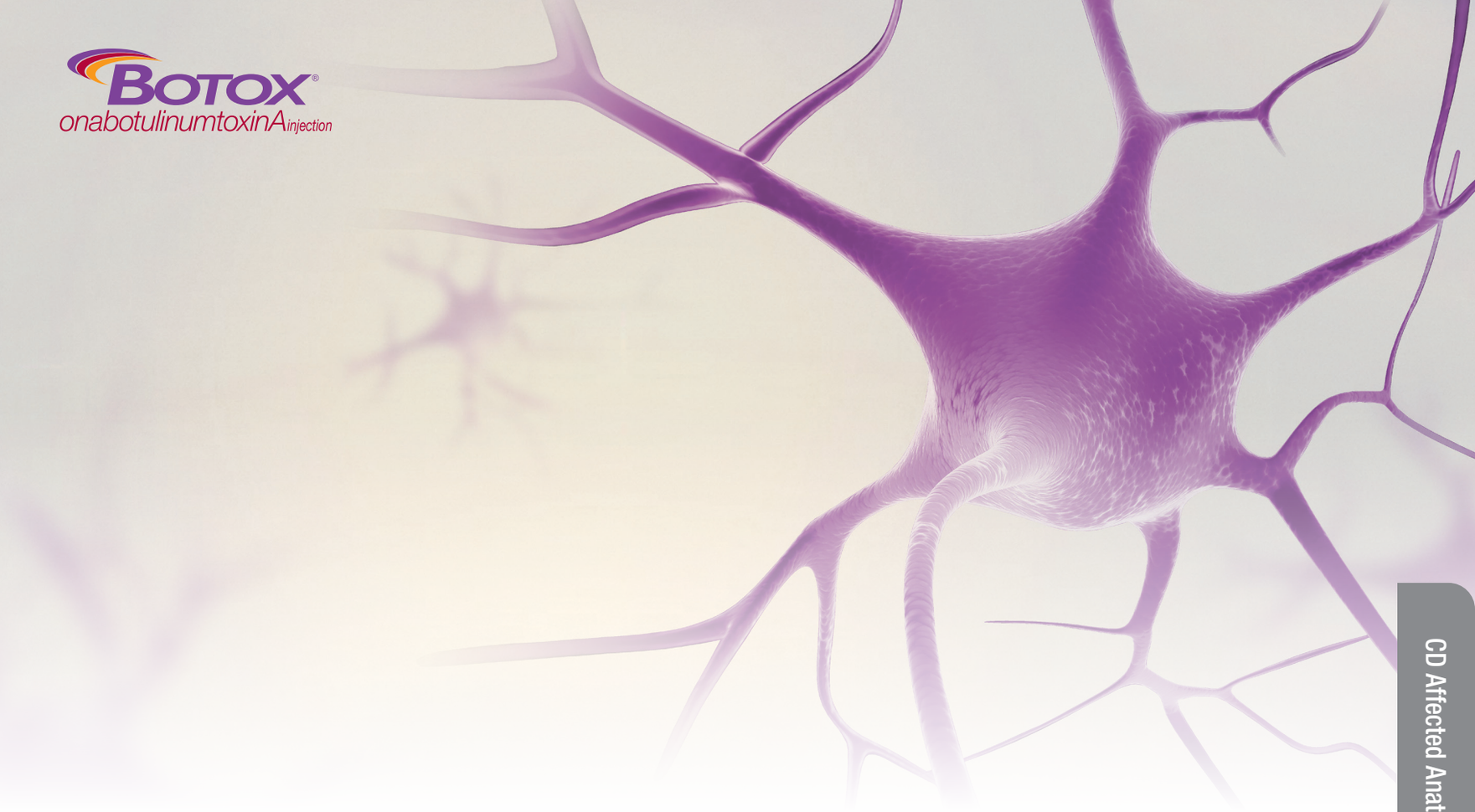
Retrobulbar Hemorrhages in Patients Treated With BOTOX for Strabismus

During the administration of BOTOX for the treatment of strabismus, retrobulbar hemorrhages sufficient to compromise retinal circulation have occurred. It is recommended that appropriate instruments to decompress the orbit be accessible.

Human Albumin and Transmission of Viral Diseases

This product contains albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases and variant Creutzfeldt-Jakob disease (vCJD). There is a theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD), but if that risk actually exists, the risk of transmission would also be considered extremely remote. No cases of transmission of viral diseases, CJD, or vCJD have ever been identified for licensed albumin or albumin contained in other licensed products.

Please see additional Important Safety Information throughout.



Affected anatomy in Cervical Dystonia

- The affected anatomy content provided in this section was developed in coordination with medical professionals
- It is meant to serve as an educational resource for muscle identification and selection in Cervical Dystonia
- Combination postures shown in this section reflect those commonly seen in clinical practice
- A midline has been provided, where appropriate, to help establish a clinical baseline for head/neck positions
- For some single postures, affected anatomy has been omitted in a few images to help enhance visualization of posture progression
- For some combination postures, a single presentation has been shown from 3 different angles (anterior, lateral, posterior) to help visualize clinical impact
- Muscles cited have been identified as contributors to the specific posture:
  - **Bold purple labels = Primary contributor to specified posture and approved for BOTOX®**
  - Standard purple labels = Secondary contributor to specified posture and approved for BOTOX®
  - Black labels = Contributor to specified posture and not approved for BOTOX®; for anatomical reference only

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS
Adverse reactions to BOTOX for injection are discussed in greater detail in the following sections: *Boxed Warning*, *Contraindications*, and *Warnings and Precautions*.

Please see additional Important Safety Information throughout.

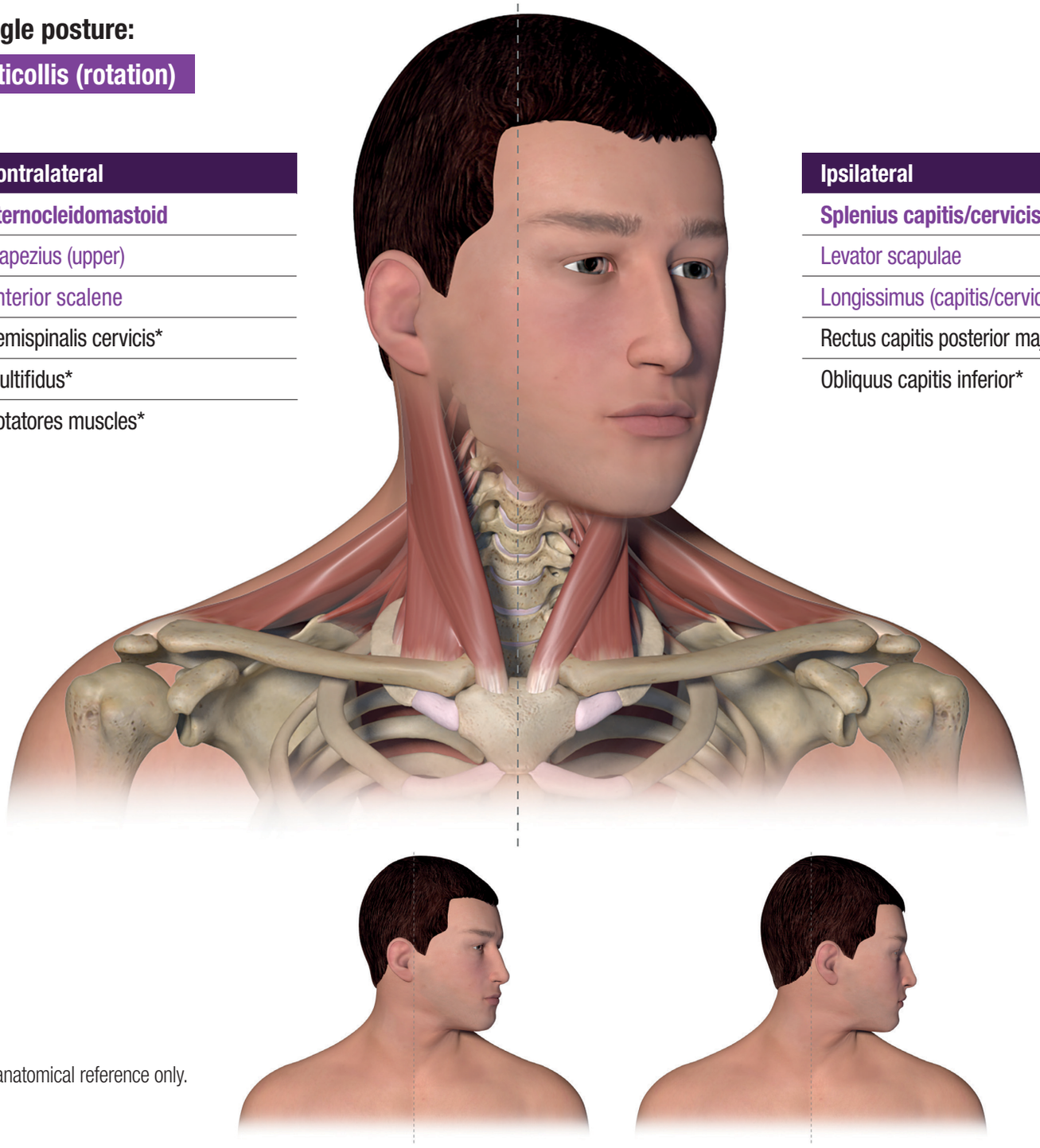
Clinical presentation of Cervical Dystonia

Single posture:

Torticollis (rotation)

Contralateral
Sternocleidomastoid
Trapezius (upper)
Anterior scalene
Semispinalis cervicis*
Multifidus*
Rotatores muscles*

Ipsilateral
Splenius capitis/cervicis
Levator scapulae
Longissimus (capitis/cervicis)
Rectus capitis posterior major*
Obliquus capitis inferior*



*For anatomical reference only.

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Cervical Dystonia
The most frequently reported adverse reactions following injection of BOTOX for cervical dystonia include dysphagia (19%), upper respiratory infection (12%), neck pain (11%), and headache (11%).

Please see additional Important Safety Information throughout.

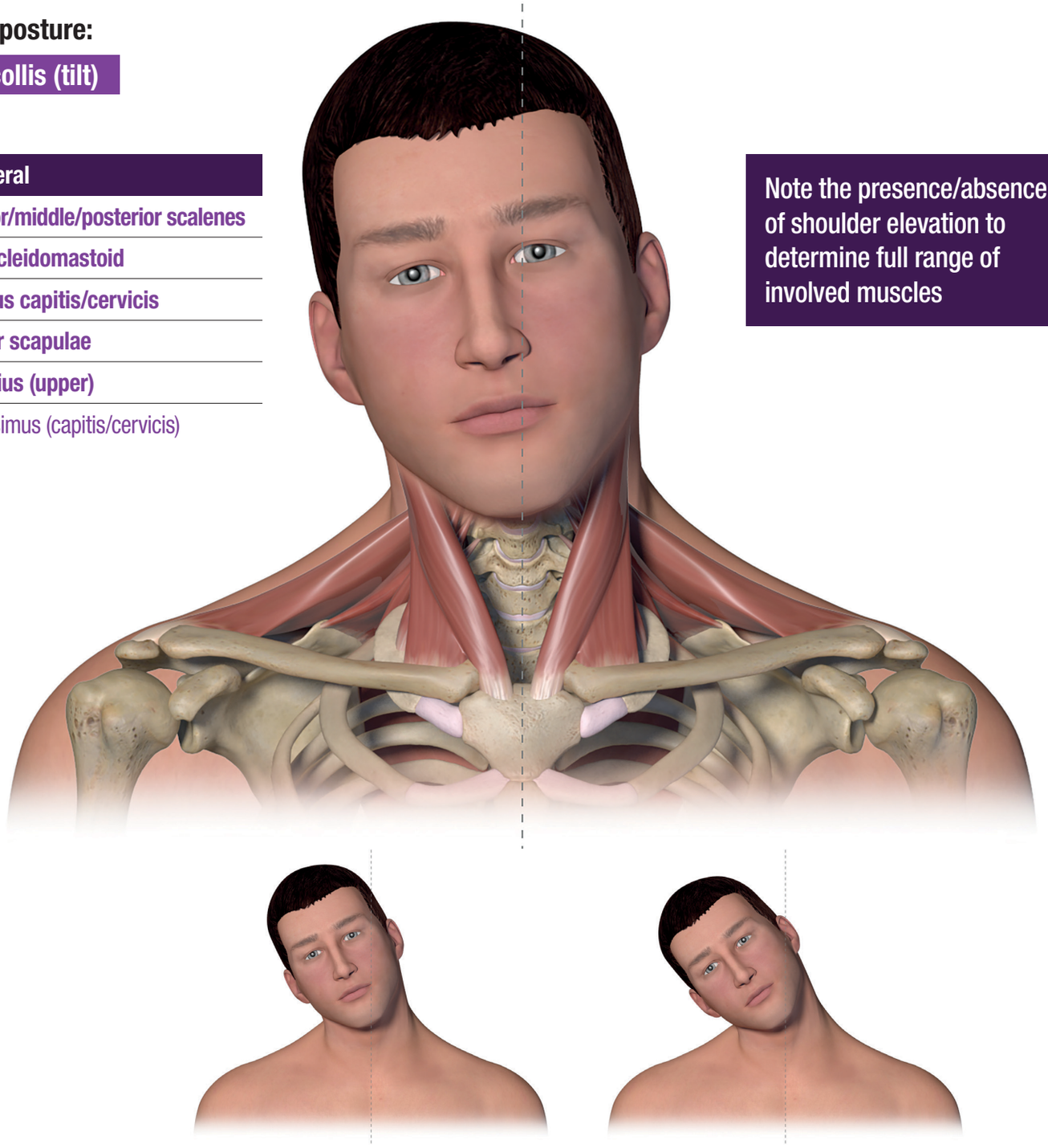
BOTOX® onabotulinumtoxinA injection

Clinical presentation of Cervical Dystonia (continued)

Single posture:

Laterocollis (tilt)

Ipsilateral
Anterior/middle/posterior scalenes
Sternocleidomastoid
Splenius capitis/cervicis
Levator scapulae
Trapezius (upper)
Longissimus (capitis/cervicis)



Note the presence/absence of shoulder elevation to determine full range of involved muscles

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)

Blepharospasm

The most frequently reported adverse reactions following injection of BOTOX for blepharospasm include ptosis (21%), superficial punctate keratitis (6%), and eye dryness (6%).

Please see additional Important Safety Information throughout.

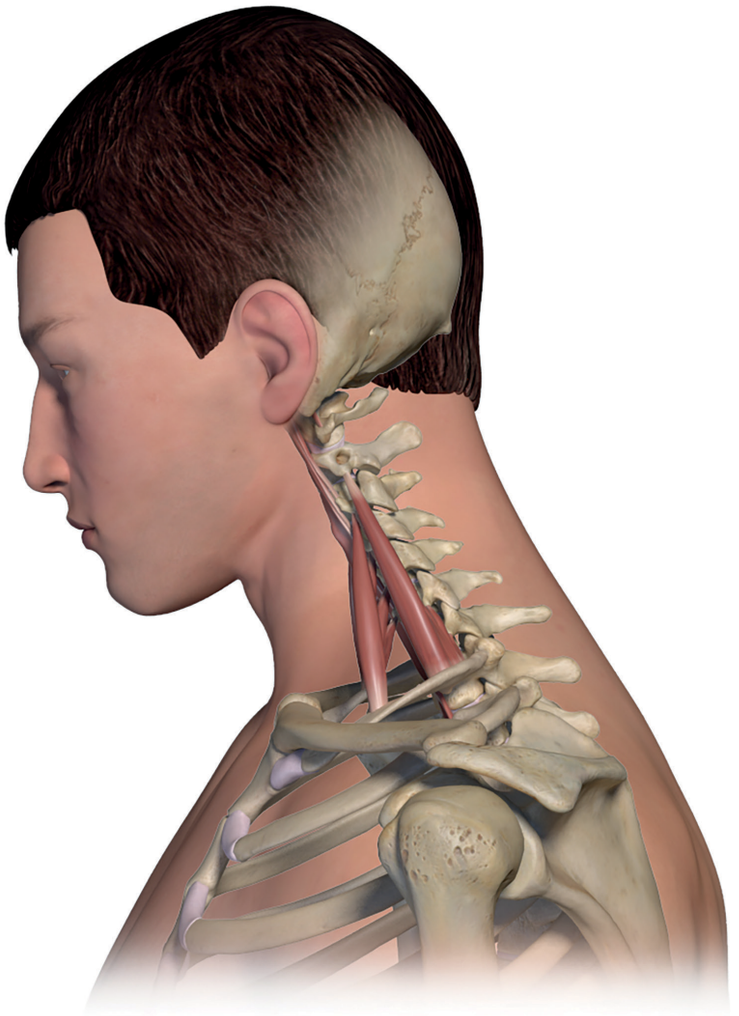
BOTOX® onabotulinumtoxinA injection

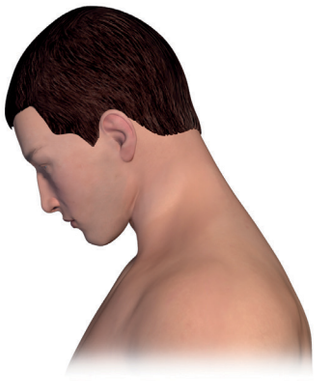
Clinical presentation of Cervical Dystonia (continued)

Single posture:

Anterocollis (flexion)

Bilateral
Anterior/middle scalenes
Longus capitis/colli*
Rectus capitis anterior*





*For anatomical reference only.

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)

Strabismus

The most frequently reported adverse events following injection of BOTOX for strabismus include ptosis (1% after inferior rectus injections, 16% after horizontal rectus injections, and 38% after superior rectus injections) and vertical deviation (17%).

Please see additional Important Safety Information throughout.

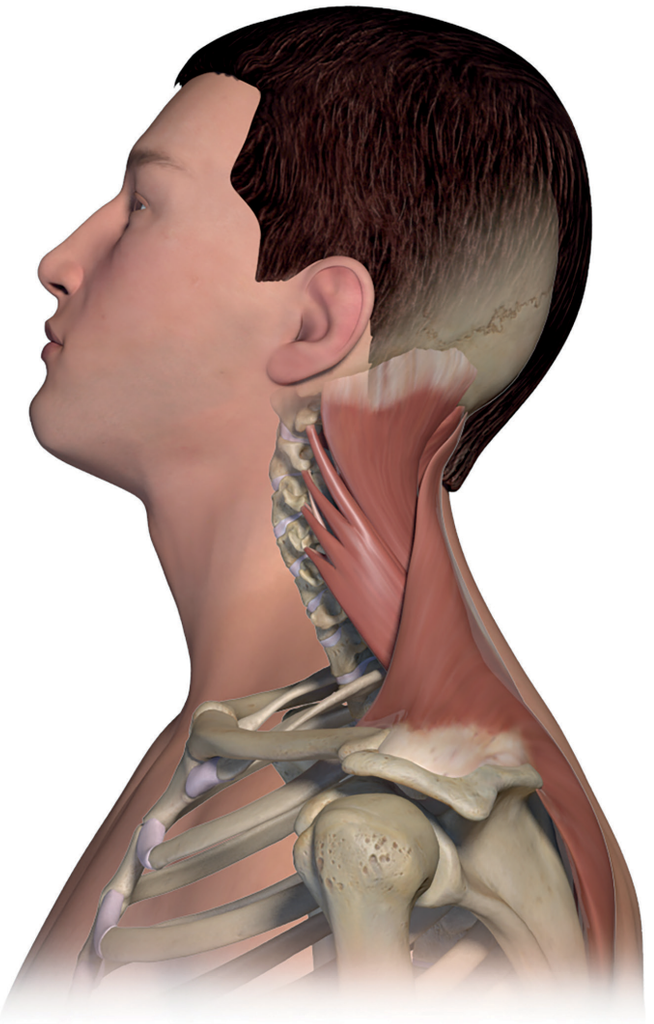
BOTOX®
onabotulinumtoxinA injection

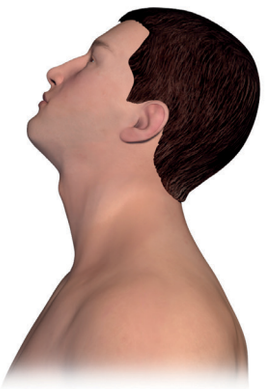
Clinical presentation of Cervical Dystonia (continued)

Single posture:

Retrocollis (extension)

Bilateral
Semispinalis capitis
Splenius capitis
Splenius cervicis
Longissimus (capitis/cervicis)
Trapezius (upper)
Levator scapulae
Semispinalis cervicis*
Rectus capitis posterior major/minor*
Obliquus capitis superior*





*For anatomical reference only.

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Postmarketing Experience
Adverse reactions that have been identified during postapproval use of BOTOX are discussed in greater detail in *Postmarketing Experience* (Section 6.3 of the Prescribing Information).

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

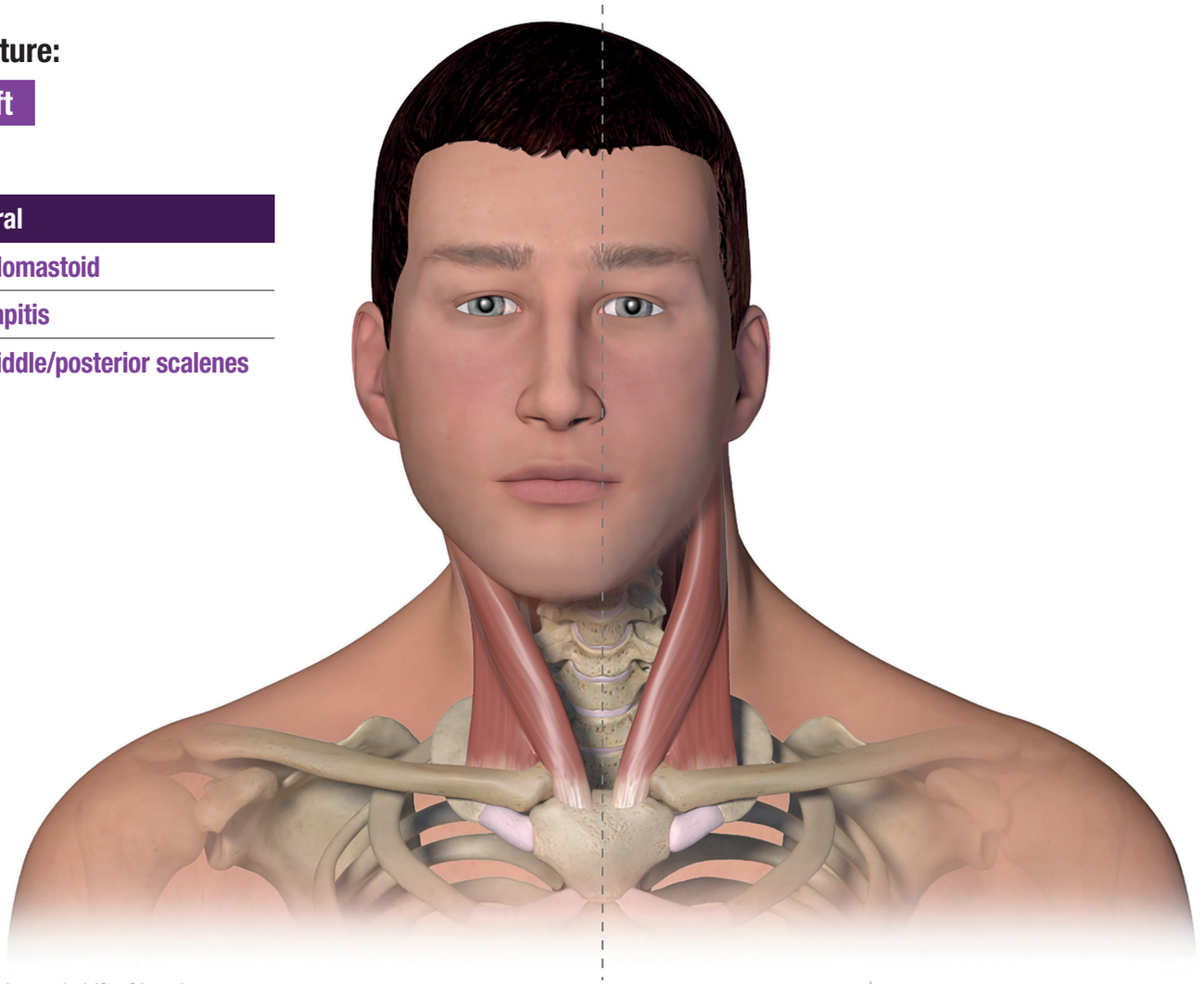
Clinical presentation of Cervical Dystonia (continued)

Single posture:

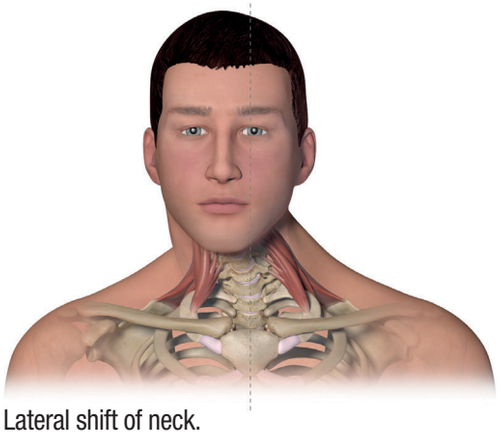
Lateral shift

Contralateral

- Sternocleidomastoid
- Splenius capitis
- Anterior/middle/posterior scalenes



Lateral shift of head.



Lateral shift of neck.

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Postmarketing Experience (continued)

There have been spontaneous reports of death, sometimes associated with dysphagia, pneumonia, and/or other significant debility or anaphylaxis, after treatment with botulinum toxin. There have also been reports of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. Some of these patients had risk factors, including cardiovascular disease. The exact relationship of these events to the botulinum toxin injection has not been established.

Please see additional Important Safety Information throughout.

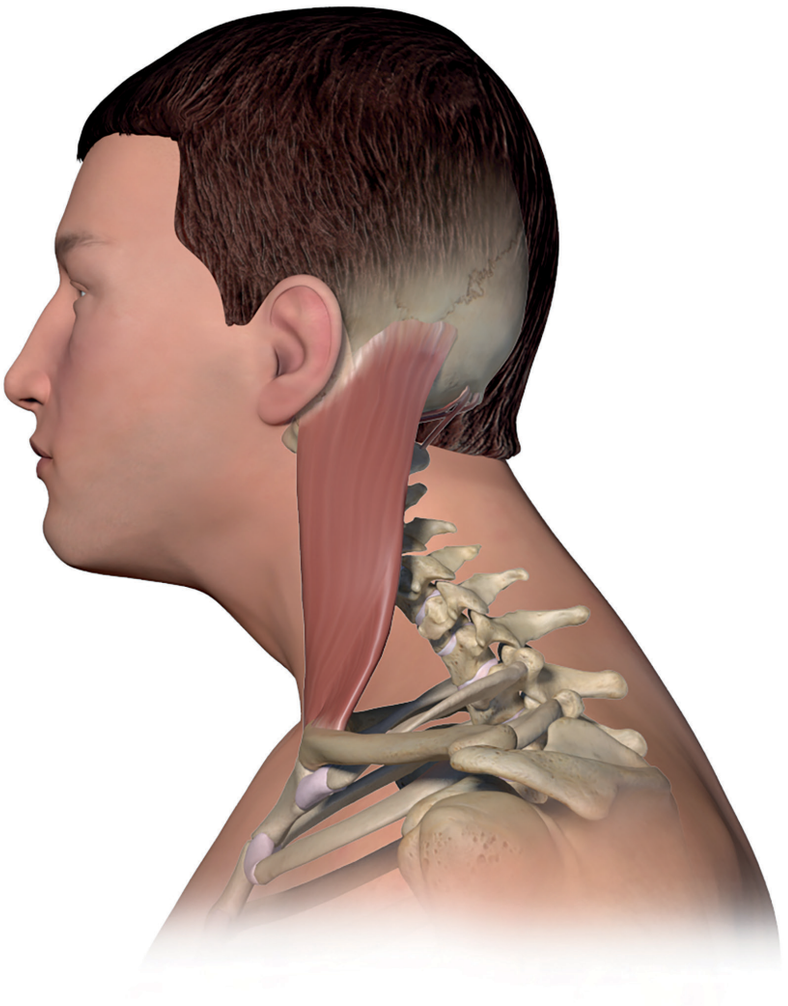
BOTOX® onabotulinumtoxinA injection

Clinical presentation of Cervical Dystonia (continued)

Single posture:

Sagittal shift

Bilateral
Sternocleidomastoid
Rectus capitis posterior major/minor*
Obliquus capitis superior*



*For anatomical reference only.

IMPORTANT SAFETY INFORMATION (continued)

DRUG INTERACTIONS

Co-administration of BOTOX and other agents interfering with neuromuscular transmission (eg, aminoglycosides, curare-like compounds) should only be performed with caution as the effect of the toxin may be potentiated. Use of anticholinergic drugs after administration of BOTOX may potentiate systemic anticholinergic effects. The effect of administering different botulinum neurotoxin products at the same time or within several months of each other is unknown. 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. Excessive weakness may also be exaggerated by administration of a muscle relaxant before or after administration of BOTOX.

Please see full Prescribing Information, including Boxed Warning and Medication Guide, or visit https://www.rxabbvie.com/pdf/botox_pi.pdf

BOTOX®
onabotulinumtoxinA injection

Clinical presentation of Cervical Dystonia (continued)

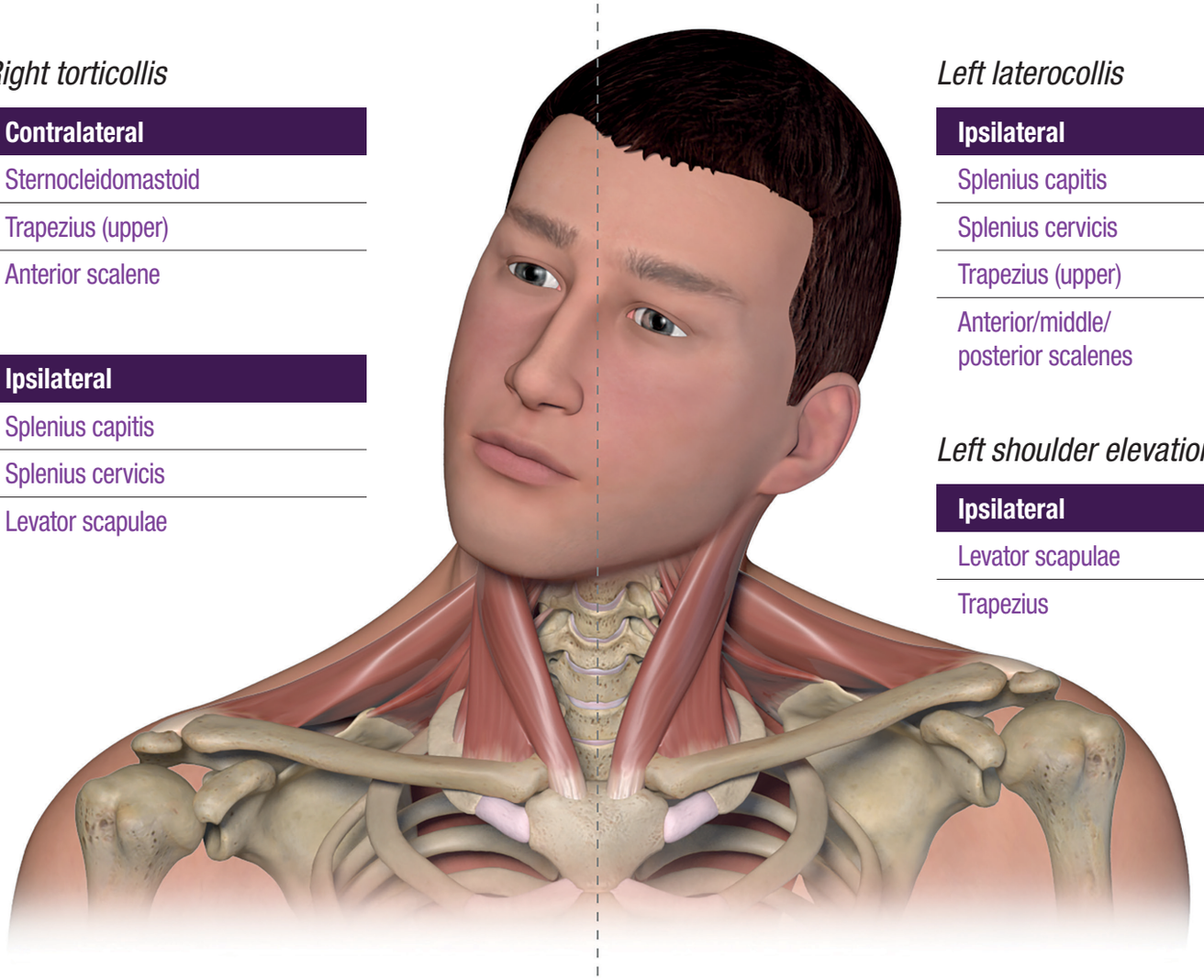
Combination posture:

Right torticollis, left laterocollis, left shoulder elevation

Right torticollis

Contralateral
Sternocleidomastoid
Trapezius (upper)
Anterior scalene

Ipsilateral
Splenius capitis
Splenius cervicis
Levator scapulae



Left laterocollis

Ipsilateral
Splenius capitis
Splenius cervicis
Trapezius (upper)
Anterior/middle/ posterior scalenes

Left shoulder elevation

Ipsilateral
Levator scapulae
Trapezius

IMPORTANT SAFETY INFORMATION (continued)
CONTRAINDICATIONS
BOTOX is contraindicated in the presence of infection at the proposed injection site(s) and in patients who are hypersensitive to any botulinum toxin product or to any of the components in the formulation.

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Clinical presentation of Cervical Dystonia (continued)

Combination posture:

Left torticollis, left laterocollis

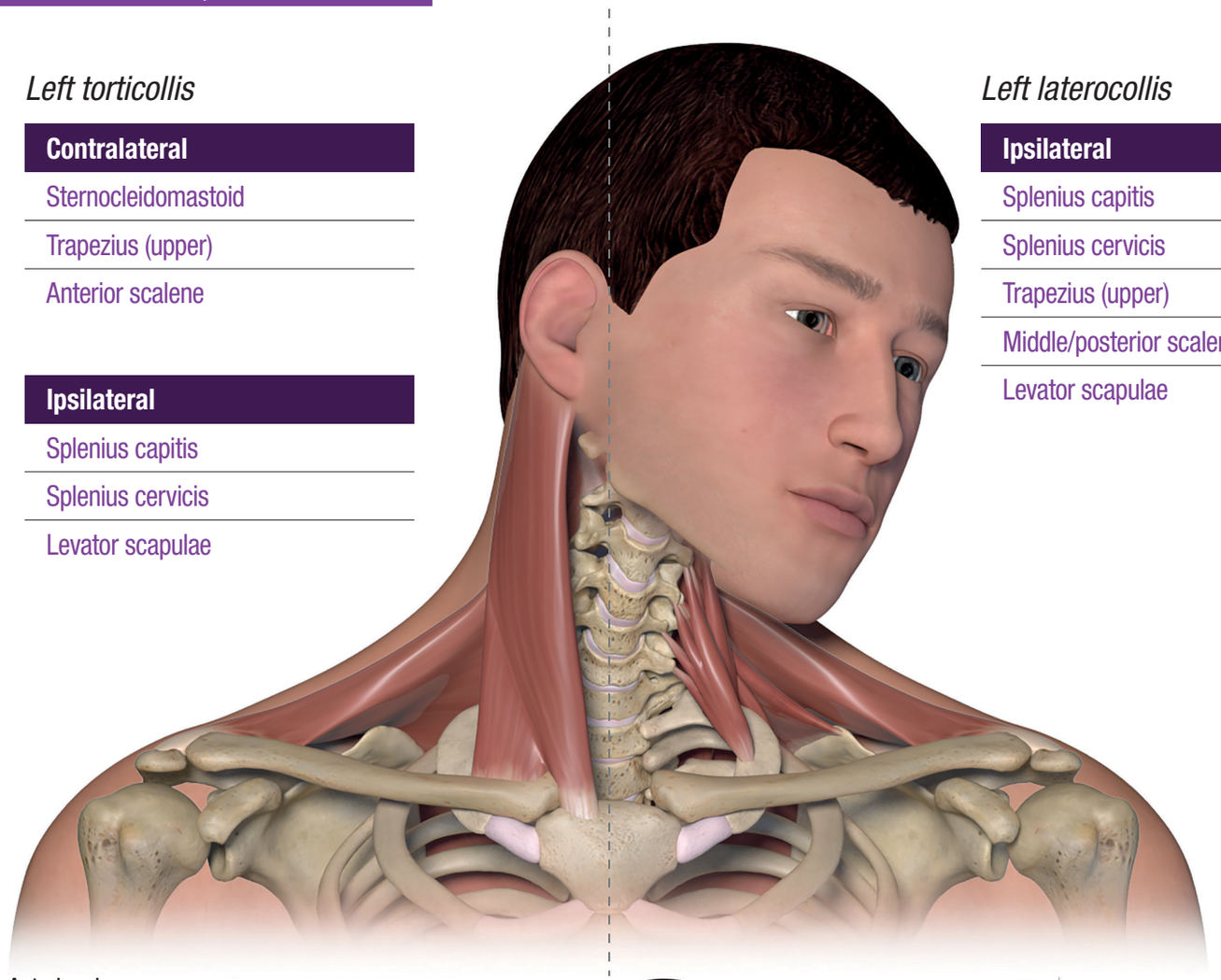
Left torticollis

Contralateral
Sternocleidomastoid
Trapezius (upper)
Anterior scalene

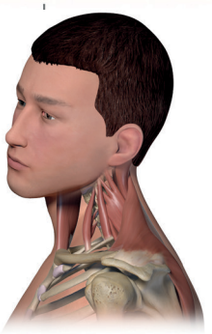
Ipsilateral
Splenius capitis
Splenius cervicis
Levator scapulae

Left laterocollis

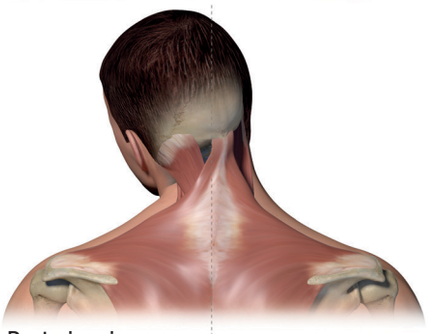
Ipsilateral
Splenius capitis
Splenius cervicis
Trapezius (upper)
Middle/posterior scalenes
Levator scapulae



Anterior view.



Lateral view.



Posterior view.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS
Spread of Toxin Effect
See *Boxed Warning*.

No definitive serious adverse event reports of distant spread of toxin effect associated with BOTOX for blepharospasm at the recommended dose (30 Units and below) or strabismus at the labeled dose have been reported.

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Clinical presentation of Cervical Dystonia (continued)

Combination posture:

Right torticollis, retrocollis, neck pain

Right torticollis

Contralateral
Sternocleidomastoid
Trapezius (upper)

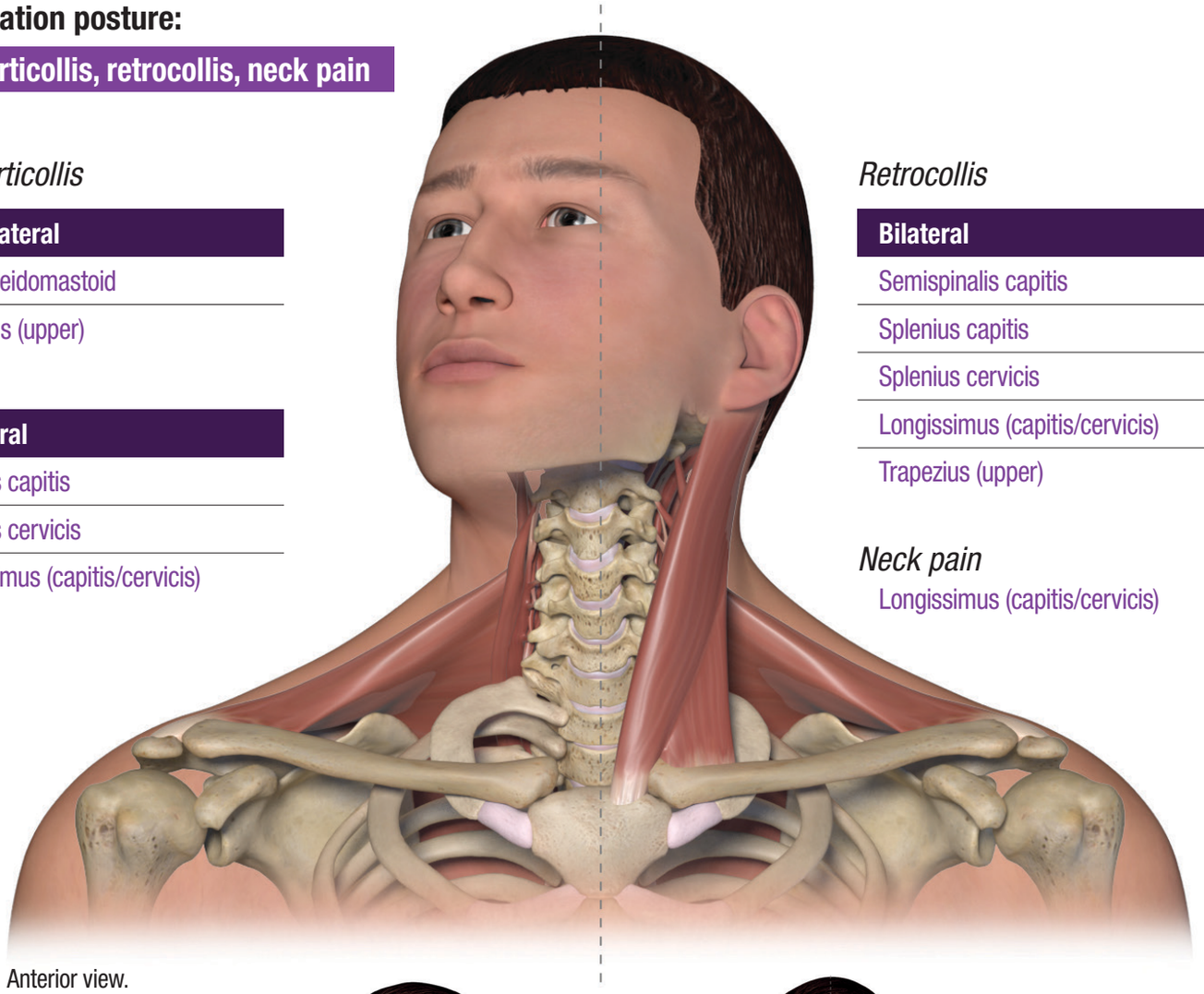
Ipsilateral
Splenius capitis
Splenius cervicis
Longissimus (capitis/cervicis)

Retrocollis

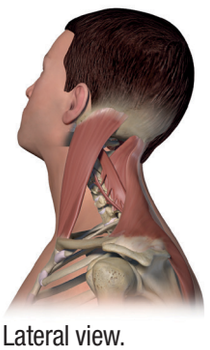
Bilateral
Semispinalis capitis
Splenius capitis
Splenius cervicis
Longissimus (capitis/cervicis)
Trapezius (upper)

Neck pain

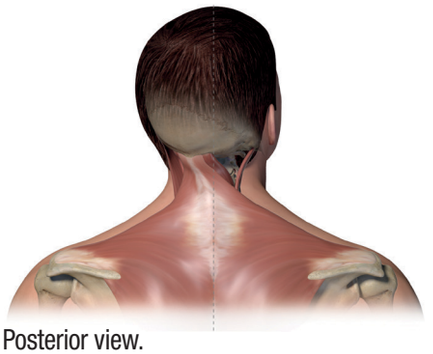
Longissimus (capitis/cervicis)



Anterior view.



Lateral view.



Posterior view.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Lack of Interchangeability Between Botulinum Toxin Products
The potency Units of BOTOX 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 BOTOX cannot be compared to nor converted into Units of any other botulinum toxin products assessed with any other specific assay method.

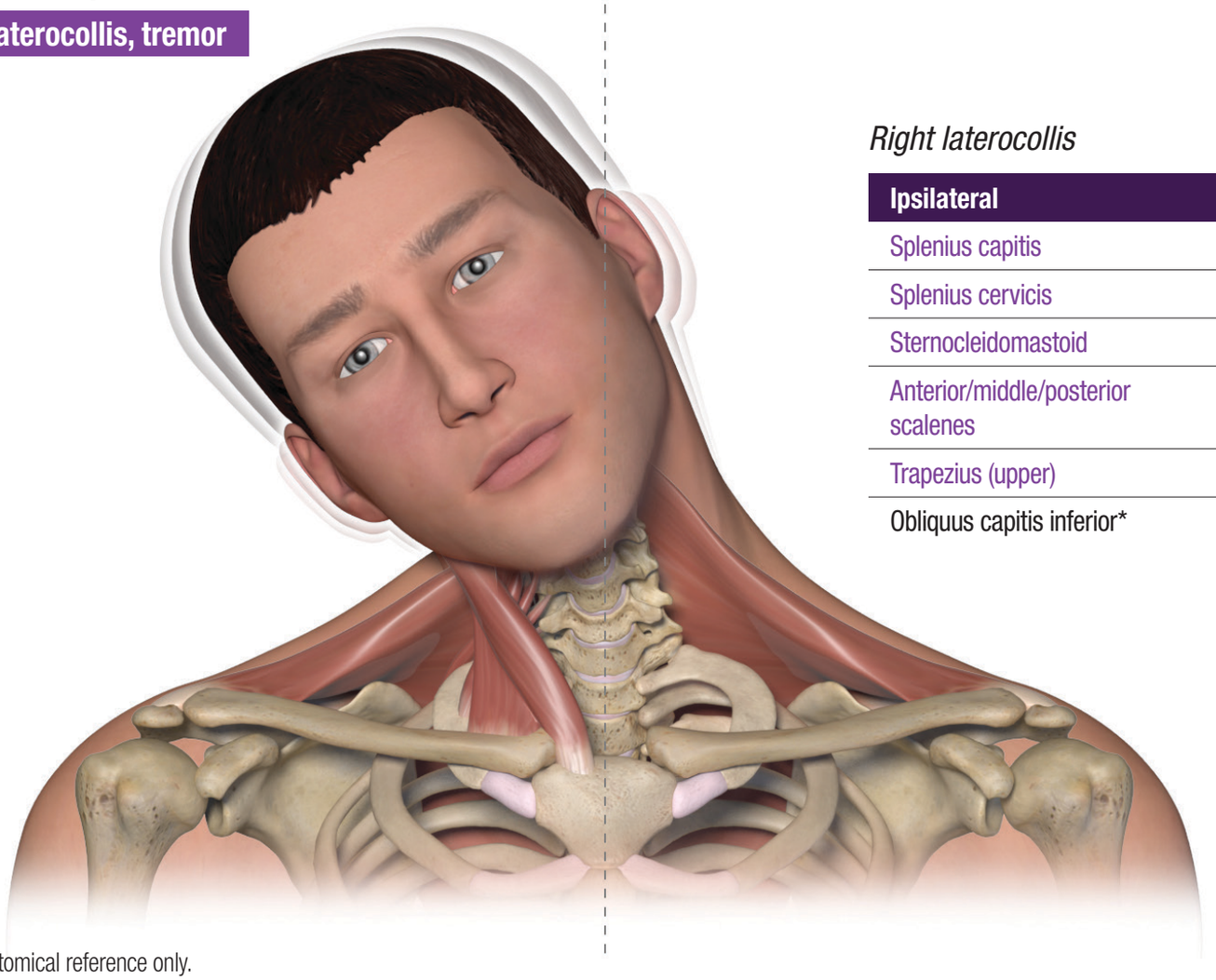
Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Clinical presentation of Cervical Dystonia (continued)

Combination posture:

Right laterocollis, tremor



Right laterocollis

Ipsilateral
Splenius capitis
Splenius cervicis
Sternocleidomastoid
Anterior/middle/posterior scalenes
Trapezius (upper)
Obliquus capitis inferior*

*For anatomical reference only.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

Serious Adverse Reactions With Unapproved Use

Serious adverse reactions, including excessive weakness, dysphagia, and aspiration pneumonia, with some adverse reactions associated with fatal outcomes, have been reported in patients who received BOTOX injections for unapproved uses. In these cases, the adverse reactions were not necessarily related to distant spread of toxin, but may have resulted from the administration of BOTOX to the site of injection and/or adjacent structures. In several of the cases, patients had preexisting dysphagia or other significant disabilities. There is insufficient information to identify factors associated with an increased risk for adverse reactions associated with the unapproved uses of BOTOX. The safety and effectiveness of BOTOX for unapproved uses have not been established.

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Muscles by posture in Cervical Dystonia

Posture	Muscles		
Single			
Torticollis	**Contralateral**	• **Sternocleidomastoid** • Trapezius (upper) • Anterior scalene	• Multifidus* • Semispinalis cervicis* • Rotatores muscles*
	Ipsilateral	• **Splenius capitis** • **Splenius cervicis** • Longissimus (capitis/cervicis) • Levator scapulae	• Obliquus capitis inferior* • Rectus capitis posterior major*
Laterocollis	**Ipsilateral**	• **Anterior/middle/posterior scalenes** • **Splenius capitis** • **Splenius cervicis** • **Trapezius (upper)**	• **Sternocleidomastoid** • **Levator scapulae** • Longissimus (capitis/cervicis)
Anterocollis	**Bilateral**	• **Anterior/middle scalenes** • Rectus capitis anterior*	• Longus capitis/colli*
Retrocollis	**Bilateral**	• **Semispinalis capitis** • **Splenius capitis** • **Splenius cervicis** • **Longissimus (capitis/cervicis)** • Trapezius (upper) • Levator scapulae	• Rectus capitis posterior major/minor* • Semispinalis cervicis* • Obliquus capitis superior*
Lateral shift	**Contralateral**	• **Sternocleidomastoid** • **Splenius capitis**	• **Anterior/middle/posterior scalenes**
Sagittal shift	**Bilateral**	• **Sternocleidomastoid**	• Obliquus capitis superior* • Rectus capitis posterior major/minor*

Bold purple labels = Primary contributor to specified posture and approved for BOTOX®.
Standard purple labels = Secondary contributor to specified posture and approved for BOTOX®.
*Black labels = Contributor to specified posture and not approved for BOTOX®; for anatomical reference only.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Hypersensitivity Reactions
Serious and/or immediate hypersensitivity reactions have been reported. These reactions include anaphylaxis, serum sickness, urticaria, soft-tissue edema, and dyspnea. If such a reaction occurs, further injection of BOTOX should be discontinued and appropriate medical therapy immediately instituted. One fatal case of anaphylaxis has been reported in which lidocaine was used as the diluent, and consequently, the causal agent cannot be reliably determined.

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Muscles by posture in Cervical Dystonia (continued)

Posture	Muscles		
Combination	**Right torticollis, left laterocollis, left shoulder elevation**		
Right torticollis	**Contralateral**	• Sternocleidomastoid • Trapezius (upper)	• Anterior scalene
	Ipsilateral	• Splenius capitis • Splenius cervicis	• Levator scapulae
Left laterocollis	**Ipsilateral**	• Splenius capitis • Splenius cervicis • Trapezius (upper)	• Anterior/middle/posterior scalenes
Left shoulder elevation	**Ipsilateral**	• Levator scapulae • Trapezius	
Combination	**Left torticollis, left laterocollis**		
Left torticollis	**Contralateral**	• Sternocleidomastoid • Trapezius (upper)	• Anterior scalene
	Ipsilateral	• Splenius capitis • Splenius cervicis	• Levator scapulae
Left laterocollis	**Ipsilateral**	• Splenius capitis • Splenius cervicis • Trapezius (upper)	• Levator scapulae • Middle/posterior scalenes
Combination	**Right torticollis, retrocollis, neck pain**		
Right torticollis	**Contralateral**	• Sternocleidomastoid	• Trapezius (upper)
	Ipsilateral	• Splenius capitis • Splenius cervicis	• Longissimus (capitis/cervicis)
Retrocollis	**Bilateral**	• Semispinalis capitis • Splenius capitis • Splenius cervicis	• Longissimus (capitis/cervicis) • Trapezius (upper)
Combination	**Right laterocollis, tremor**		
Right laterocollis	**Ipsilateral**	• Splenius capitis • Splenius cervicis • Sternocleidomastoid	• Trapezius (upper) • Anterior/middle/posterior scalenes • Obliquus capitis inferior*

Standard purple labels = May be a contributor to specified posture and approved for BOTOX®.

*Black labels = Contributor to specified posture and not approved for BOTOX®; for anatomical reference only.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Increased Risk of Clinically Significant Effects With Preexisting Neuromuscular Disorders

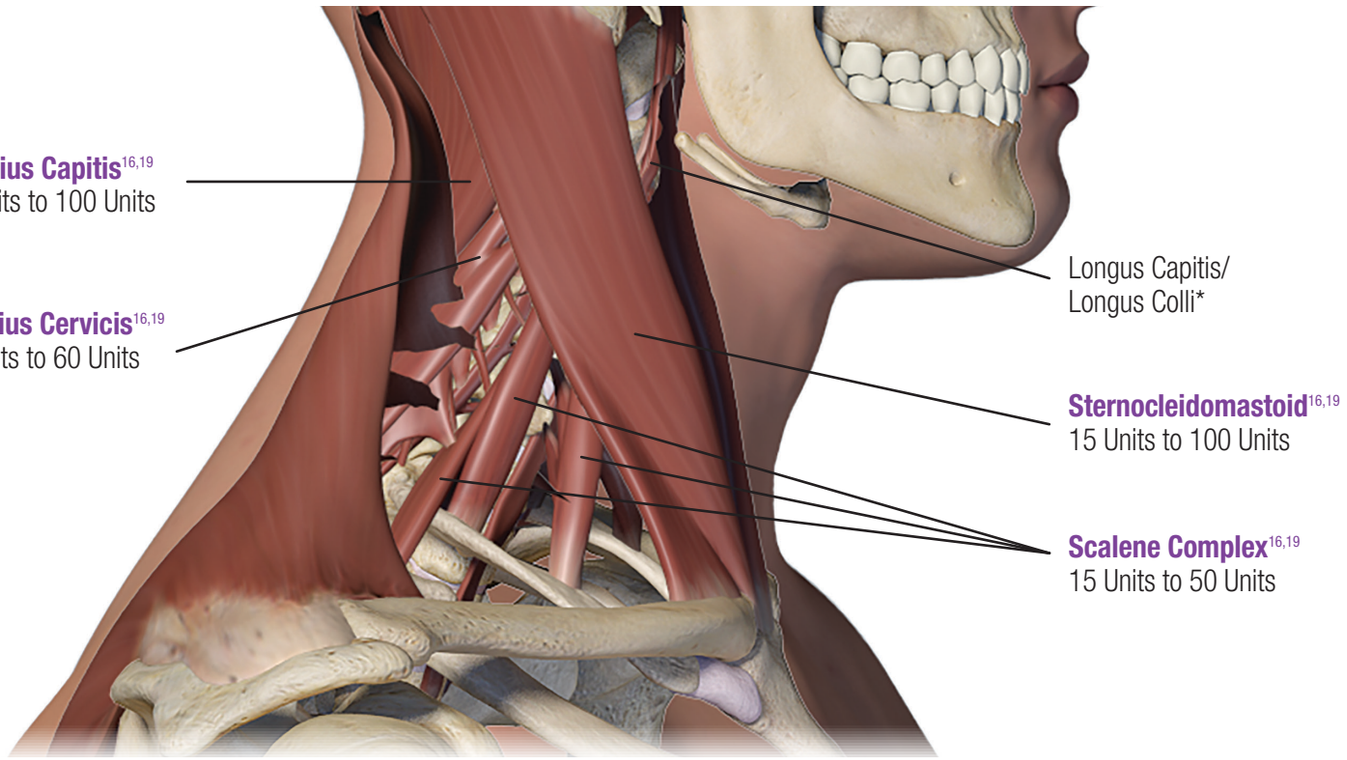
Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis (ALS), or neuromuscular junction disorders (eg, myasthenia gravis or Lambert-Eaton syndrome) should be monitored when given botulinum toxin.

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Main muscles involved in Cervical Dystonia

Muscles listed in purple are those approved for BOTOX® injection[16]



*For anatomical reference only.
Lines indicate muscle location and do not point out sites for injection.

236 Units = median BOTOX® dose in CD pivotal study[16]
(25th to 75th percentile range was 198 Units to 300 Units)

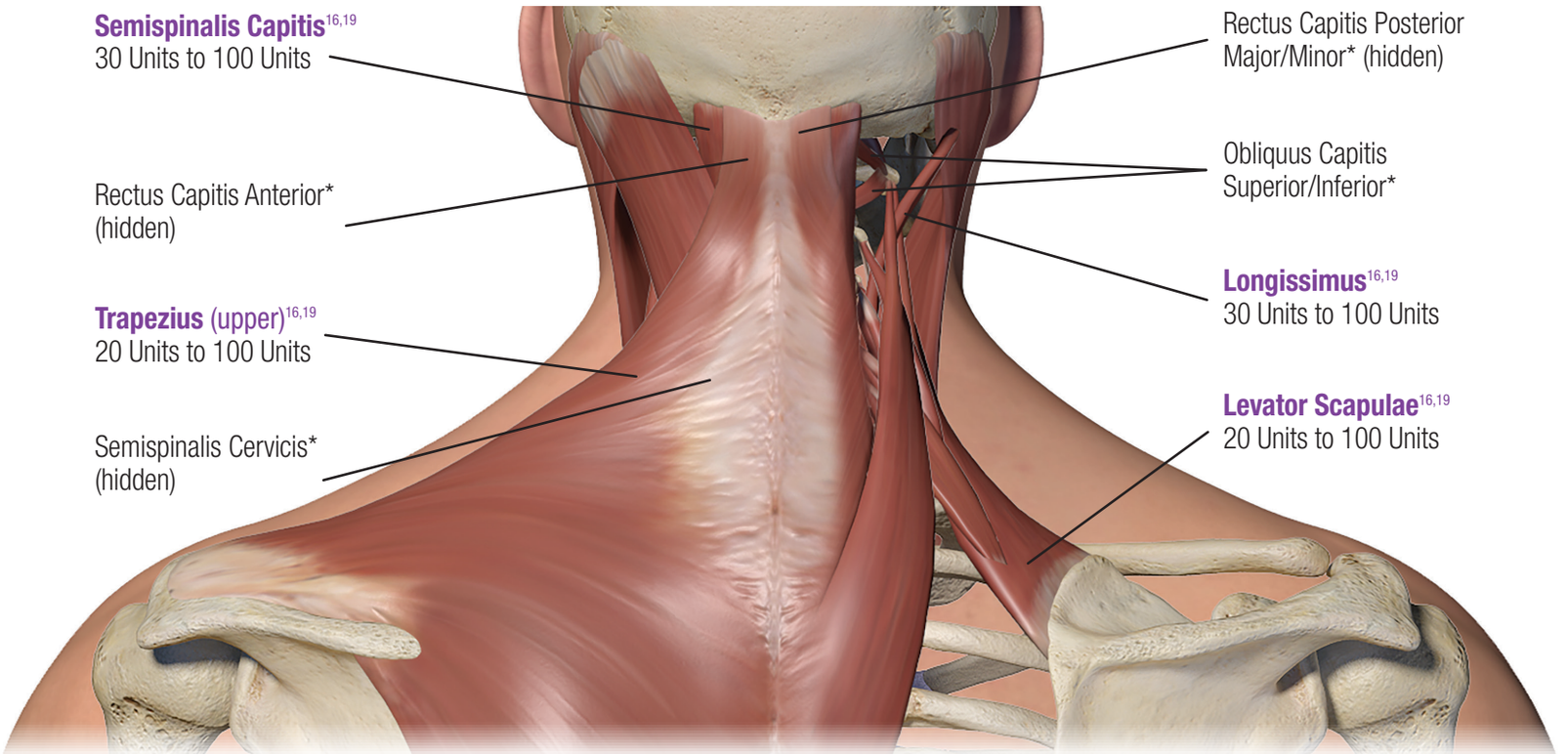
IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Increased Risk of Clinically Significant Effects With Preexisting Neuromuscular Disorders (continued)
Patients with known or unrecognized neuromuscular disorders or neuromuscular junction disorders may be at increased risk of clinically significant effects, including generalized muscle weakness, diplopia, ptosis, dysphonia, dysarthria, severe dysphagia, and respiratory compromise from therapeutic doses of BOTOX (see *Warnings and Precautions*).

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Main muscles involved in Cervical Dystonia (continued)

Muscles listed in purple are those approved for BOTOX® injection[16]



*For anatomical reference only.
Lines indicate muscle location and do not point out sites for injection.

236 Units = median BOTOX® dose in CD pivotal study[16]
(25th to 75th percentile range was 198 Units to 300 Units)

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Dysphagia and Breathing Difficulties
Treatment with BOTOX and other botulinum toxin products can result in swallowing or breathing difficulties. Patients with preexisting swallowing or breathing difficulties may be more susceptible to these complications. In most cases, this is a consequence of weakening of muscles in the area of injection that are involved in breathing or oropharyngeal muscles that control swallowing or breathing (see *Boxed Warning*).

Please see additional Important Safety Information throughout.

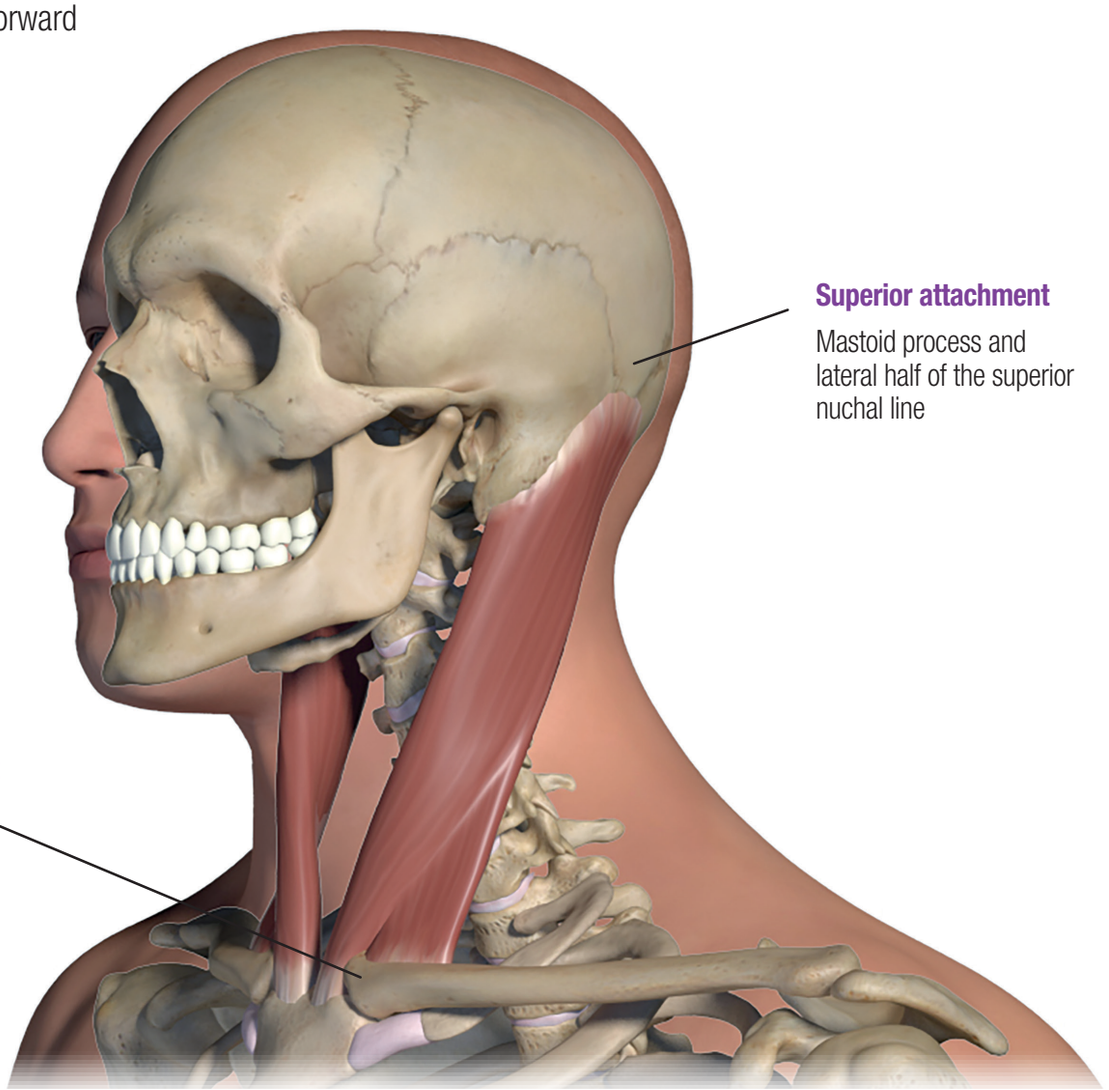
BOTOX®
onabotulinumtoxinA injection

Sternocleidomastoid

▶ BOTOX® dose: 15 Units to 100 Units

Muscle action[25]

Unilaterally bends the head to the same side and rotates the head to the opposite side. Bilaterally extends the head, then pulls the neck forward



Superior attachment

Mastoid process and lateral half of the superior nuchal line

Inferior attachment

Manubrium and medial one-third of the clavicle

Involved postures

- Torticollis
- Laterocollis
- Lateral shift
- Sagittal shift
- Left torticollis, left laterocollis
- Right torticollis, retrocollis
- Right laterocollis, tremor
- Right torticollis, left laterocollis, shoulder elevation

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

Corneal Exposure and Ulceration in Patients Treated With BOTOX for Blepharospasm

Reduced blinking from BOTOX injection of the orbicularis muscle can lead to corneal exposure, persistent epithelial defect, and corneal ulceration, especially in patients with VII nerve disorders.

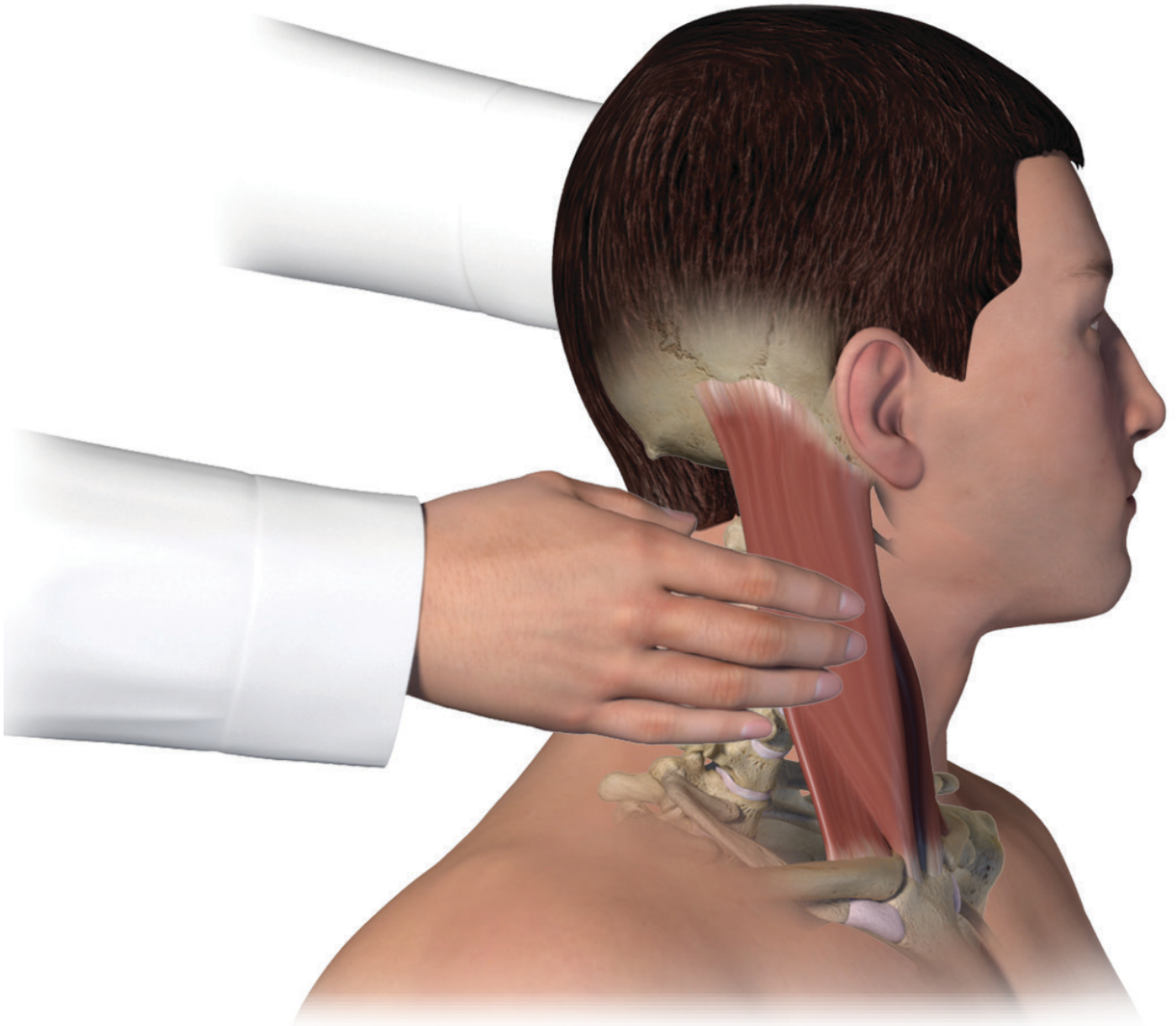
Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Sternocleidomastoid (continued)

Localization

Readily localized with contralateral rotation of the head. Providing resistance to rotation may accentuate the muscle further



IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

Retrobulbar Hemorrhages in Patients Treated With BOTOX for Strabismus

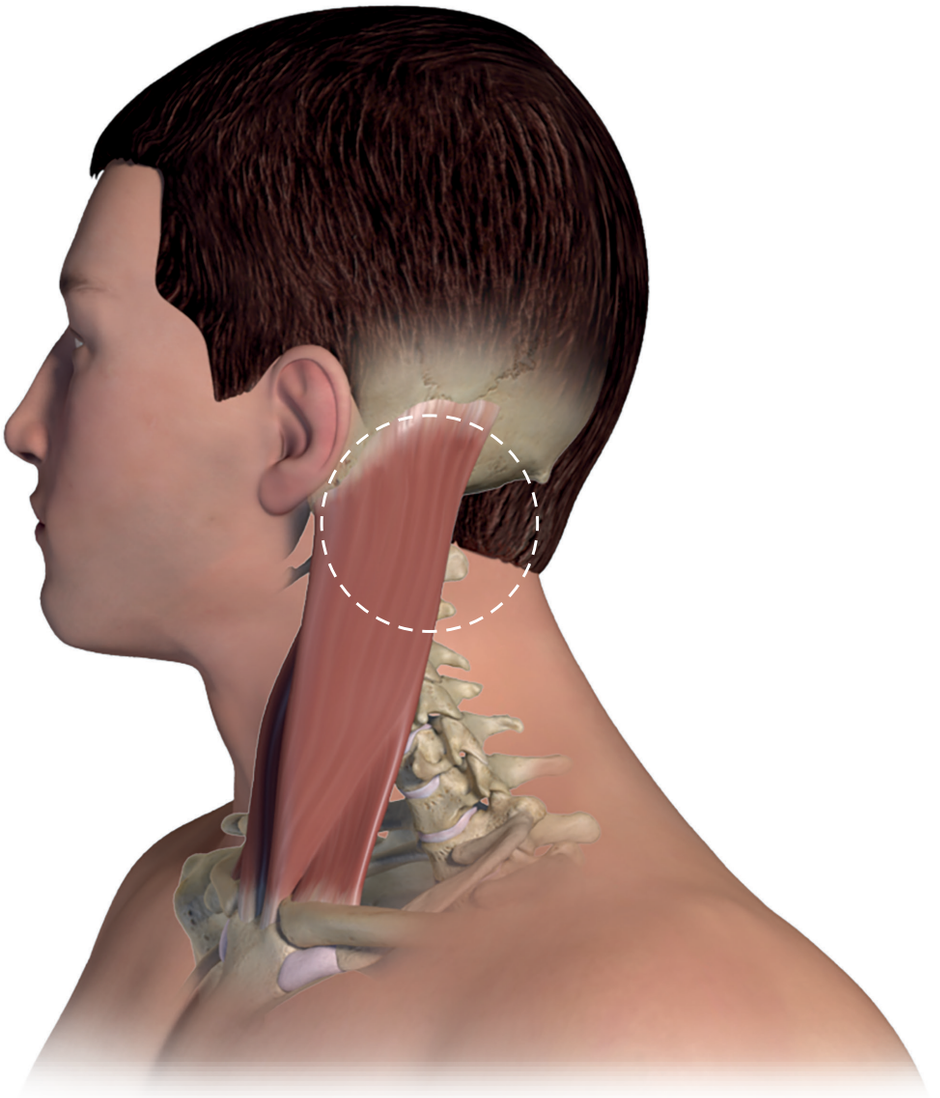
During the administration of BOTOX for the treatment of strabismus, retrobulbar hemorrhages sufficient to compromise retinal circulation have occurred. It is recommended that appropriate instruments to decompress the orbit be accessible.

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Sternocleidomastoid (continued)

Injection considerations



- Consider a starting dose at the lower end of the approved dosing range and split total dose evenly for bilateral injections
- Grasping the muscle between the index finger and thumb may facilitate injection
- Injecting outside the posterior and superior portions of the muscle may inadvertently increase the risk of dysphagia
- This muscle may become thin after repeat injections, so consider a longitudinal approach due to proximity to the neurovascular bundle
- Have patient activate muscle to facilitate localization

BOTOX® onabotulinumtoxinA injection

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Notes

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Human Albumin and Transmission of Viral Diseases (continued)
There is a theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD), but if that risk actually exists, the risk of transmission would also be considered extremely remote. No cases of transmission of viral diseases, CJD, or vCJD have ever been identified for licensed albumin or albumin contained in other licensed products.

Please see additional Important Safety Information throughout.

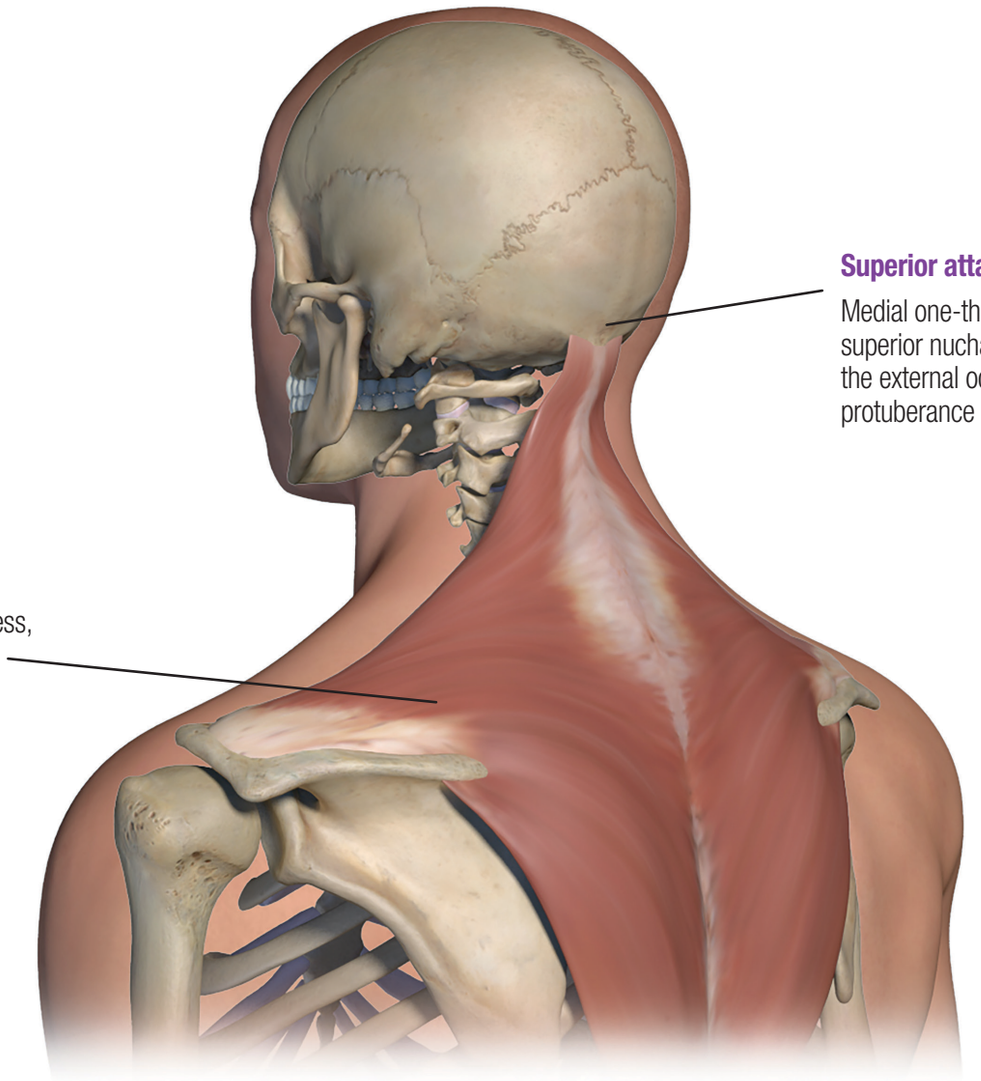
BOTOX®
onabotulinumtoxinA injection

Trapezius (upper)

▶ BOTOX® dose: 20 Units to 100 Units

Muscle action[25, 26]

Unilaterally rotates the head to the opposite side and bends it to the same side. Bilaterally extends the head



Superior attachment

Medial one-third of the superior nuchal line and the external occipital protuberance

Inferior attachment

Lateral one-third of the clavicle, acromion process, and scapular spine; spinous processes of the thoracic and lower cervical vertebrae

Involved postures

- Torticollis
- Laterocollis
- Retrocollis
- Right torticollis, left laterocollis, shoulder elevation
- Left torticollis, left laterocollis
- Right torticollis, retrocollis
- Right laterocollis, tremor

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS
Adverse reactions to BOTOX for injection are discussed in greater detail in the following sections: *Boxed Warning*, *Contraindications*, and *Warnings and Precautions*.

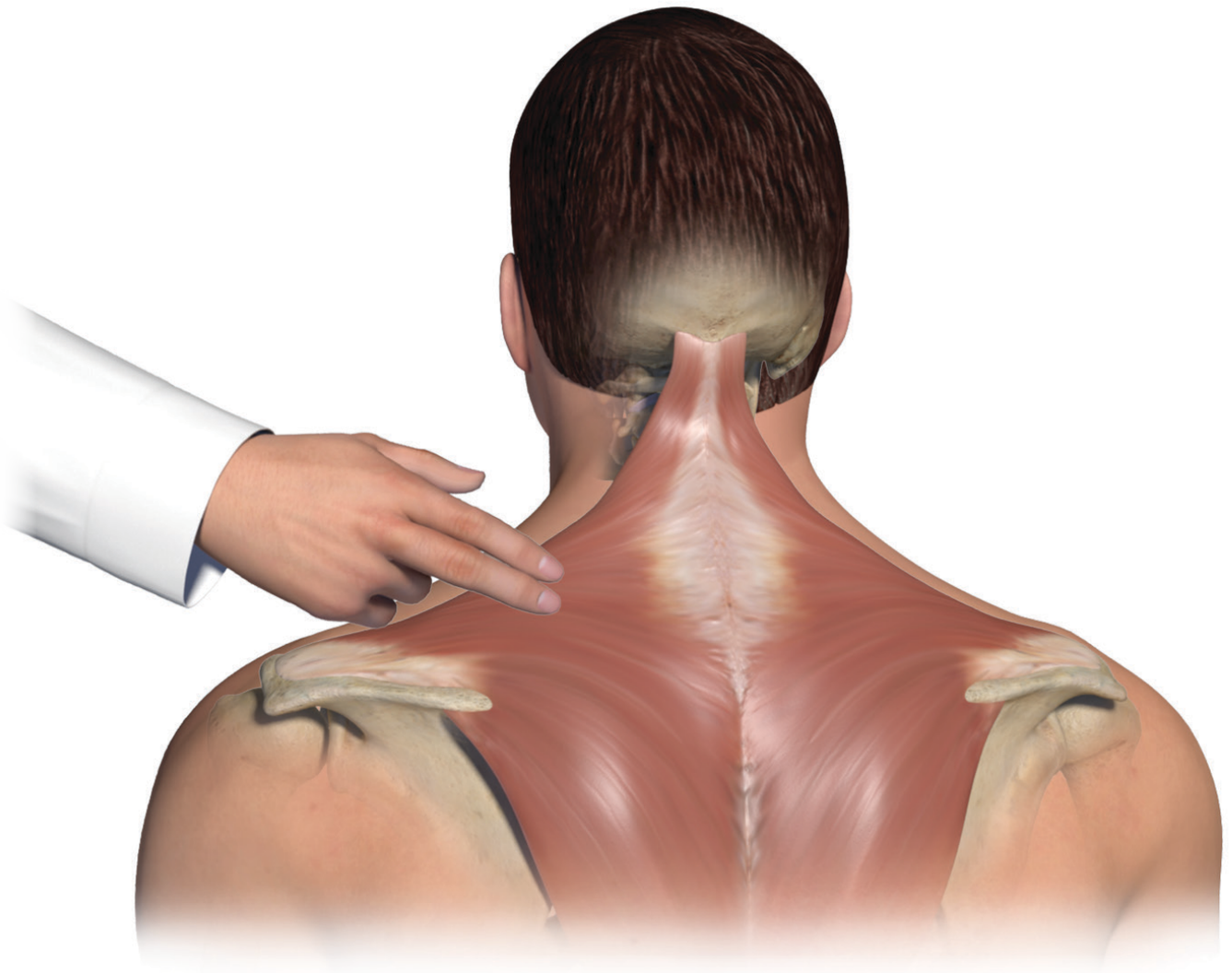
Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Trapezius (upper) (continued)

Localization

Localized between the inflection point of the neck (necklace line) and the acromioclavicular joint



IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)

Cervical Dystonia

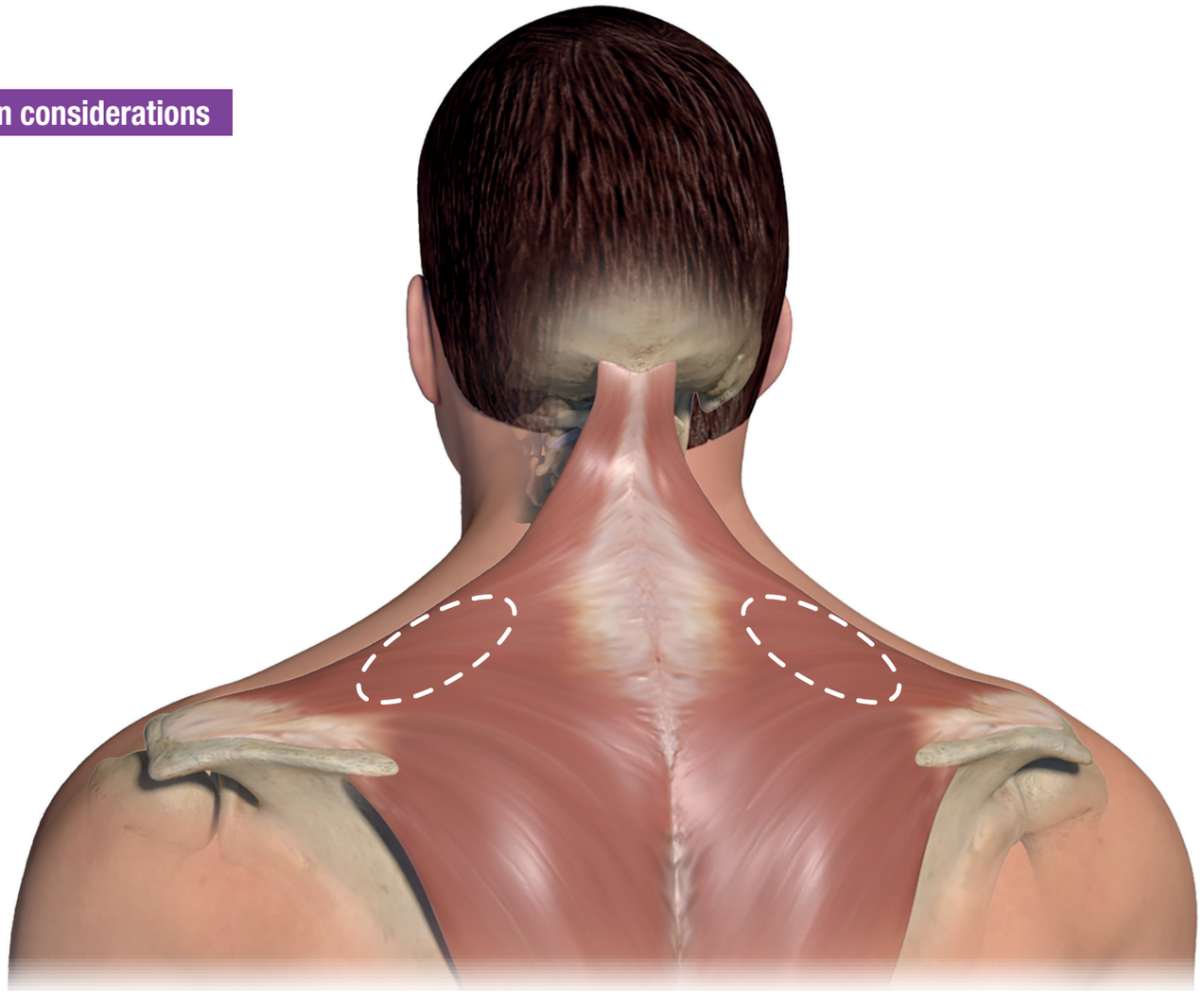
The most frequently reported adverse reactions following injection of BOTOX for cervical dystonia include dysphagia (19%), upper respiratory infection (12%), neck pain (11%), and headache (11%).

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Trapezius (upper) (continued)

Injection considerations



- Target this muscle in the presence of contralateral rotation and/or shoulder elevation
- Given the size of this muscle, multiple injection sites may be useful (keeping total dose within approved range)
- Injecting outside the upper/lower portions of this muscle and/or with too high a dose may inadvertently cause muscle weakness and head drop
- Medial portion has more vertical muscle fiber orientation and may be a weak contributor to contralateral rotation. This part of the muscle is very thin
- Consider injecting at a 0 degree angle, horizontal to the muscle to avoid injecting too deep
- Avoid injecting too deep as this is a very superficial muscle

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)

Blepharospasm

The most frequently reported adverse reactions following injection of BOTOX for blepharospasm include ptosis (21%), superficial punctate keratitis (6%), and eye dryness (6%).

Please see additional Important Safety Information throughout.

BOTOX®
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IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)

Strabismus

The most frequently reported adverse events following injection of BOTOX for strabismus include ptosis (1% after inferior rectus injections, 16% after horizontal rectus injections, and 38% after superior rectus injections) and vertical deviation (17%).

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Scalene complex

▶ BOTOX® dose: 15 Units to 50 Units

Muscle action[25, 26]

Anterior scalene = Unilaterally bends the neck to the same side and rotates the head to the opposite side. Bilaterally flexes the neck

Middle scalene = Unilaterally bends the neck to the same side. Bilaterally flexes the neck

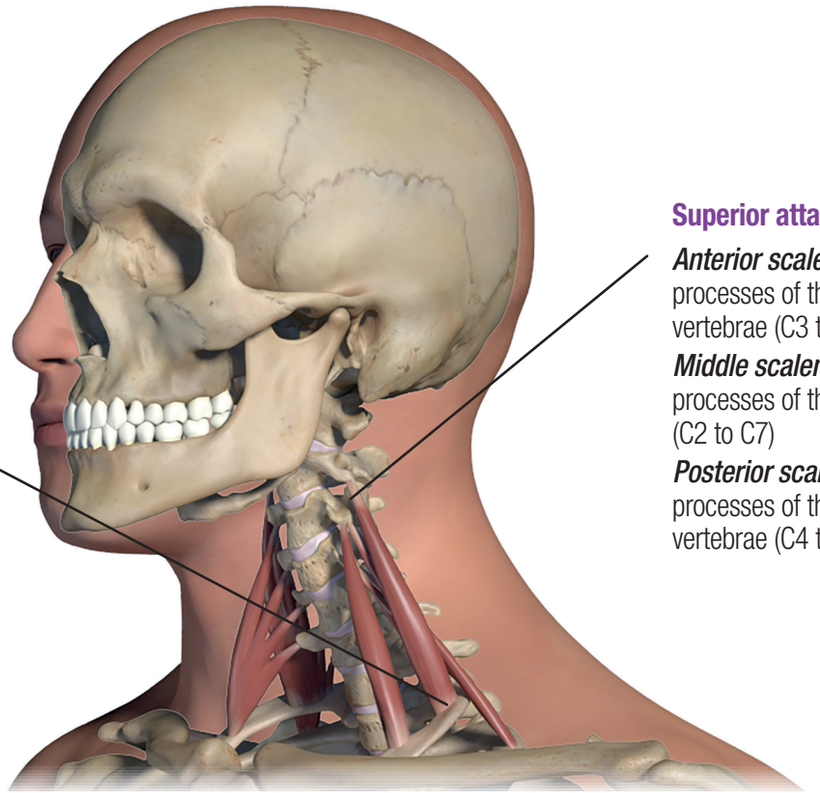
Posterior scalene = Unilaterally bends the neck to the same side

Inferior attachment

Anterior scalene = First rib anterior to the groove for the subclavian artery

Middle scalene = First rib posterior to the groove for the subclavian artery

Posterior scalene = Posterior aspect of the second rib



Superior attachment

Anterior scalene = Transverse processes of the middle cervical vertebrae (C3 to C6)

Middle scalene = Transverse processes of the cervical vertebrae (C2 to C7)

Posterior scalene = Transverse processes of the middle cervical vertebrae (C4 to C6)

Involved postures

Anterior scalene:
- Torticollis
- Laterocollis
- Anterocollis
- Lateral shift
- Left torticollis, left laterocollis
- Right laterocollis, tremor
- Right torticollis, left laterocollis, shoulder elevation

Middle scalene:
- Laterocollis
- Anterocollis
- Lateral shift
- Right torticollis, left laterocollis, shoulder elevation
- Left torticollis, left laterocollis
- Right laterocollis, tremor

Posterior scalene:
- Laterocollis
- Lateral shift
- Right torticollis, left laterocollis, shoulder elevation
- Left torticollis, left laterocollis
- Right laterocollis, tremor

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)

Postmarketing Experience

Adverse reactions that have been identified during postapproval use of BOTOX are discussed in greater detail in *Postmarketing Experience* (Section 6.3 of the Prescribing Information).

Please see additional Important Safety Information throughout.

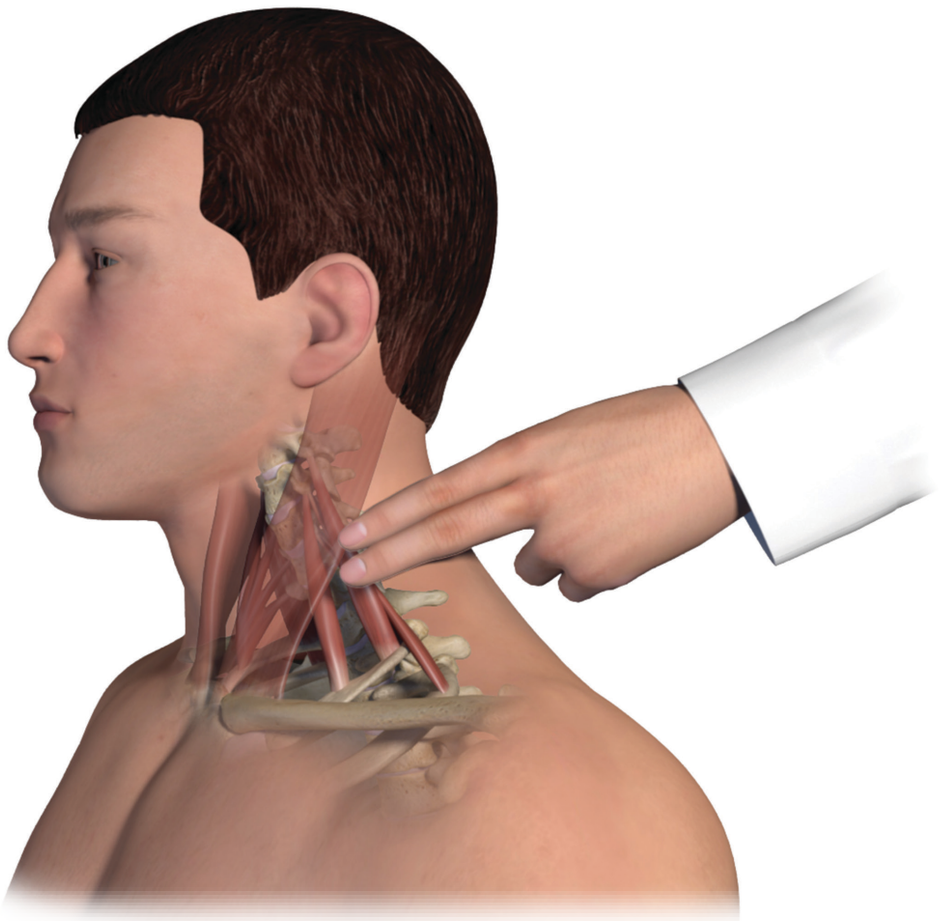
BOTOX® onabotulinumtoxinA injection

Scalene complex (continued)

Localization

Middle scalene = At the angle of the neck, 2 fingerbreadths anterior to the border of the trapezius and just posterior to the posterior border of the sternocleidomastoid. Lies on the anterior surface of the transverse processes

Anterior scalene = Immediately posterior to the clavicular head of the sternocleidomastoid

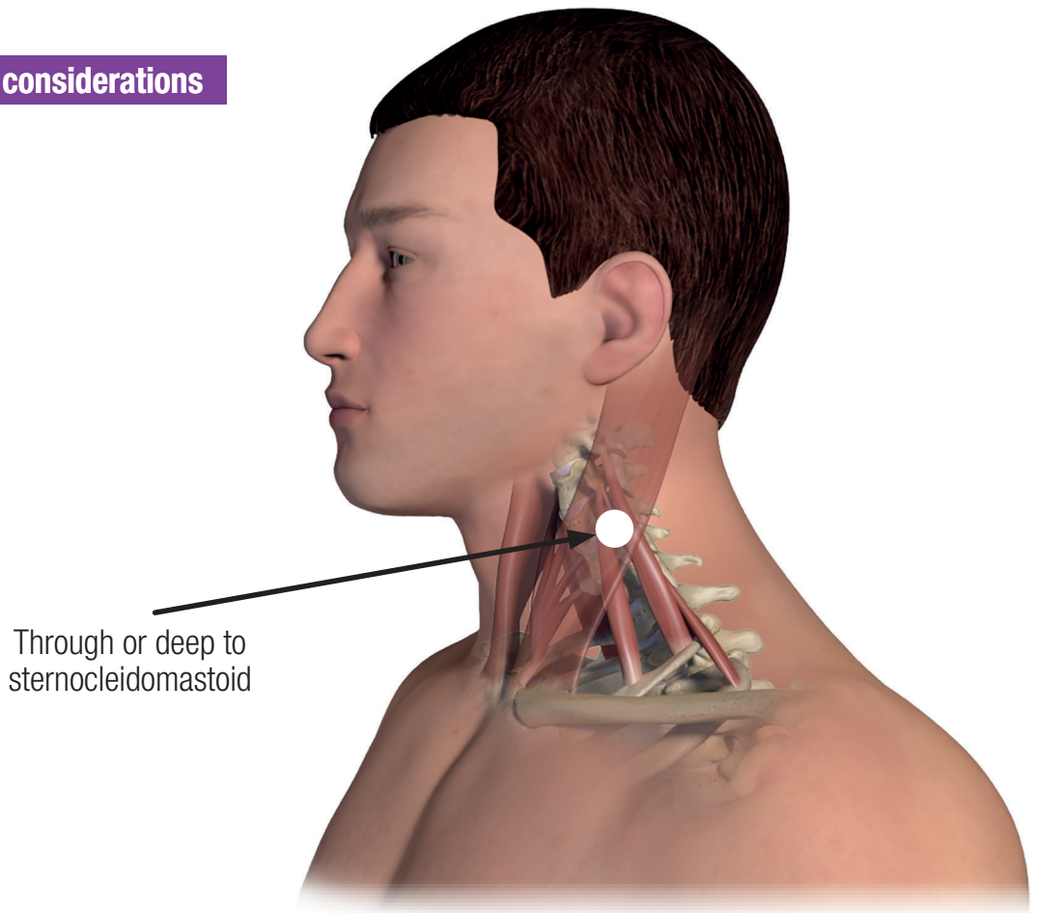


IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Postmarketing Experience (continued)
There have been spontaneous reports of death, sometimes associated with dysphagia, pneumonia, and/or other significant debility or anaphylaxis, after treatment with botulinum toxin. There have also been reports of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. Some of these patients had risk factors, including cardiovascular disease. The exact relationship of these events to the botulinum toxin injection has not been established.

Please see additional Important Safety Information throughout.

Scalene complex (continued)

Injection considerations



- Consider targeting the anterior scalene in the presence of anterocollis:
  - The clavicular head of the sternocleidomastoid (SCM) can act as an anatomical landmark for localization
  - Injection may be accomplished by going through the SCM or moving the SCM and going behind it
- Consider positioning needle perpendicular to muscle with thumb and index fingers palpating the levator scapulae and SCM to frame your approach
- Use small, careful movements when injecting this muscle group due to proximity of vital structures (eg, brachial plexus, vasculature, apex of lung)
- Staying approximately 2 fingerbreadths above the clavicle may lessen the odds of hitting the brachial plexus
- Consider a starting dose at the lower end of the approved dosing range and adjust accordingly based on treatment response

IMPORTANT SAFETY INFORMATION (continued)
DRUG INTERACTIONS
Co-administration of BOTOX and other agents interfering with neuromuscular transmission (eg, aminoglycosides, curare-like compounds) should only be performed with caution as the effect of the toxin may be potentiated.

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

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IMPORTANT SAFETY INFORMATION (continued)
DRUG INTERACTIONS (continued)
Use of anticholinergic drugs after administration of BOTOX may potentiate systemic anticholinergic effects. The effect of administering different botulinum neurotoxin products at the same time or within several months of each other is unknown. 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. Excessive weakness may also be exaggerated by administration of a muscle relaxant before or after administration of BOTOX.

Please see full Prescribing Information, including Boxed Warning and Medication Guide, or visit https://www.rxabbvie.com/pdf/botox_pi.pdf

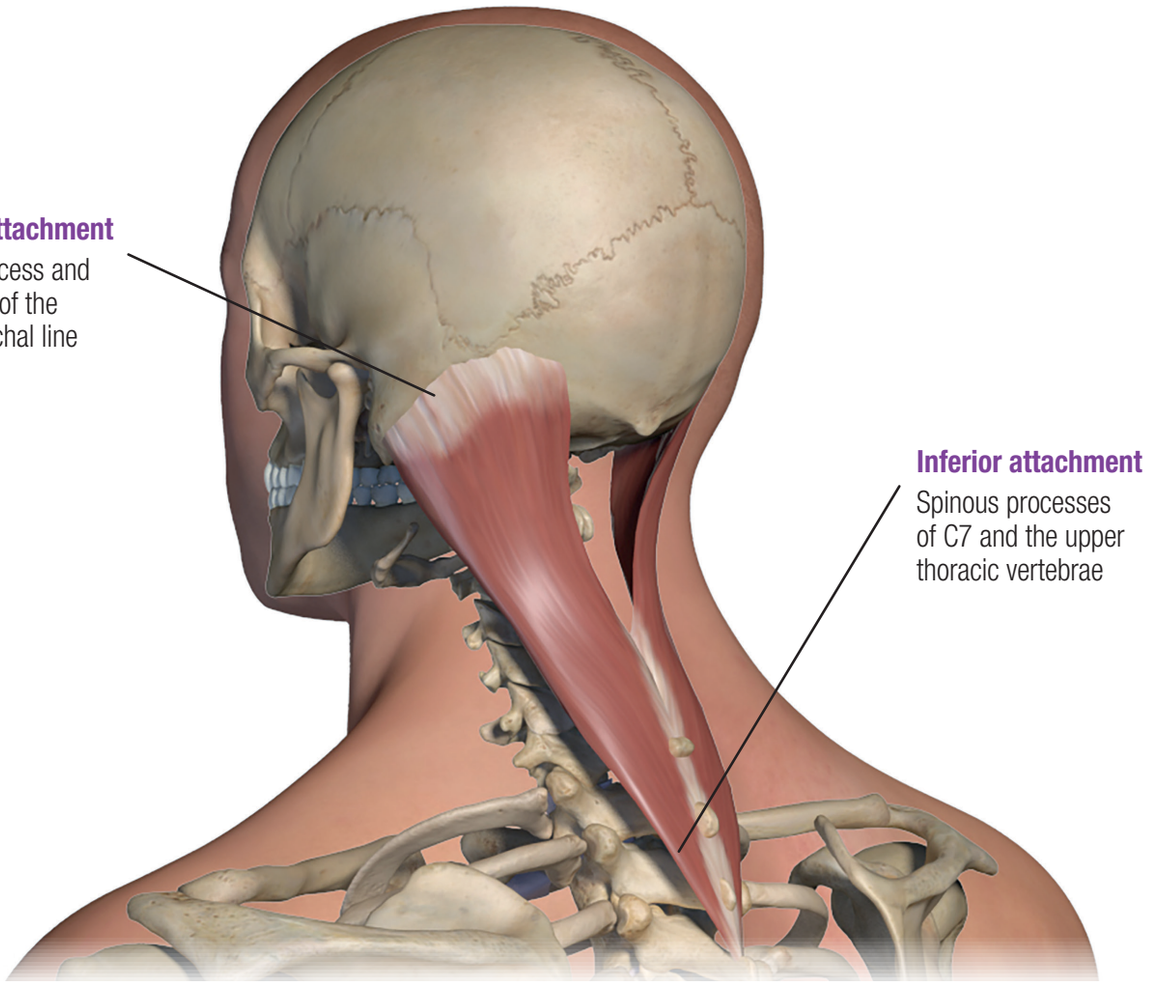
BOTOX® onabotulinumtoxinA injection

Splenius capitis

▶ BOTOX® dose: 15 Units to 100 Units

Muscle action[25]

Unilaterally rotates the head to the same side and bends it to the same side. Bilaterally extends the head



Involved postures

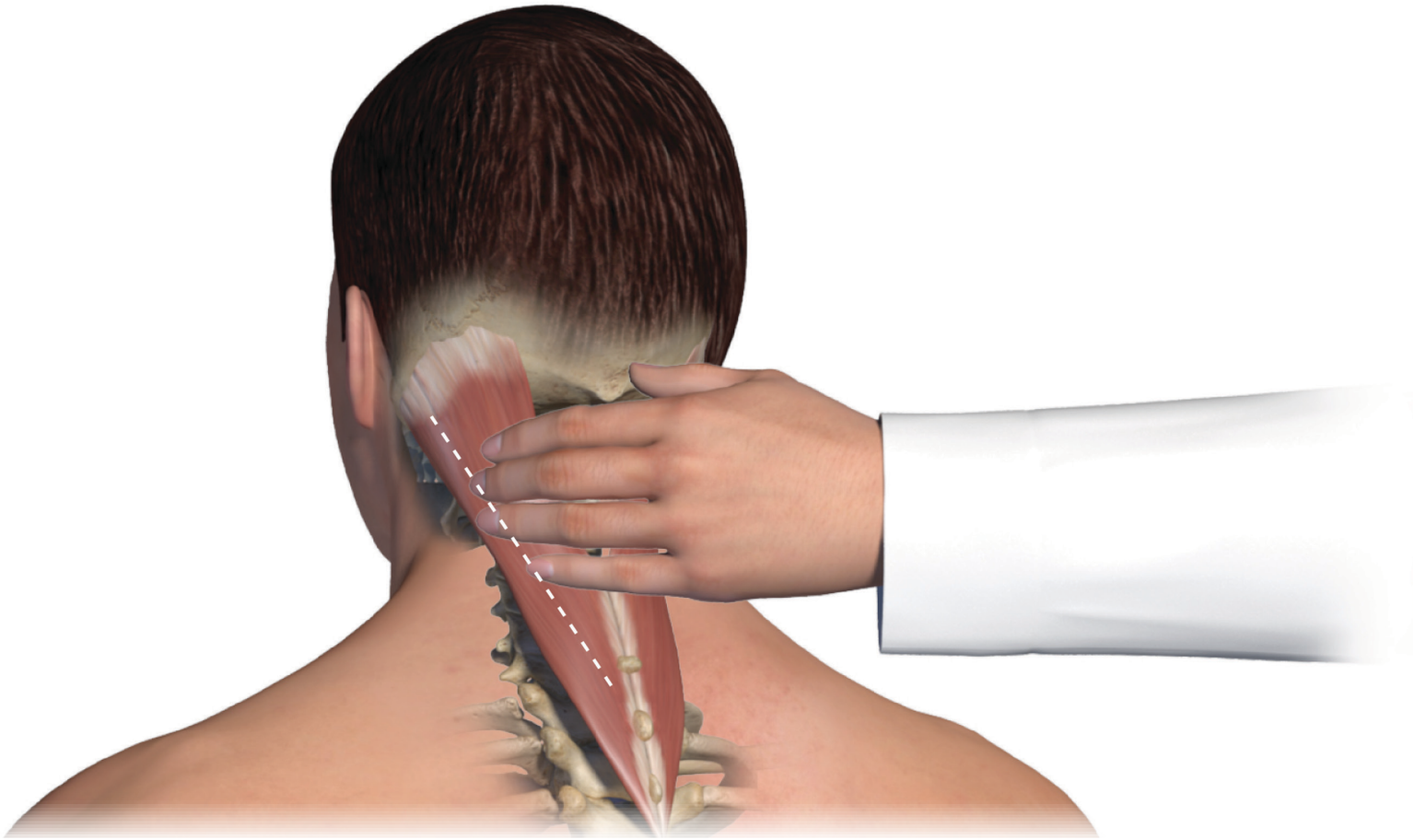
- Torticollis
- Laterocollis
- Retrocollis
- Lateral shift
- Right torticollis, left laterocollis, shoulder elevation
- Left torticollis, left laterocollis
- Right torticollis, retrocollis
- Right laterocollis, tremor

BOTOX®
onabotulinumtoxinA injection

Splenius capitis (continued)

Localization

Two fingerbreadths inferior to the occipital protuberance and 3 fingerbreadths lateral to the midline, anterior to the trapezius and posterior to the sternocleidomastoid



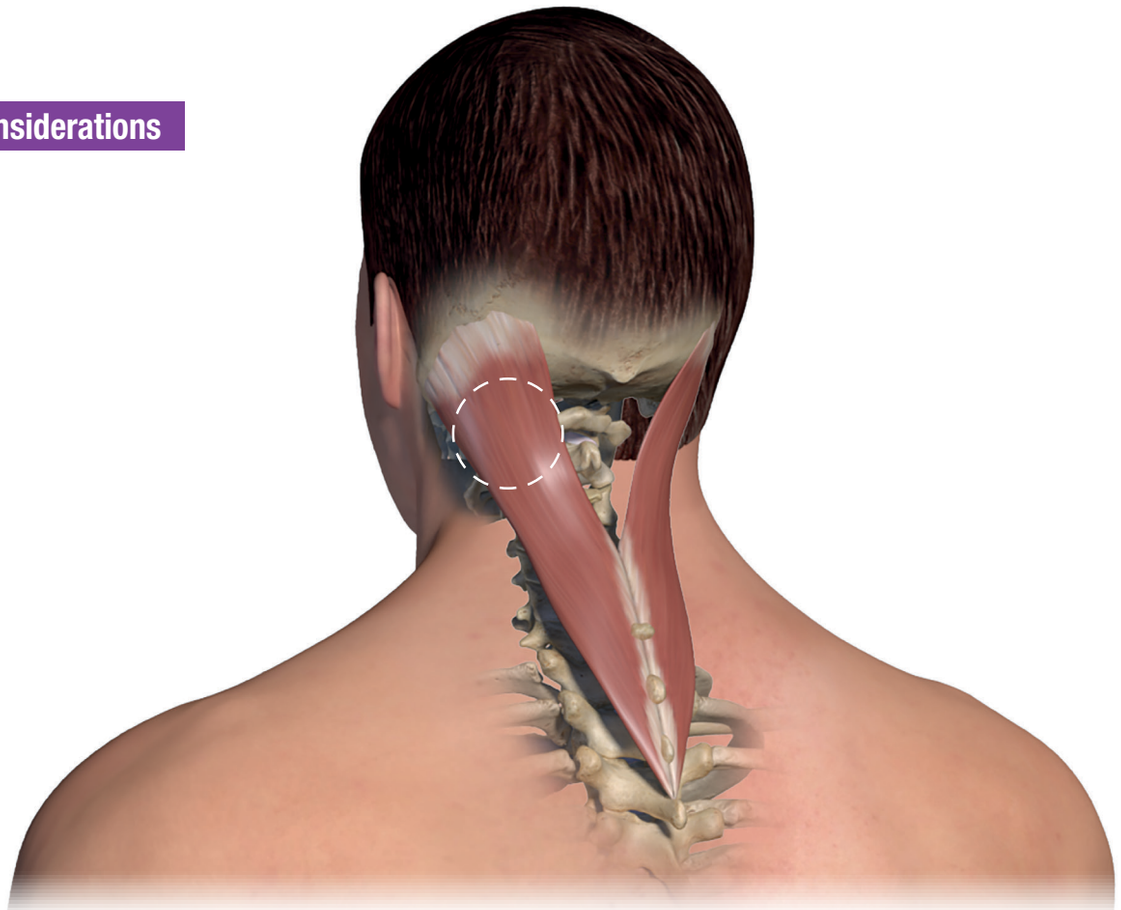
IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS
Spread of Toxin Effect
See *Boxed Warning*.

No definitive serious adverse event reports of distant spread of toxin effect associated with BOTOX for blepharospasm at the recommended dose (30 Units and below) or strabismus at the labeled dose have been reported.

Please see additional Important Safety Information throughout.

Splenius capitis (continued)

Injection considerations



- A common target in CD, the splenius capitis and cervicis are considered together as a single functional group and usually require multiple injections
- When treating retrocollis, consider approaching the splenius group bilaterally
- Use caution when injecting the splenius capitis as it is a flat and thin muscle:
  - Consider approaching more laterally and closer to the occiput
  - This is often a painful injection, so consider advising patient accordingly
- An aggressive starting dose may inadvertently cause head drop, especially in patients with limited rotation or extension
  - Consider a starting dose at the lower end of the approved dosing range and adjust accordingly based on treatment response
- Position patient's head in a neutral position during injection, if possible

BOTOX® onabotulinumtoxinA injection

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IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Serious Adverse Reactions With Unapproved Use
Serious adverse reactions, including excessive weakness, dysphagia, and aspiration pneumonia, with some adverse reactions associated with fatal outcomes, have been reported in patients who received BOTOX injections for unapproved uses. In these cases, the adverse reactions were not necessarily related to distant spread of toxin, but may have resulted from the administration of BOTOX to the site of injection and/or adjacent structures. In several of the cases, patients had preexisting dysphagia or other significant disabilities. There is insufficient information to identify factors associated with an increased risk for adverse reactions associated with the unapproved uses of BOTOX. The safety and effectiveness of BOTOX for unapproved uses have not been established.

Please see additional Important Safety Information throughout.

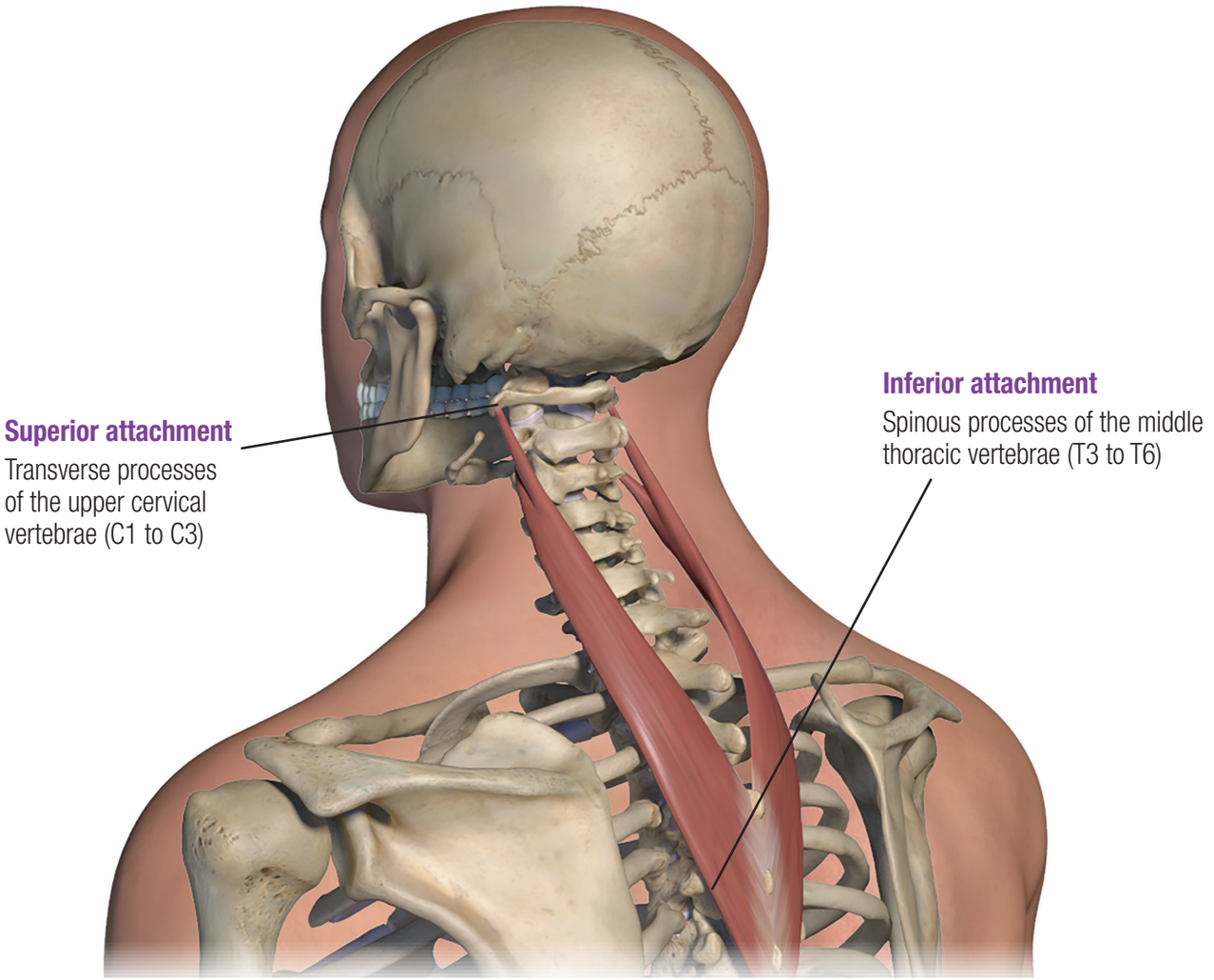
BOTOX® onabotulinumtoxinA injection

Splenius cervicis

▶ BOTOX® dose: 20 Units to 60 Units

Muscle action[25, 26]

Unilaterally rotates the upper neck and bends it to the same side. Bilaterally extends the upper cervical spine



Involved postures

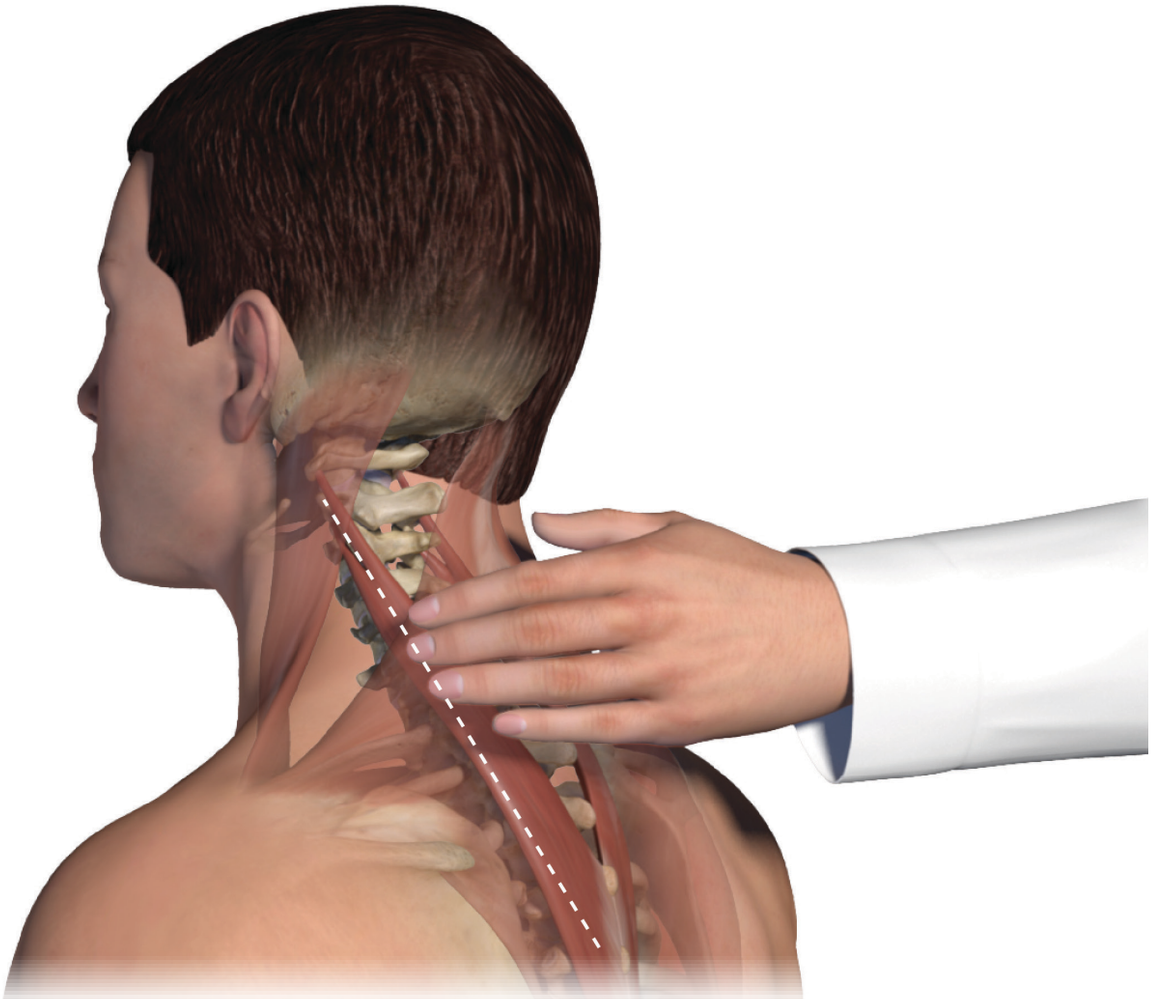
- Torticollis
- Laterocollis
- Retrocollis
- Right torticollis, left laterocollis, shoulder elevation
- Left torticollis, left laterocollis
- Right torticollis, retrocollis
- Right laterocollis, tremor

BOTOX® onabotulinumtoxinA injection

Splenius cervicis (continued)

Localization

At the angle of the neck, anterior to the trapezius, posterior to the SCM, in between and parallel to the splenius capitis and levator scapulae

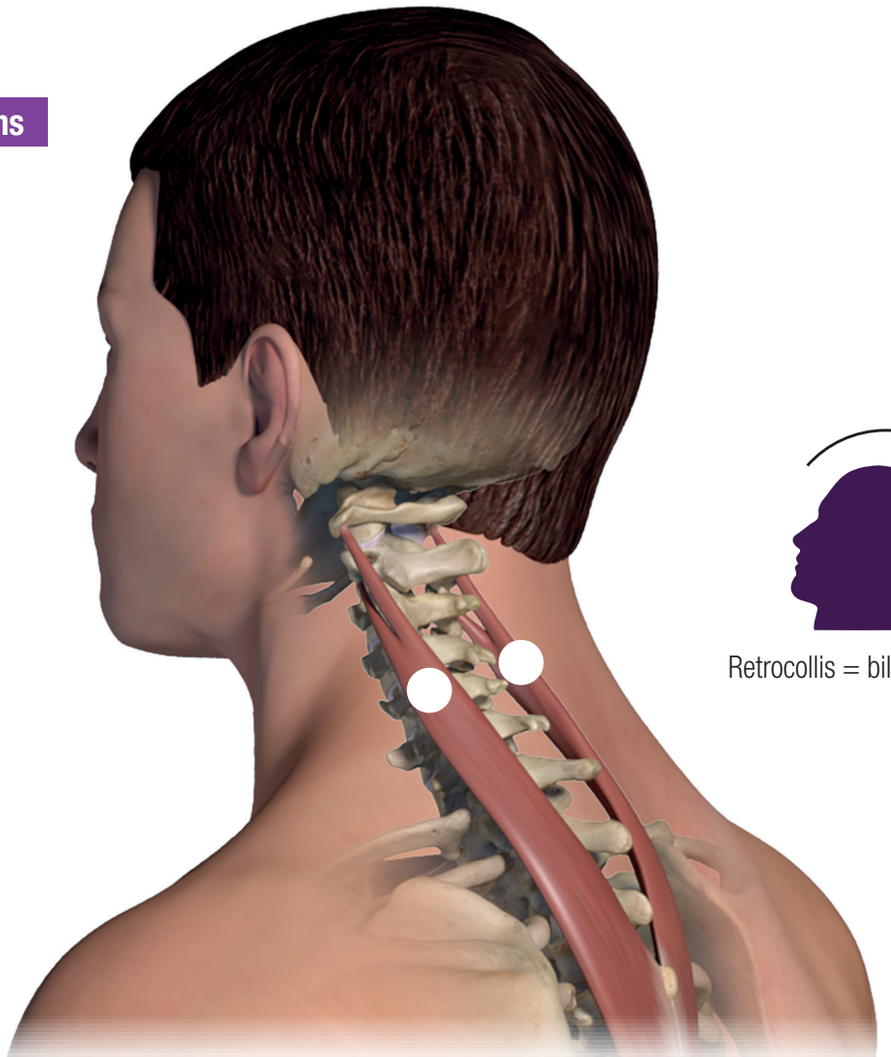


IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Hypersensitivity Reactions (continued)
These reactions include anaphylaxis, serum sickness, urticaria, soft-tissue edema, and dyspnea. If such a reaction occurs, further injection of BOTOX should be discontinued and appropriate medical therapy immediately instituted. One fatal case of anaphylaxis has been reported in which lidocaine was used as the diluent, and consequently, the causal agent cannot be reliably determined.

Please see additional Important Safety Information throughout.

Splenius cervicis (continued)

Injection considerations



Retrocollis = bilateral approach

- A common target in CD, the splenius capitis and cervicis are considered together as a single functional group and usually require multiple injections
- When treating retrocollis, consider approaching the splenius group bilaterally
- Consider injecting the cervicis in its superior part
- An aggressive starting dose may inadvertently cause head drop, especially in patients with limited rotation or extension
  - Consider a starting dose at the lower end of the approved dosing range and adjust accordingly based on treatment response
- Position patient's head in a neutral position during injection, if possible

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

Increased Risk of Clinically Significant Effects With Preexisting Neuromuscular Disorders

Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis (ALS), or neuromuscular junction disorders (eg, myasthenia gravis or Lambert-Eaton syndrome) should be monitored when given botulinum toxin.

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

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Or visit
BOTOXDigitalTools.com

Notes

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Increased Risk of Clinically Significant Effects With Preexisting Neuromuscular Disorders (continued)
Patients with known or unrecognized neuromuscular disorders or neuromuscular junction disorders may be at increased risk of clinically significant effects, including generalized muscle weakness, diplopia, ptosis, dysphonia, dysarthria, severe dysphagia, and respiratory compromise from therapeutic doses of BOTOX (see *Warnings and Precautions*).

Please see additional Important Safety Information throughout.

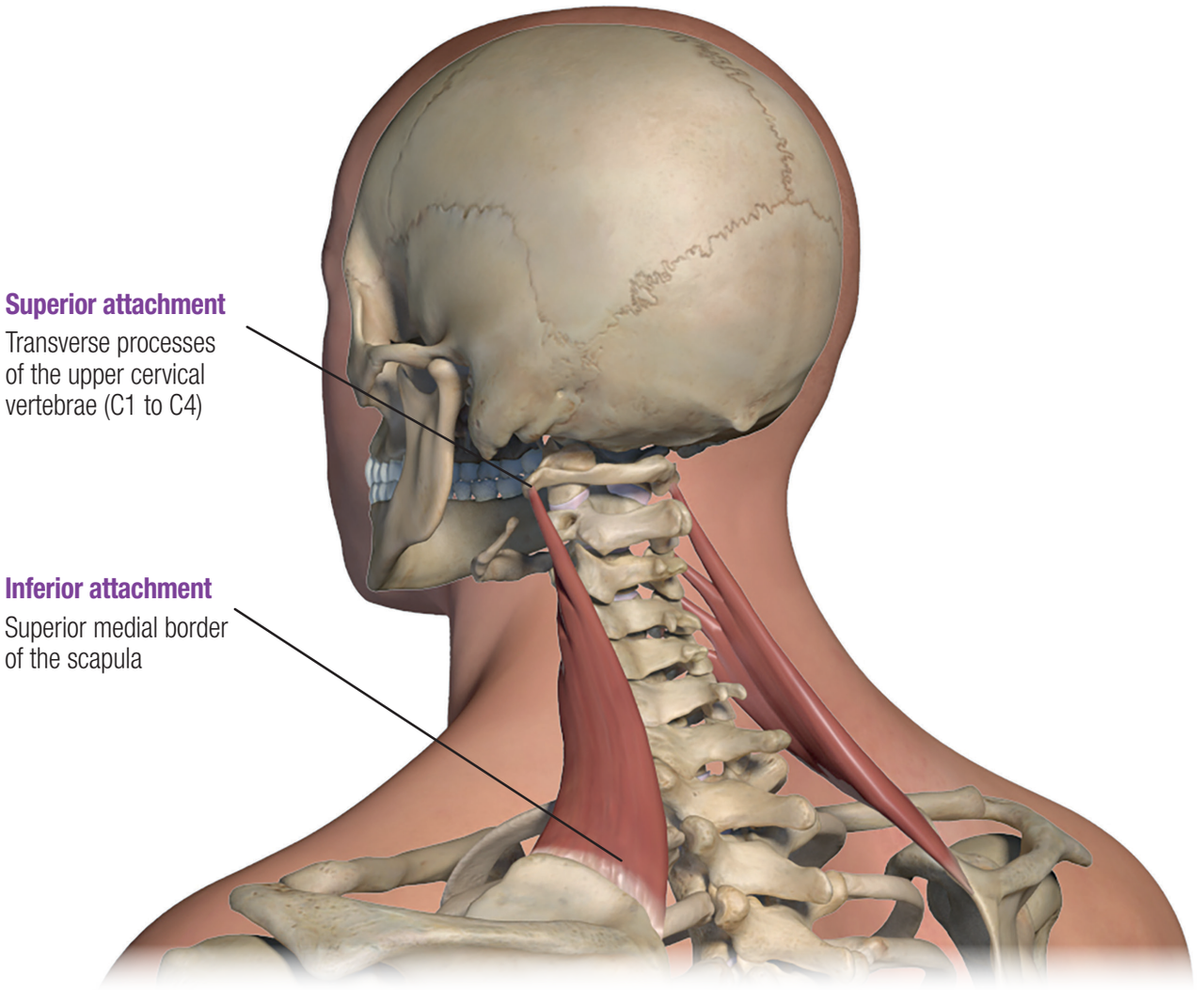
BOTOX®
onabotulinumtoxinA injection

Levator scapulae

▶ BOTOX® dose: 20 Units to 100 Units

Muscle action[25, 26]

Unilaterally rotates the neck to the same side and bends it to the same side. Bilaterally extends the neck



Involved postures

- Torticollis
- Laterocollis
- Retrocollis
- Right torticollis, left laterocollis, shoulder elevation
- Left torticollis, left laterocollis

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

Dysphagia and Breathing Difficulties

Treatment with BOTOX and other botulinum toxin products can result in swallowing or breathing difficulties. Patients with preexisting swallowing or breathing difficulties may be more susceptible to these complications. In most cases, this is a consequence of weakening of muscles in the area of injection that are involved in breathing or oropharyngeal muscles that control swallowing or breathing (see *Boxed Warning*).

Please see additional Important Safety Information throughout.

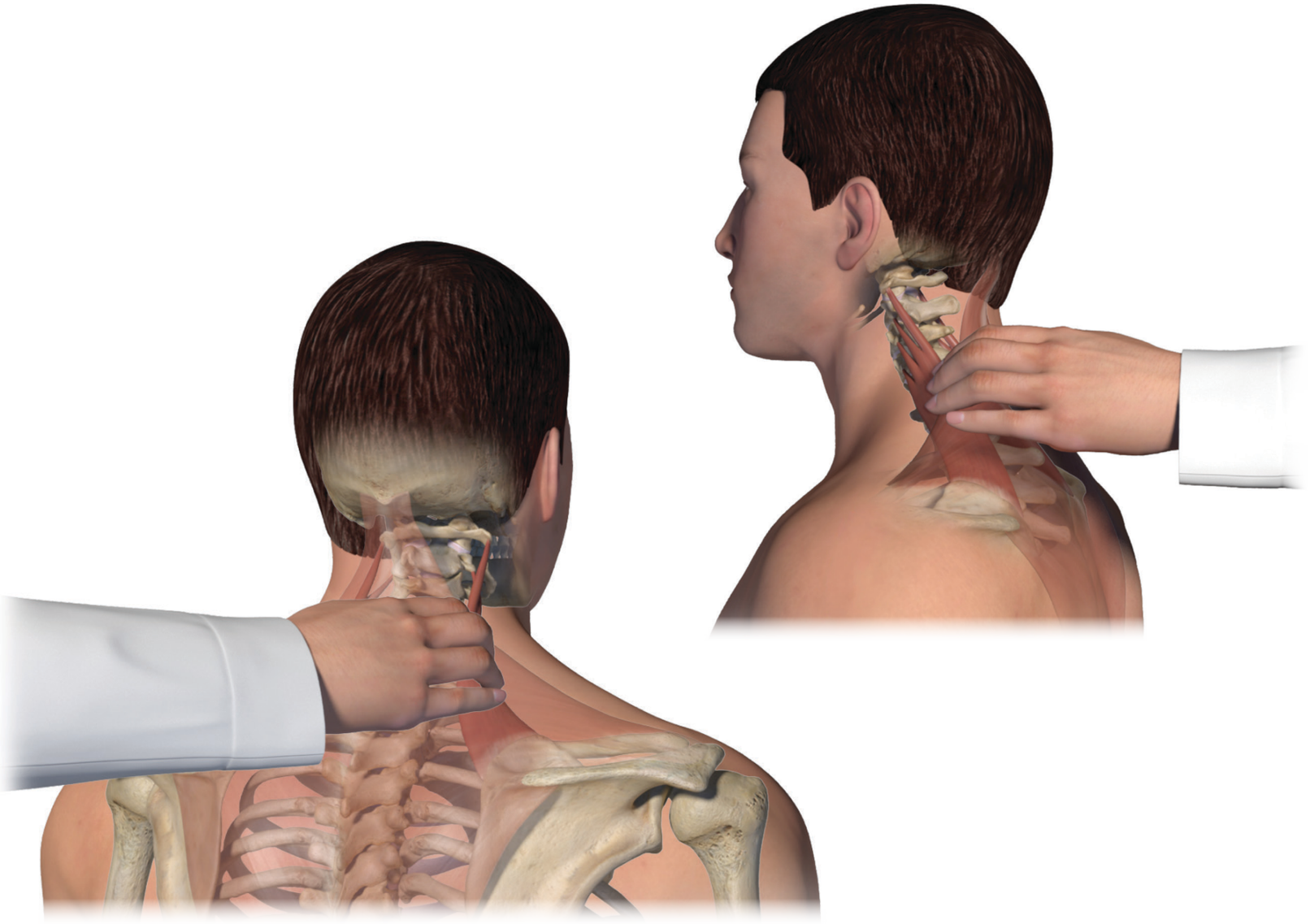
BOTOX® onabotulinumtoxinA injection

Levator scapulae (continued)

Localization

Superior = At the angle of the neck, immediately anterior to the trapezius

Inferior = One fingerbreadth medial and 1 fingerbreadth superior to the superior, medial border of the scapula



IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Corneal Exposure and Ulceration in Patients Treated With BOTOX for Blepharospasm

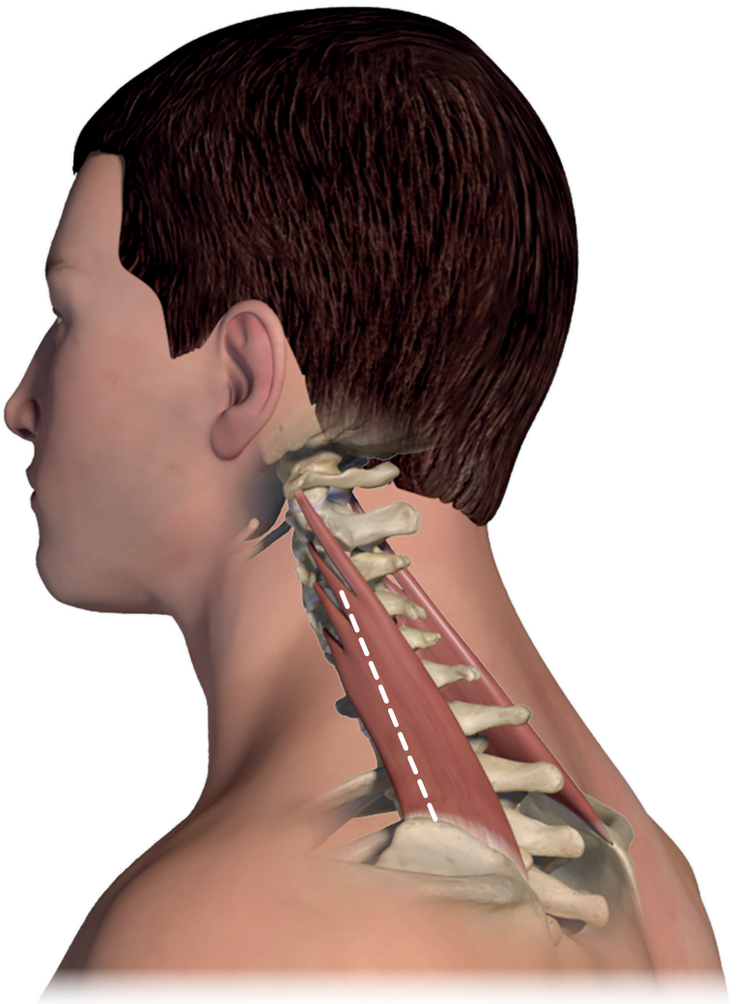
Reduced blinking from BOTOX injection of the orbicularis muscle can lead to corneal exposure, persistent epithelial defect, and corneal ulceration, especially in patients with VII nerve disorders.

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Levator scapulae (continued)

Injection considerations



- Consider targeting this muscle in the presence of shoulder elevation and significant neck pain
- If localization is difficult, instruct patient to activate muscle by shrugging their shoulders or putting their hand in a back pocket
- Although a superficial muscle, the electrically active parts may be at some depth, occasionally up to 3 cm
- When injecting, consider drawing an imaginary line from the medial border of the scapula to the upper neck (C3/C4) and inject over this line at 2 to 3 fingerbreadths from scapular insertion to hit lower half of muscle
- When injecting the inferior portion, consider approaching at a 45 degree angle in line with muscle orientation
- Consider a starting dose around 20 Units to 25 Units and titrate in 10 Unit to 20 Unit increments
- Consider dividing higher doses between the superior and inferior portions of the muscle

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

Retrobulbar Hemorrhages in Patients Treated With BOTOX for Strabismus

During the administration of BOTOX for the treatment of strabismus, retrobulbar hemorrhages sufficient to compromise retinal circulation have occurred. It is recommended that appropriate instruments to decompress the orbit be accessible.

Please see additional Important Safety Information throughout.

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Notes

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

Human Albumin and Transmission of Viral Diseases

This product contains albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases and variant Creutzfeldt-Jakob disease (vCJD). There is a theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD), but if that risk actually exists, the risk of transmission would also be considered extremely remote. No cases of transmission of viral diseases, CJD, or vCJD have ever been identified for licensed albumin or albumin contained in other licensed products.

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Longissimus (capitis/cervicis)

▶ BOTOX® dose: 30 Units to 100 Units

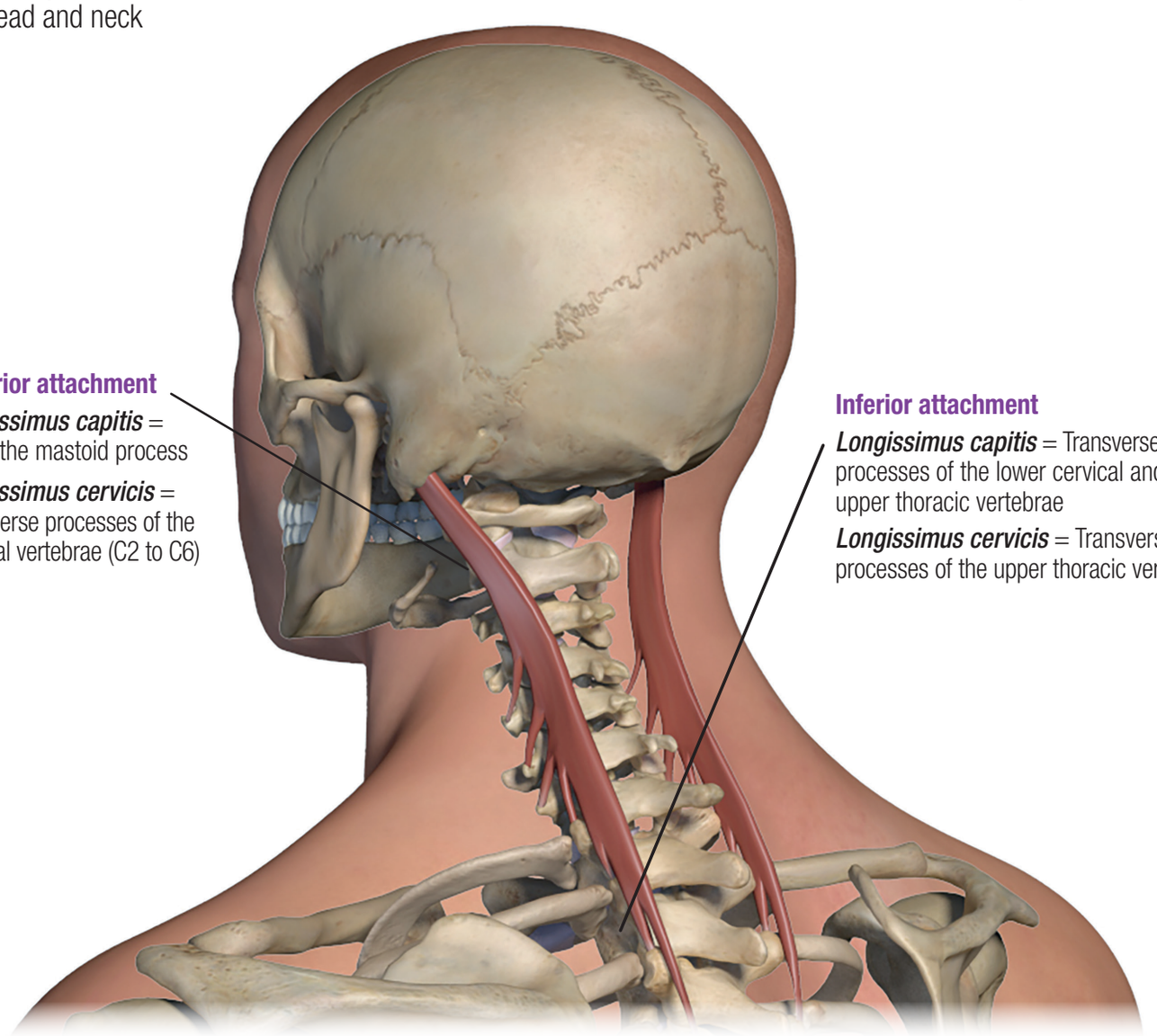
Muscle action[25, 26]

Unilaterally rotates the head and neck to the same side and bends them to the same side. Bilaterally extends the head and neck

Superior attachment

Longissimus capitis = Tip of the mastoid process

Longissimus cervicis = Transverse processes of the cervical vertebrae (C2 to C6)



Inferior attachment

Longissimus capitis = Transverse processes of the lower cervical and upper thoracic vertebrae

Longissimus cervicis = Transverse processes of the upper thoracic vertebrae

Involved postures

- Torticollis
- Laterocollis
- Retrocollis
- Right torticollis, retrocollis (for neck pain)

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS
Adverse reactions to BOTOX for injection are discussed in greater detail in the following sections: *Boxed Warning*, *Contraindications*, and *Warnings and Precautions*.

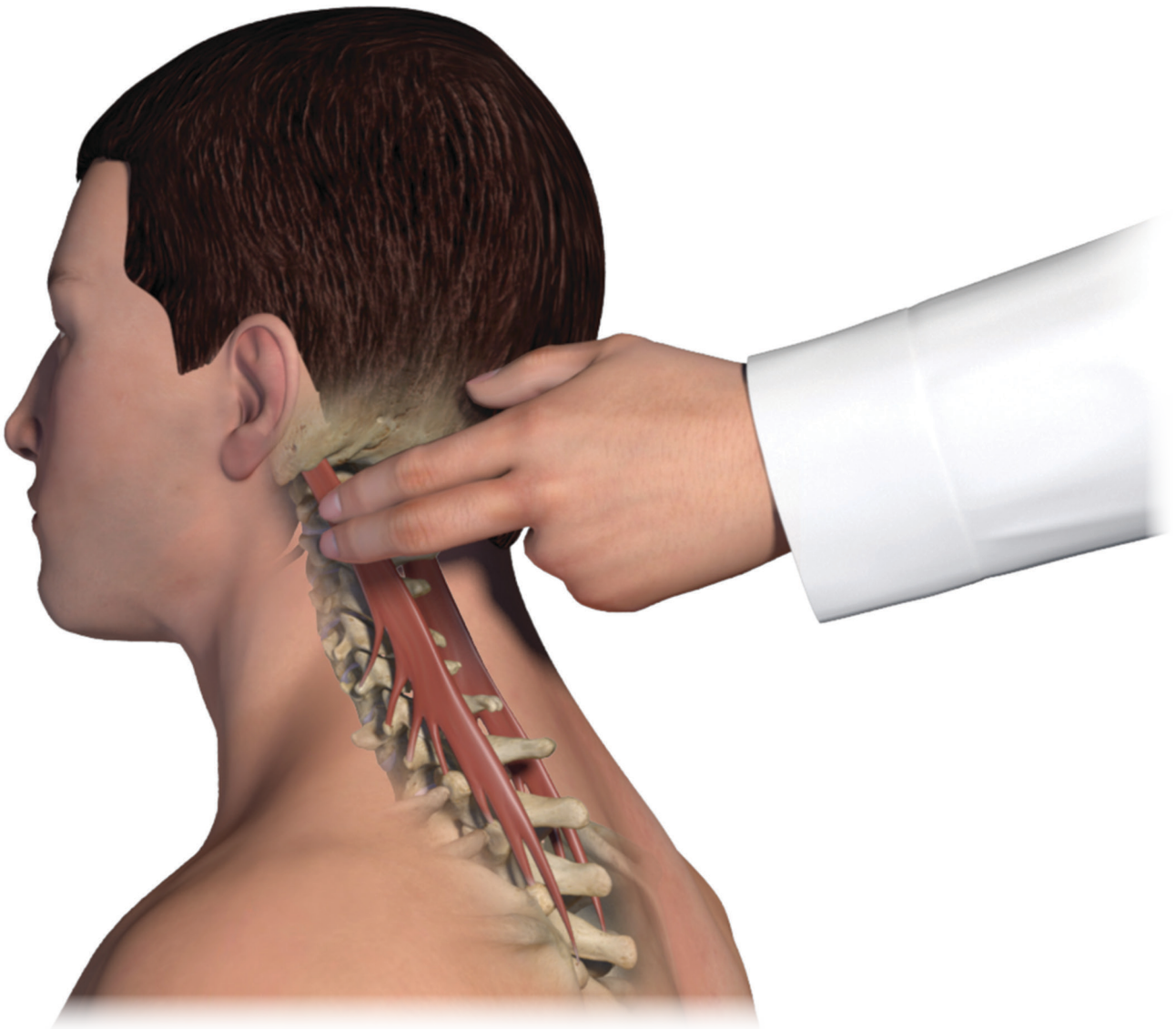
Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Longissimus (capitis/cervicis) (continued)

Localization

Palpate the transverse processes approximately 2 fingerbreadths inferior to the mastoid process. Lies parallel and just medial to the splenius cervicis. May feel like a rod or pencil when dystonic



IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)

Cervical Dystonia

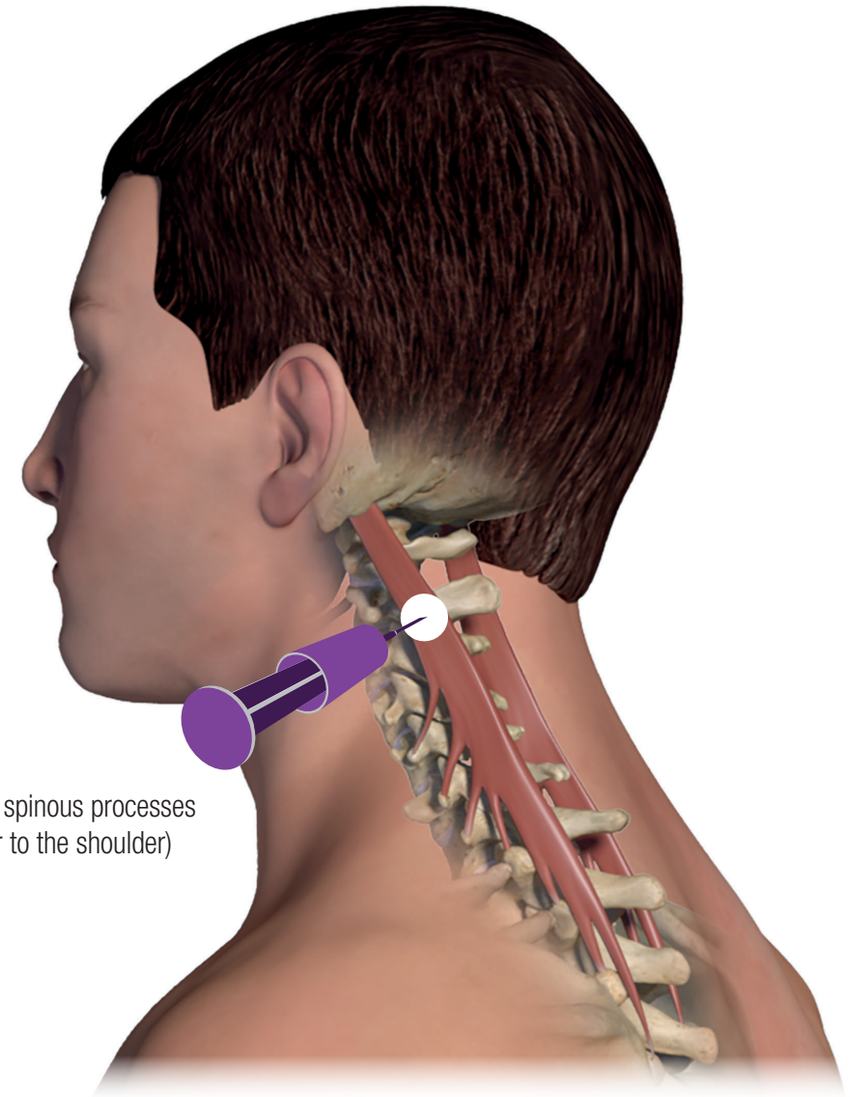
The most frequently reported adverse reactions following injection of BOTOX for cervical dystonia include dysphagia (19%), upper respiratory infection (12%), neck pain (11%), and headache (11%).

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Longissimus (capitis/cervicis) (continued)

Injection considerations



Parallel to the spinous processes
(perpendicular to the shoulder)

- This muscle is relatively easy to palpate and may feel like a pencil extending from the tip of the mastoid process
- This muscle should be targeted in patients with retrocollis (bilaterally), ipsilateral torticollis (unilaterally), and significant posterior or lateral axial neck pain
- Consider injecting just medial of the mastoid process at a depth of approximately 2 cm (enough to pass through the splenius capitis)
- This muscle often responds to smaller doses of BOTOX®, so consider starting in the lower end of the approved dosing range

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)

Blepharospasm

The most frequently reported adverse reactions following injection of BOTOX for blepharospasm include ptosis (21%), superficial punctate keratitis (6%), and eye dryness (6%).

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

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Notes

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)

Strabismus

The most frequently reported adverse events following injection of BOTOX for strabismus include ptosis (1% after inferior rectus injections, 16% after horizontal rectus injections, and 38% after superior rectus injections) and vertical deviation (17%).

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

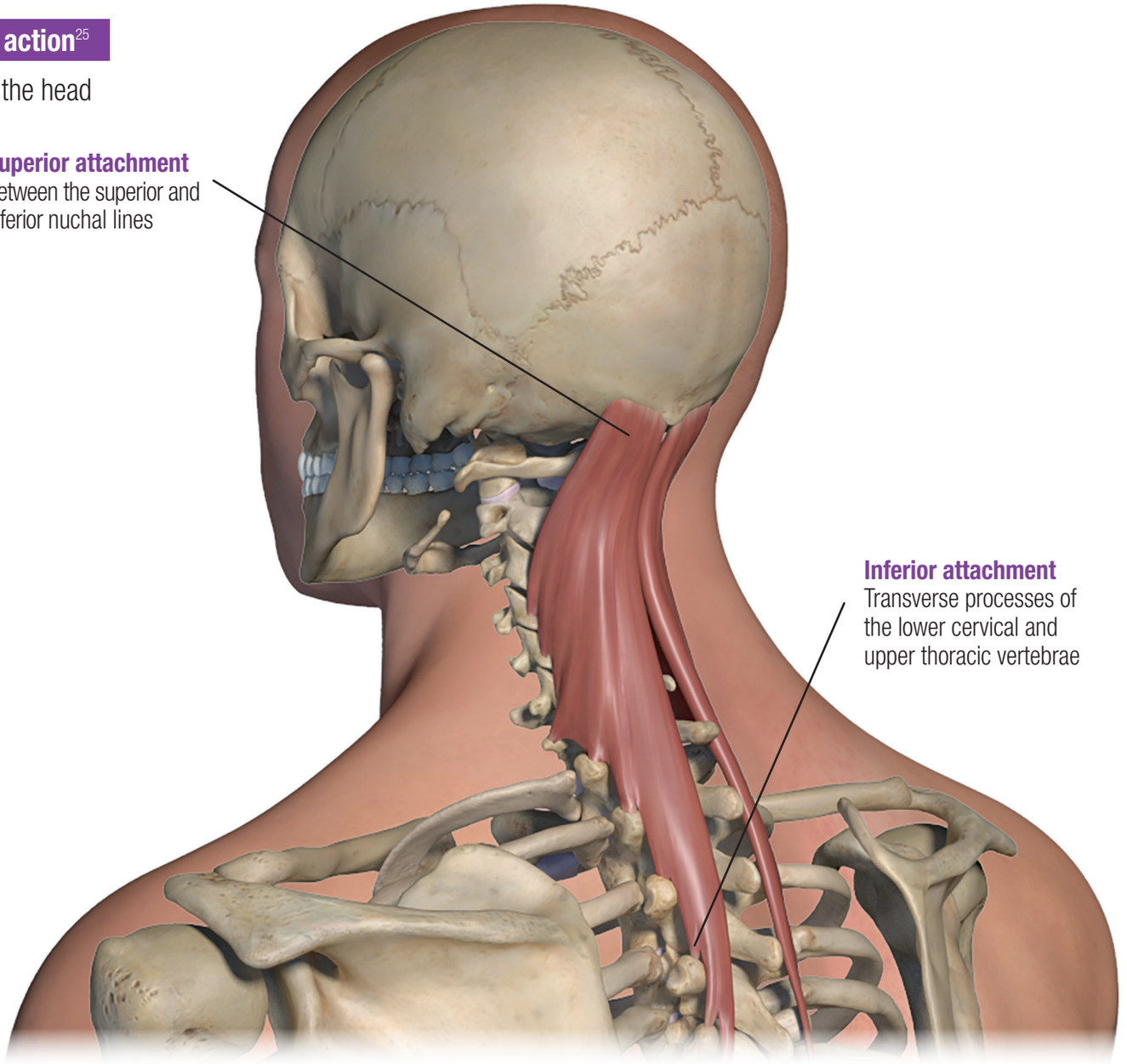
Semispinalis capitis

▶ BOTOX® dose: 30 Units to 100 Units

Muscle action[25]

Extends the head

Superior attachment
Between the superior and inferior nuchal lines



Inferior attachment
Transverse processes of the lower cervical and upper thoracic vertebrae

Involved postures

- Retrocollis
- Right torticollis, retrocollis

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)

Postmarketing Experience

Adverse reactions that have been identified during postapproval use of BOTOX are discussed in greater detail in *Postmarketing Experience* (Section 6.3 of the Prescribing Information).

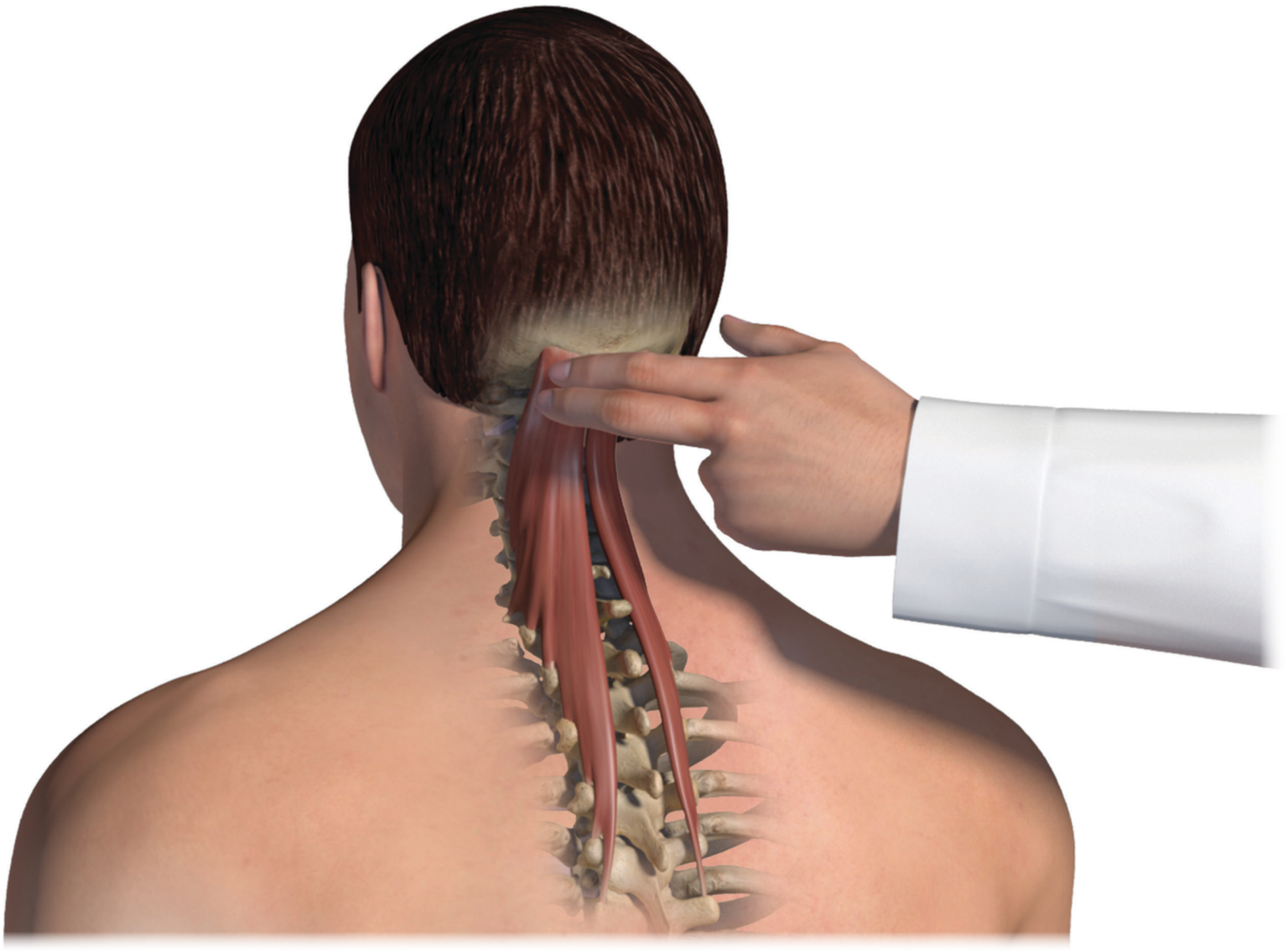
Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Semispinalis capitis (continued)

Localization

Two fingerbreadths below the occipital protuberance and 2 fingerbreadths lateral to the midline, anterior/deep to the trapezius and splenius capitis



IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Postmarketing Experience (continued)
There have been spontaneous reports of death, sometimes associated with dysphagia, pneumonia, and/or other significant debility or anaphylaxis, after treatment with botulinum toxin. There have also been reports of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. Some of these patients had risk factors, including cardiovascular disease. The exact relationship of these events to the botulinum toxin injection has not been established.

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Semispinalis capitis (continued)

Injection considerations

Also consider with neck pain

- Besides retrocollis, this muscle may also be considered with:
  - Torticollis (contralateral)
  - Laterocollis
  - Neck pain (due to presence of greater occipital nerve)
- When injecting this muscle, keep the following in mind:
  - It is deep to the trapezius and splenius capitis
  - A more inferior injection approach may result in diffusion of BOTOX® into a neighboring muscle (ie, splenius capitis)
  - This is often a painful injection, so consider advising patient accordingly
- An aggressive starting dose may lead to head drop, so consider the lower end of the approved range

IMPORTANT SAFETY INFORMATION (continued)
DRUG INTERACTIONS
Co-administration of BOTOX and other agents interfering with neuromuscular transmission (eg, aminoglycosides, curare-like compounds) should only be performed with caution as the effect of the toxin may be potentiated.

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

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Notes

IMPORTANT SAFETY INFORMATION (continued)
DRUG INTERACTIONS (continued)
Use of anticholinergic drugs after administration of BOTOX may potentiate systemic anticholinergic effects. The effect of administering different botulinum neurotoxin products at the same time or within several months of each other is unknown. 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. Excessive weakness may also be exaggerated by administration of a muscle relaxant before or after administration of BOTOX.

Please see full Prescribing Information, including Boxed Warning and Medication Guide, or visit https://www.rxabbvie.com/pdf/botox_pi.pdf

BOTOX® onabotulinumtoxinA injection

Dilution and reconstitution

Follow general dilution instructions for BOTOX® vials (100 Units and 200 Units)[16]

100-Unit BOTOX® Vial		
0.9% Sodium Chloride* per vial	Dose per 1 mL syringe	Dose per 0.1 mL
1 mL	100 Units	10 Units
2 mL	50 Units	5 Units
4 mL	25 Units	2.5 Units
8 mL	12.5 Units	1.25 Units
10 mL	10 Units	1 Unit

200-Unit BOTOX® Vial		
0.9% Sodium Chloride* per vial	Dose per 1 mL syringe	Dose per 0.1 mL
1 mL	200 Units	20 Units
2 mL	100 Units	10 Units
4 mL	50 Units	5 Units
8 mL	25 Units	2.5 Units
16 mL	12.5 Units	1.25 Units
20 mL	10 Units	1 Unit

*Preservative-free 0.9% Sodium Chloride Injection, USP only.

- The recommended dilution is 200 Units/2 mL, 200 Units/4 mL, 100 Units/1 mL, or 100 Units/2 mL with preservative-free 0.9% Sodium Chloride Injection, USP (see tables above)
- Administer the 200-Unit vial or 100-Unit vial of BOTOX® within 24 hours after reconstitution in the vial
- Unused reconstituted BOTOX® should be stored in the refrigerator (2ºC to 8ºC) for up to 24 hours until time of use
- BOTOX® vials are for single-dose only. Discard any unused portion
- Unopened vials of BOTOX® should be stored in a refrigerator (between 2ºC to 8ºC or 36ºF to 46ºF)

IMPORTANT SAFETY INFORMATION (continued)
CONTRAINDICATIONS
BOTOX is contraindicated in the presence of infection at the proposed injection site(s) and in patients who are hypersensitive to any botulinum toxin product or to any of the components in the formulation.

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Reconstitution procedures

Using the reconstitution needle, draw up the proper amount of saline (see Dilution Table) in the appropriately sized sterile syringe. A 21-gauge, 2-inch needle is recommended for reconstitution. Reconstituted BOTOX® should be clear, colorless, and free of particulate matter.

Insert the needle straight into the vial, then tilt the vial at a 45° angle. Slowly inject the saline into the BOTOX® neurotoxin vial. Vacuum is present in the vial, which demonstrates that the sterility of the vial is intact. Do not use the vial if the vacuum does not pull the saline into the vial.

Release the vacuum by disconnecting the syringe from the needle and allowing air to flow into the vial. Gently mix BOTOX® with the saline by moving the vial side to side or rotating the vial.

Draw the fluid into the injection syringe by placing the needle into the bottom corner of the vial for full extraction.

Disconnect the injection syringe from the vial and attach an appropriate needle for injection. A 25- to 30-gauge needle may be used for superficial muscles, and a longer 22-gauge needle may be used for deeper musculature.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS

Spread of Toxin Effect

See *Boxed Warning*.

No definitive serious adverse event reports of distant spread of toxin effect associated with BOTOX for blepharospasm at the recommended dose (30 Units and below) or strabismus at the labeled dose have been reported.

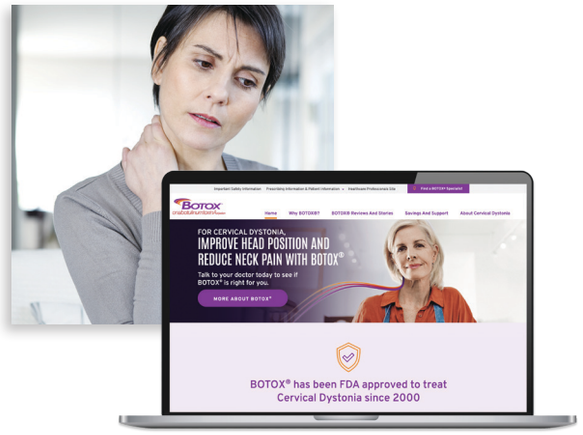
Lack of Interchangeability Between Botulinum Toxin Products

The potency Units of BOTOX 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 BOTOX cannot be compared to nor converted into Units of any other botulinum toxin products assessed with any other specific assay method.

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

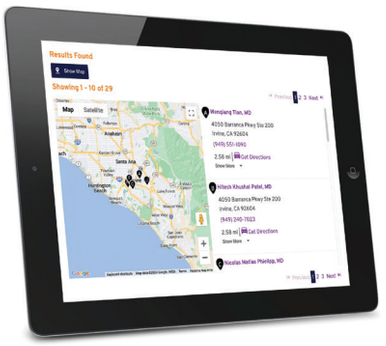
Resources available to help your patients access BOTOX®



Patient Education

- Brochures are available for both current and prospective patients to help them understand what to expect with BOTOX® treatment
- In-office materials are available to help educate patients about their condition and BOTOX®
- Patients can also visit: BOTOXCervicalDystonia.com

Contact your Account Specialist to learn how to get these materials for your patients



Support

- The Find a BOTOX® Specialist tool helps patients/caregivers seeking treatment find providers and practices
- Create and customize your profile with multiple options (eg, name and photo, specialty). Once your profile has been created, you may be included in patient search results on the Find a BOTOX® Specialist tool

Learn more at BOTOXOne.com

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

Serious Adverse Reactions With Unapproved Use

Serious adverse reactions, including excessive weakness, dysphagia, and aspiration pneumonia, with some adverse reactions associated with fatal outcomes, have been reported in patients who received BOTOX injections for unapproved uses. In these cases, the adverse reactions were not necessarily related to distant spread of toxin, but may have resulted from the administration of BOTOX to the site of injection and/or adjacent structures. In several of the cases, patients had preexisting dysphagia or other significant disabilities. There is insufficient information to identify factors associated with an increased risk for adverse reactions associated with the unapproved uses of BOTOX. The safety and effectiveness of BOTOX for unapproved uses have not been established.

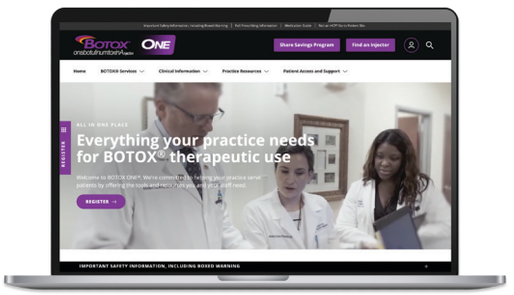
Please see additional Important Safety Information throughout.

Resources available to help clinicians and office staff

Peer-to-peer training

- Both live and virtual training programs are available for BOTOX® injection training
- Anatomical models and injection simulators offer the ability to practice localizing and injecting muscles for Cervical Dystonia treatment

Contact your Account Specialist to learn more about our training offerings



BOTOXOne.com

- Clinical and injection training information, tools, videos, and patient support materials
- Easy access to BOTOX® ordering
- Personalized dashboard
- Comprehensive reimbursement support
- BOTOX® Savings Program patient eligibility and claim status tools

Register at BOTOXOne.com to access these resources and more

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

Hypersensitivity Reactions
Serious and/or immediate hypersensitivity reactions have been reported. These reactions include anaphylaxis, serum sickness, urticaria, soft-tissue edema, and dyspnea. If such a reaction occurs, further injection of BOTOX should be discontinued and appropriate medical therapy immediately instituted. One fatal case of anaphylaxis has been reported in which lidocaine was used as the diluent, and consequently, the causal agent cannot be reliably determined.

Increased Risk of Clinically Significant Effects With Preexisting Neuromuscular Disorders
Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis (ALS), or neuromuscular junction disorders (eg, myasthenia gravis or Lambert-Eaton syndrome) should be monitored when given botulinum toxin. Patients with known or unrecognized neuromuscular disorders or neuromuscular junction disorders may be at increased risk of clinically significant effects, including generalized muscle weakness, diplopia, ptosis, dysphonia, dysarthria, severe dysphagia, and respiratory compromise from therapeutic doses of BOTOX (see *Warnings and Precautions*).

Dysphagia and Breathing Difficulties
Treatment with BOTOX and other botulinum toxin products can result in swallowing or breathing difficulties. Patients with preexisting swallowing or breathing difficulties may be more susceptible to these complications. In most cases, this is a consequence of weakening of muscles in the area of injection that are involved in breathing or oropharyngeal muscles that control swallowing or breathing (see *Boxed Warning*).

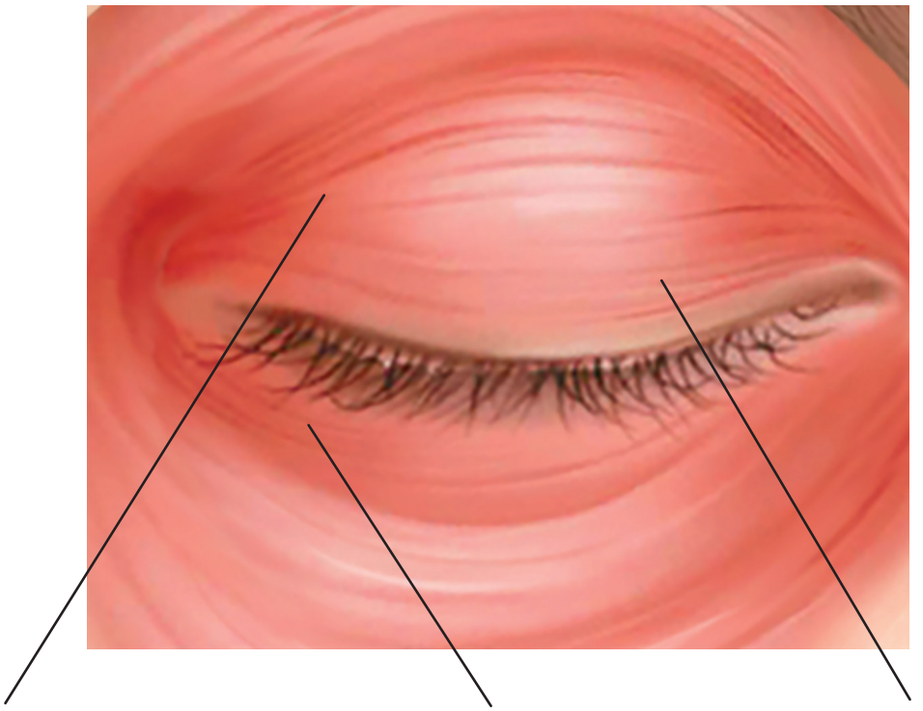
Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Understanding BOTOX® treatment for Blepharospasm

A proven first-line option for treating Blepharospasm since 1989

Approved injection sites/dosing[16]



Lateral pretarsal orbicularis oculi (upper lid)
1.25 Units to 2.5 Units

Lateral pretarsal orbicularis oculi (lower lid)
1.25 Units to 2.5 Units

Medial pretarsal orbicularis oculi (upper lid)
1.25 Units to 2.5 Units

Note: These are general areas, not the specific injection sites.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

Corneal Exposure and Ulceration in Patients Treated With BOTOX for Blepharospasm
Reduced blinking from BOTOX injection of the orbicularis muscle can lead to corneal exposure, persistent epithelial defect, and corneal ulceration, especially in patients with VII nerve disorders.

Retrobulbar Hemorrhages in Patients Treated With BOTOX for Strabismus
During the administration of BOTOX for the treatment of strabismus, retrobulbar hemorrhages sufficient to compromise retinal circulation have occurred. It is recommended that appropriate instruments to decompress the orbit be accessible.

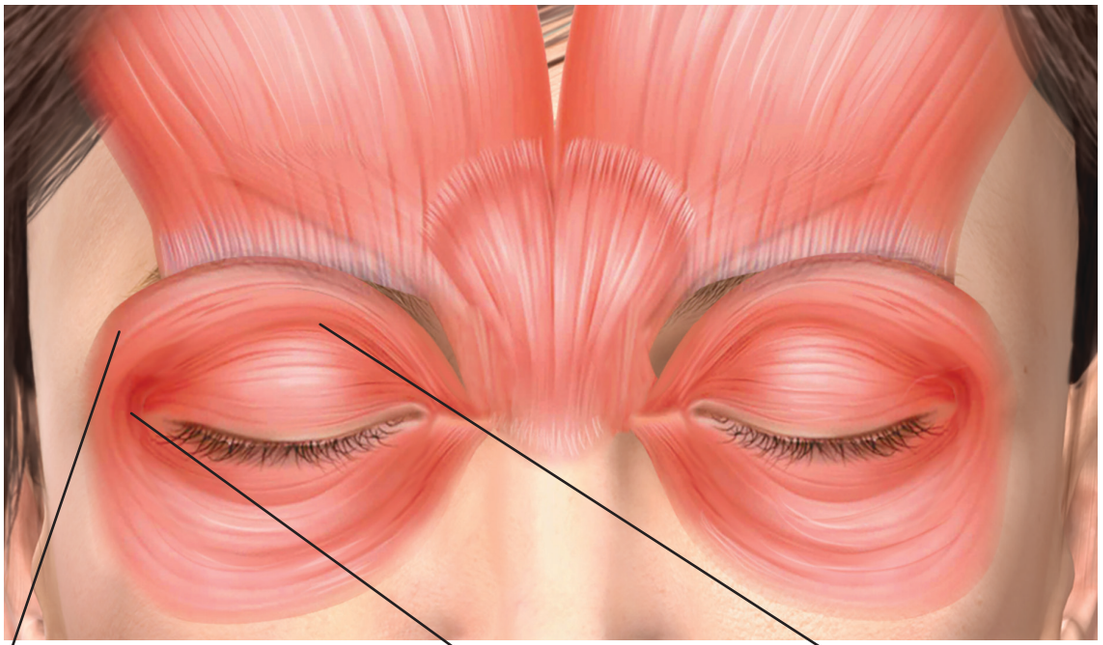
Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Orbicularis oculi

Muscle action

Closes eyelids; palpebral part closes lids gently; orbital part closes lids tightly[25]



Insertion

Orbital part: Skin and subcutaneous tissue of the eyebrow, adjacent muscles (levator labii superioris alaeque nasi, levator labii superioris, and zygomaticus minor), and the temporal extension of the epicranial aponeurosis

Palpebral part: Lateral palpebral raphe

Lacrimal part: Fascia of the nasolacrimal sac, tarsi of the eyelids, and the lateral palpebral raphe

Localization

Follow the circumference of the orbit as the muscle spreads into the adjacent regions of the eyelids, anterior temporal region, infraorbital cheek, and superciliary region

Origin

Orbital part: Nasal component of the frontal bone, the frontal process of the maxilla, and from the medial palpebral ligament

Palpebral part: Medial palpebral ligament

Lacrimal part: Upper part of the lacrimal bone

BOTOX®
onabotulinumtoxinA injection

Blepharospasm dosing guidelines

- The initial recommended dose is 1.25 Units to 2.5 Units (0.05 mL to 0.1 mL volume at each site). The recommended dilution to achieve 1.25 Units is 100 Units/8 mL; for 2.5 Units it is 100 Units/4 mL[16]
- The cumulative dose of BOTOX® treatment for Blepharospasm in a 30-day period should not exceed 200 Units[16]
- Reconstituted BOTOX® is injected using a sterile, 27- to 30-gauge needle without electromyographic guidance[16]
- Avoiding injection near the levator palpebrae superioris may reduce the complication of ptosis[16]
- Avoiding medial lower lid injections may reduce the complication of diplopia. Ecchymosis can be prevented by applying pressure at the injection site immediately after injection[16]
- Initial effect of the injections is generally seen within 3 days and reaches a peak 1 to 2 weeks posttreatment. Each treatment lasts approximately 3 months, following which the procedure can be repeated[16]
- At repeat treatment sessions, the dose may be increased up to two-fold if the response from the initial treatment is considered insufficient, usually defined as an effect that does not last longer than 2 months. However, there appears to be little benefit obtainable from injecting more than 5 Units per site. Some tolerance may be found when BOTOX® is used in treating Blepharospasm if treatments are given any more frequently than every 3 months, and it is rare to have the effect be permanent[16]

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS
Adverse reactions to BOTOX for injection are discussed in greater detail in the following sections: *Boxed Warning*, *Contraindications*, and *Warnings and Precautions*.

Cervical Dystonia
The most frequently reported adverse reactions following injection of BOTOX for cervical dystonia include dysphagia (19%), upper respiratory infection (12%), neck pain (11%), and headache (11%).

Please see additional Important Safety Information throughout.

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IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)

Blepharospasm

The most frequently reported adverse reactions following injection of BOTOX for blepharospasm include ptosis (21%), superficial punctate keratitis (6%), and eye dryness (6%).

Strabismus

The most frequently reported adverse events following injection of BOTOX for strabismus include ptosis (1% after inferior rectus injections, 16% after horizontal rectus injections, and 38% after superior rectus injections) and vertical deviation (17%).

Postmarketing Experience

Adverse reactions that have been identified during postapproval use of BOTOX are discussed in greater detail in *Postmarketing Experience* (Section 6.3 of the Prescribing Information).

There have been spontaneous reports of death, sometimes associated with dysphagia, pneumonia, and/or other significant debility or anaphylaxis, after treatment with botulinum toxin. There have also been reports of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. Some of these patients had risk factors, including cardiovascular disease. The exact relationship of these events to the botulinum toxin injection has not been established.

DRUG INTERACTIONS

Co-administration of BOTOX and other agents interfering with neuromuscular transmission (eg, aminoglycosides, curare-like compounds) should only be performed with caution as the effect of the toxin may be potentiated. Use of anticholinergic drugs after administration of BOTOX may potentiate systemic anticholinergic effects. The effect of administering different botulinum neurotoxin products at the same time or within several months of each other is unknown. 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. Excessive weakness may also be exaggerated by administration of a muscle relaxant before or after administration of BOTOX.

Please see full Prescribing Information, including Boxed Warning and Medication Guide, or visit https://www.rxabbvie.com/pdf/botox_pi.pdf

Helpful phone numbers and websites

ORDERING

AllerganDirect.com or call 1-800-44-BOTOX (1-800-442-6869)

CUSTOMER SERVICE

1-800-44-BOTOX (1-800-442-6869)

MEDICAL INFORMATION LINE

1-800-678-1605

PATIENT SAVINGS PROGRAM

For commercially insured patients: BOTOXSavingsProgram.com

PROFESSIONAL EDUCATION AND RESOURCES

For injection training opportunities: Contact your Account Specialist

For injection and reconstitution videos, plus downloadable patient education and more: BOTOXOne.com

Please see Important Safety Information, including Boxed Warning, inside.
Please see full Prescribing Information, including Boxed Warning and Medication Guide, or visit https://www.rxabbvie.com/pdf/botox_pi.pdf

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