Injection Workbook for **Movement Disorders**

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

Treatment Considerations for Blepharospasm

Indications

Cervical Dystonia

BOTOX® 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

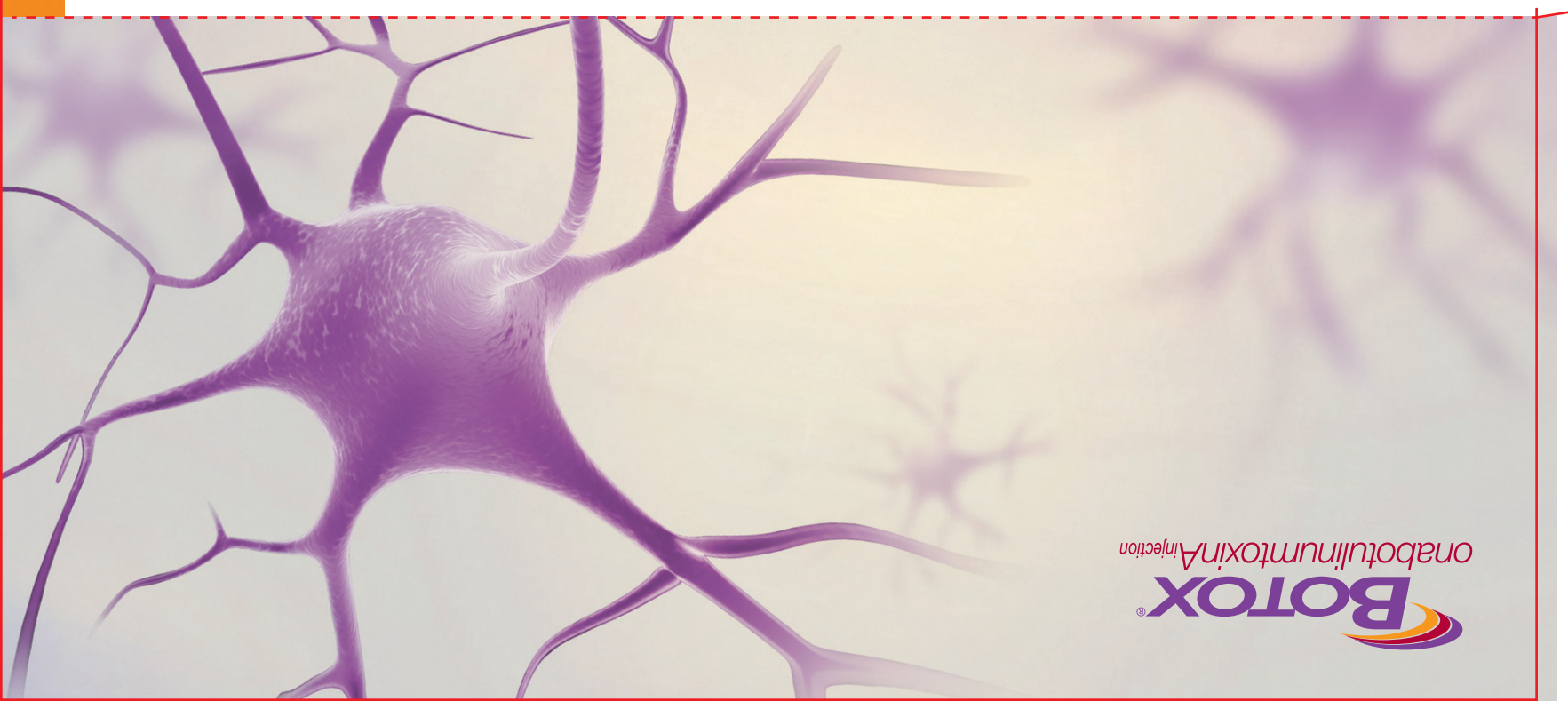
BOTOX® is indicated for the treatment of Strabismus and Blepharospasm associated with dystonia, including benign essential blepharospasm or VII nerve disorders in patients 12 years of age and older.

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 in approved indications, cases of spread of effect have been reported at doses comparable to those used to treat Cervical Dystonia and spasticity and at lower doses.

Please see additional Indications and Important Safety Information about BOTOX® inside.



BOTOX® onabotulinumtoxinA injection

Introduction

This workbook is designed to help advance your skill set for identifying Cervical Dystonia (CD) and Blepharospasm patients and implementing BOTOX® treatment. What you will learn today can have a tremendous impact on the patients you treat. Refer to this workbook often and use it as a resource for your practice.

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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.

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 about BOTOX® on following pages.

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 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

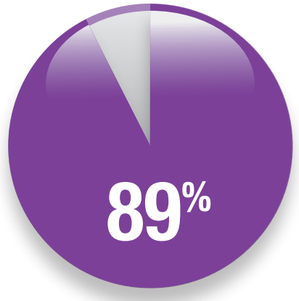
Time from Cervical Dystonia onset to diagnosis (mean)[3]

1.2 years

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

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)

Consider symptoms beyond neck pain and tremor

- Sensory tricks[6,7]
- Morning benefit (symptoms are milder in the morning)[6]
- Tenderness on palpation[6]
- Exacerbating factors—may be frequent and prominent[6]
  - 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 pre-existing 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 about BOTOX® on following pages.

BOTOX® onabotulinumtoxinA injection

Use screening techniques to help identify Cervical Dystonia

Ask the patient if they've been experiencing neck pain[6]

Look for patient's use of sensory tricks, or *gestes antagonistes*[6]

Distinguish between Cervical Dystonia tremor and other tremors, such as Parkinson disease[2,6]

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[6]

Observe head position during patient's gait[6]

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 about BOTOX® on following pages.

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[8]

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[6]

Does the patient have…

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

- ☐ Sensory tricks
- ☐ Morning benefit
- ☐ Neck pain
- ☐ Common exacerbating factors
  - – Fatigue; stress; motor tasks such as driving, walking, or writing
- ☐ 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[6]

1. Etiology:

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

2. Rule out nondystonic causes such as:

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

3. Rule out other hyperkinetic movement disorders such as:

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

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

Overview of the BOTOX® Treatment Framework

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

Increased Risk of Clinically Significant Effects With Pre-existing 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*).

Please see additional Important Safety Information about BOTOX® on following pages.

Consider bringing the framework into your BOTOX® treatment strategy

The right goals

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

- **Common goals** of BOTOX® treatment are often to **improve the severity of head deviation and reduce neck pain** associated with Cervical Dystonia
- When using BOTOX®, it's important to **set expectations** to help ensure the patient **follows the treatment plan**

The right muscles/dose

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

- **Identify muscles** contributing to the posture(s) and symptoms
- Select the right muscles and adequate dose to **get a response that the patient will notice**
  - Determine which posture(s) or symptom(s) (eg, neck pain) to initially target

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The right plan

Establish a plan to re-evaluate the performance of BOTOX® over initial and subsequent treatment sessions

- **Every patient is different** and will respond to treatment differently
- Goals as well as muscles/dose selection **should be evaluated at each treatment,** since the patient's condition may change over time
- Based on patient treatment goals and response to previous treatment, an **adjustment in BOTOX® dose or injected muscles may be needed**

Discuss specific and realistic goals with each patient

Goal-setting considerations:

- Common goals often include improving the severity of head deviation and reducing neck pain associated with Cervical Dystonia
- Effect of condition on patient (eg, discomfort while driving) and exacerbating factors
- Patient's response to treatment
- Time frame within which the patient hopes to achieve his/her goals
- Goals should be agreed upon by you and the patient

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 pre-existing 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*).

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.

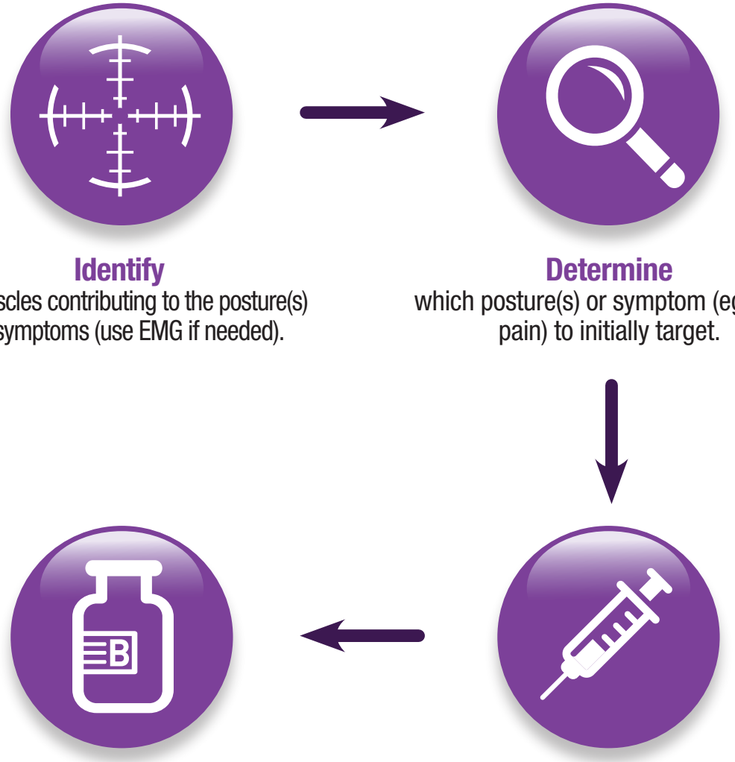
Retrobulbar Hemorrhages in Patients Treated With BOTOX® for Strabismus
During the administration of BOTOX® for the treatment of Strabismus, retrobulbar hemorrhages sufficient to compromise retinal circulation have occurred. It is recommended that appropriate instruments to decompress the orbit be accessible.

Please see additional Important Safety Information about BOTOX® on following pages.

Manage patient expectations for BOTOX® treatment

- BOTOX® is **not a cure;** it helps reduce the severity of abnormal head position and neck pain associated with Cervical Dystonia
- **Fine needles** are used during injections
- **Subsequent injection** sessions may be needed
- Patient should **return for a 2- to 6-week follow-up evaluation**
- Review insurance plans to **determine out-of-pocket costs**
  - Patients may be able to **save on treatment costs** (see page 76)

Steps to use when targeting muscles for injection



Identify
the muscles contributing to the posture(s) and symptoms (use EMG if needed).

Determine
which posture(s) or symptom (eg, neck pain) to initially target.

Plan
adjustments of muscles/dose in subsequent treatments.

Select
the right muscles and adequate dose for a proper initial response.

A low starting dose across multiple muscles may not elicit a response after the initial injection. Select a starting dose within the approved dose range

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[9]
- 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[9]
- In treating adult patients for 1 or more indications, the maximum cumulative dose should not exceed 400 Units in a 3-month interval[9]
- 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[9]
- Clinical improvement generally begins within the first 2 weeks after injection, with maximum clinical benefit at approximately 6 weeks post injection. In clinical studies, most subjects were observed to have returned to pretreatment status by 3 months post treatment[9]

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 about BOTOX® on following pages.

Key principles to setting up an effective treatment plan

Every patient is different and will respond to treatment differently

Muscle/dose selection should be evaluated and/or adjusted at each treatment depending on treatment goals and response

Patients may be re-treated at 12 weeks* to optimize BOTOX® dose and muscles

Be sure to discuss goals and reinforce expectations at each patient visit

*Patients should be considered for reinjection when the clinical effect of the previous injection has diminished but no sooner than 12 weeks from the previous injection.

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 about BOTOX® on following pages.

Monitor goals and treatment response across multiple BOTOX® sessions

Treatment-planning considerations

- Each patient will respond to treatment differently
- Re-evaluate goals and muscle/dose selection at each treatment
- Adjustments to dose and muscle selection may be needed

Treatment 1

- Check on goal status and set expectations with the patient
- For the initial injection, determine the right muscles and dose needed for a proper initial response
- For subsequent treatment sessions, determine if adjustments in muscles/dose are needed
- At the end of the treatment session, have the patient schedule a 2- to 6-week follow-up as well as their regular visit for treatment

2- to 6-week follow-up

- Discuss response to treatment and point out improvements (eg, degree of head deviation, neck pain)
- Based on response, discuss re-treatment and plan for potential muscle/dose adjustment for subsequent treatment

Future treatments

- Check on goals and determine if adjustments are needed

Help patients understand that their plan may include multiple BOTOX® treatments

BOTOX®
onabotulinumtoxinA injection

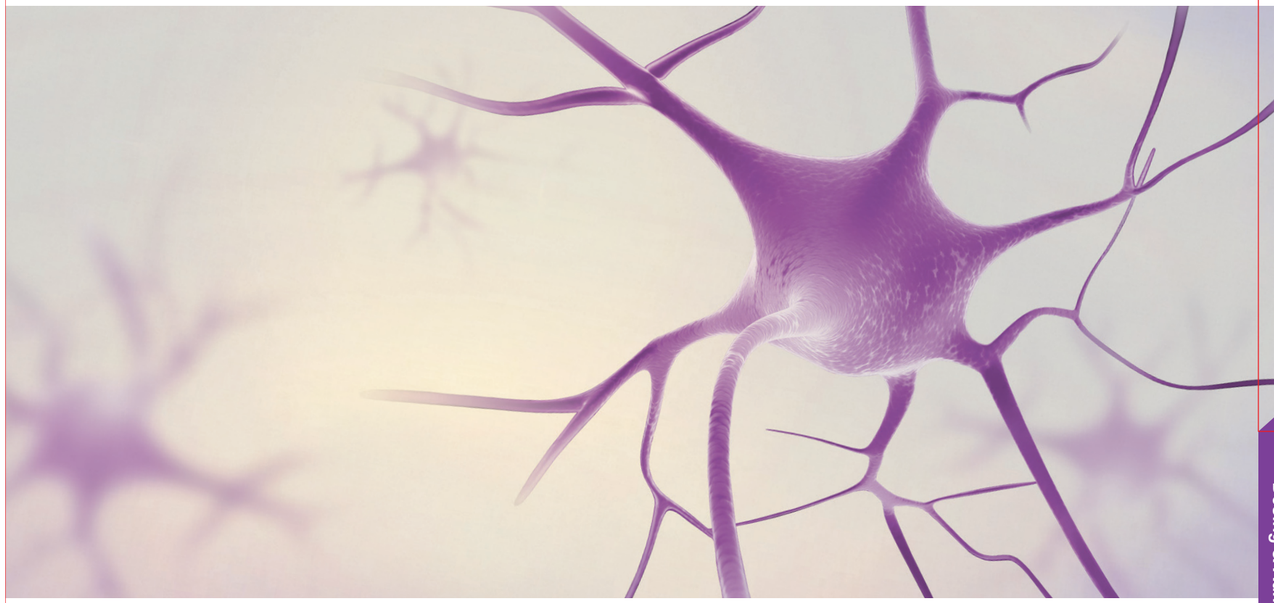
Notes

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 (15.7%) and vertical deviation (16.9%).

Please see additional Important Safety Information about BOTOX® on following pages.



Affected anatomy in Cervical Dystonia

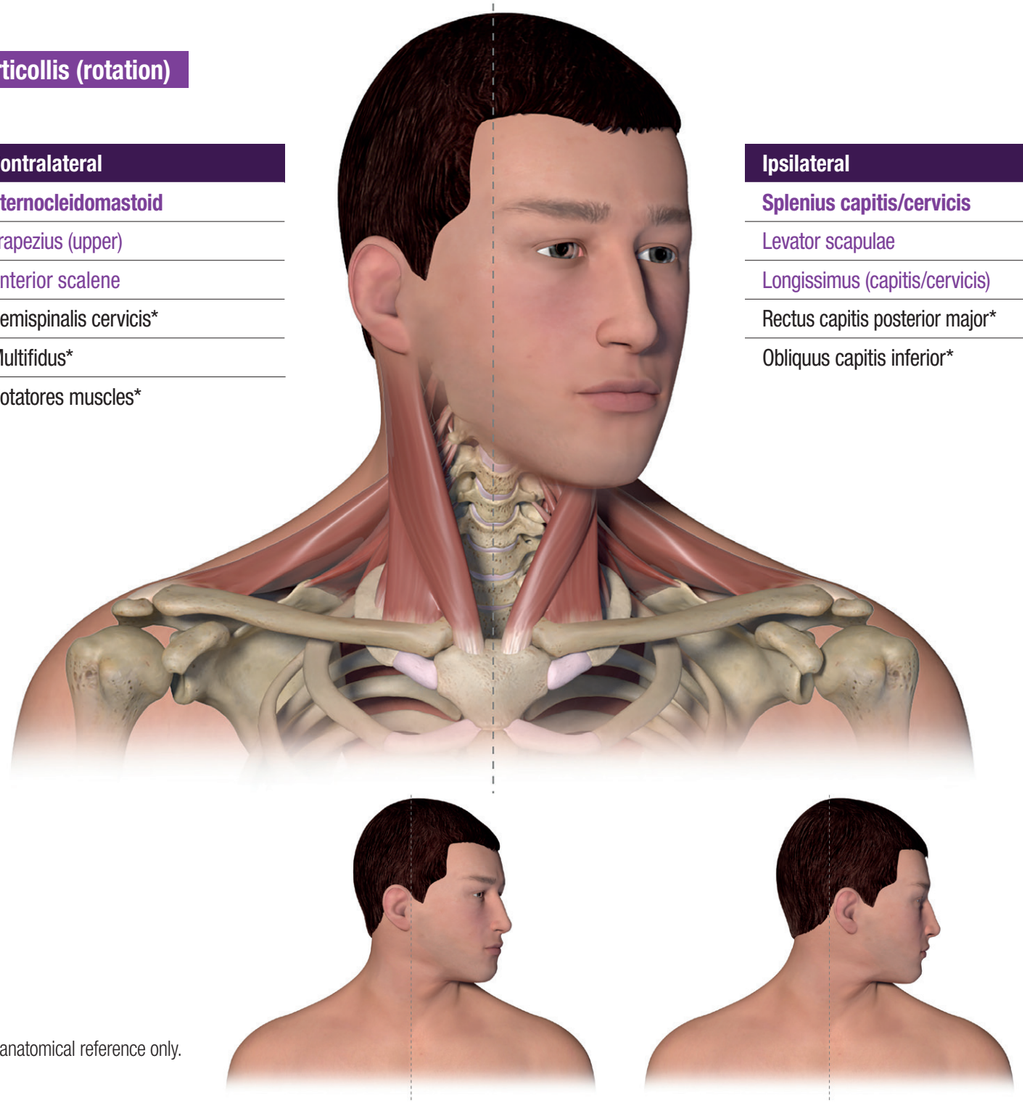
- The affected anatomy content provided in this section was developed in coordination with medical professionals
- It is meant to serve as an educational resource for muscle identification and selection in Cervical Dystonia
- Combination postures shown in this section reflect those commonly seen in clinical 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

Clinical presentation of Cervical Dystonia

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.

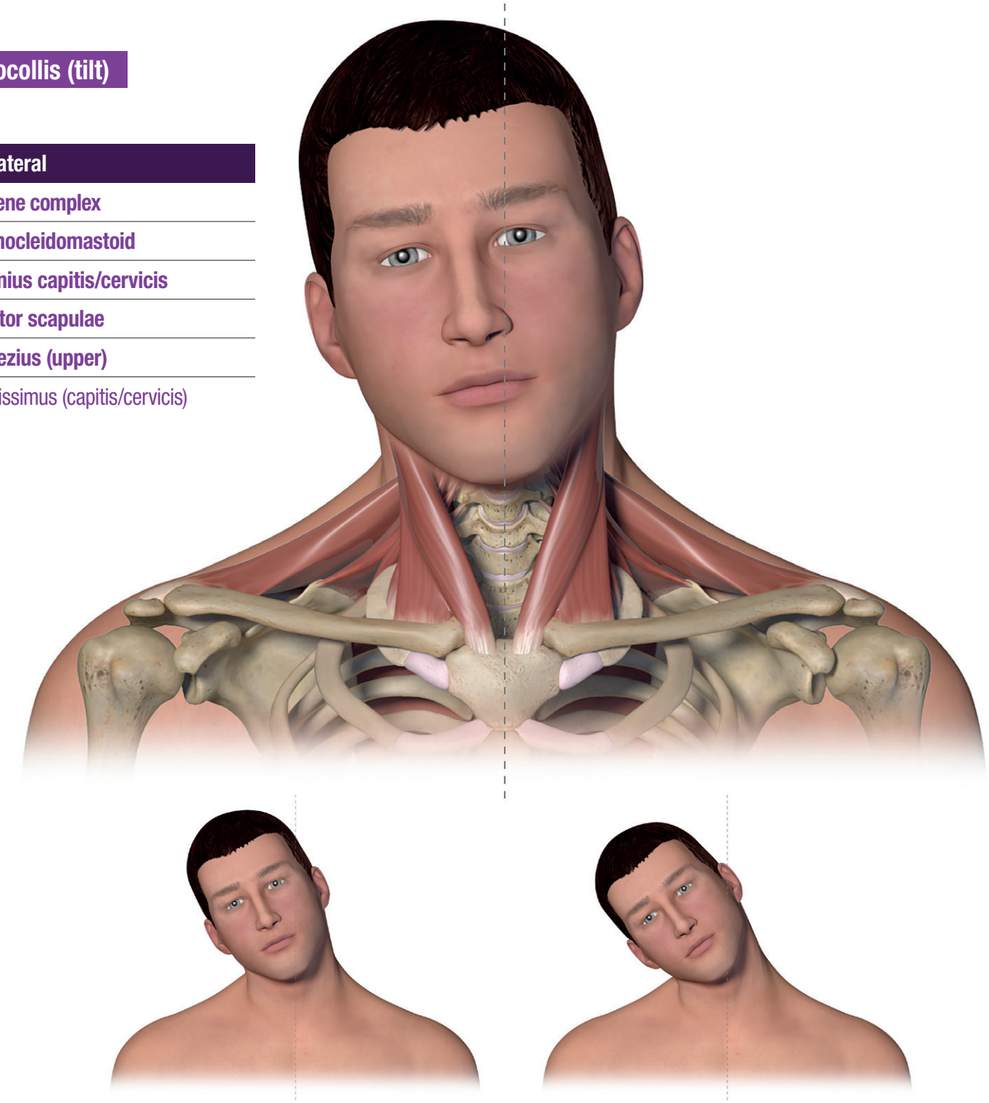
IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Postmarketing Experience
Adverse reactions that have been identified during postapproval use of BOTOX® are discussed in greater detail in Postmarketing Experience (Section 6.3 of the Prescribing Information).

Please see additional Important Safety Information about BOTOX® on following pages.

Clinical presentation of Cervical Dystonia (continued)

Laterocollis (tilt)

Ipsilateral
Scalene complex
Sternocleidomastoid
Splenius capitis/cervicis
Levator scapulae
Trapezius (upper)
Longissimus (capitis/cervicis)

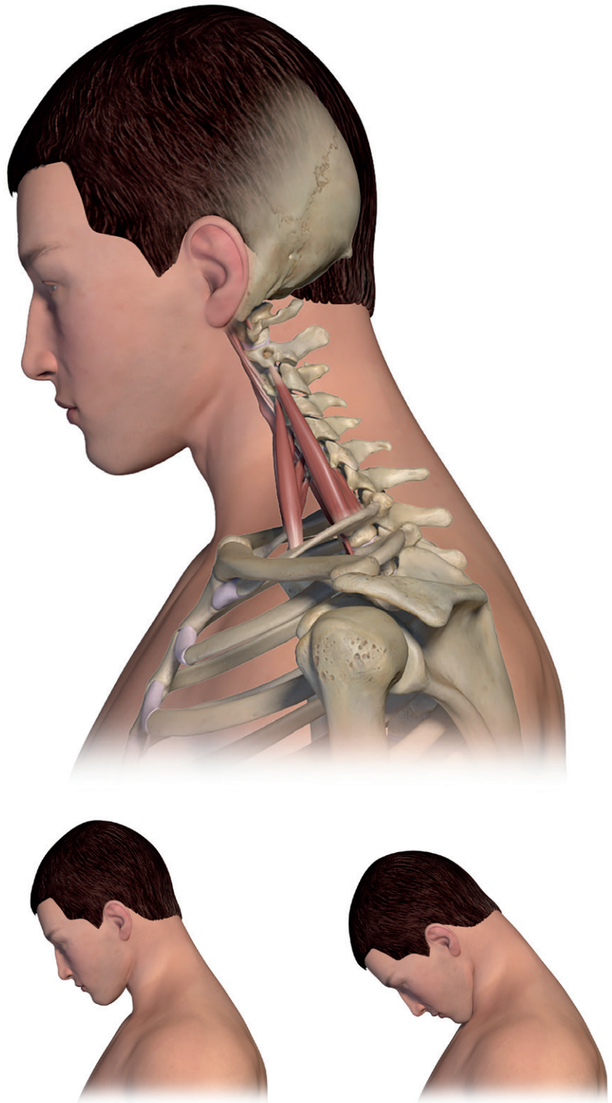


Note presence/absence of shoulder elevation to determine full range of involved muscles

Clinical presentation of Cervical Dystonia (continued)

Anterocollis (flexion)

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

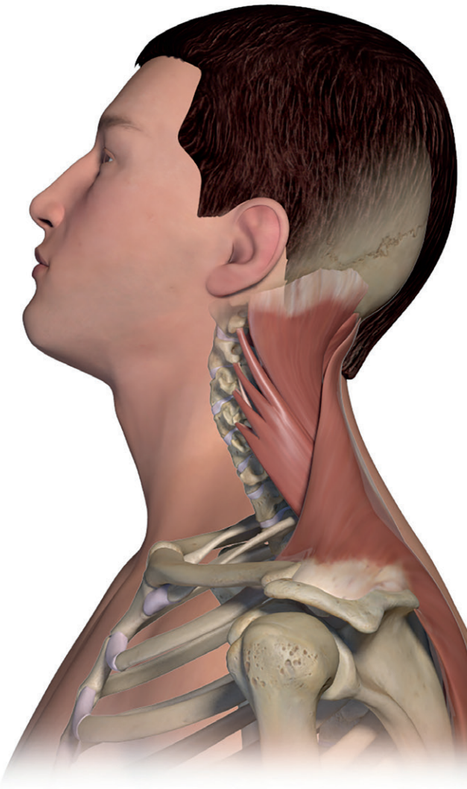


*For anatomical reference only.

Clinical presentation of Cervical Dystonia (continued)

Retrocollis (extension)

Bilateral
Semispinalis capitis
Splenius capitis/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 (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.

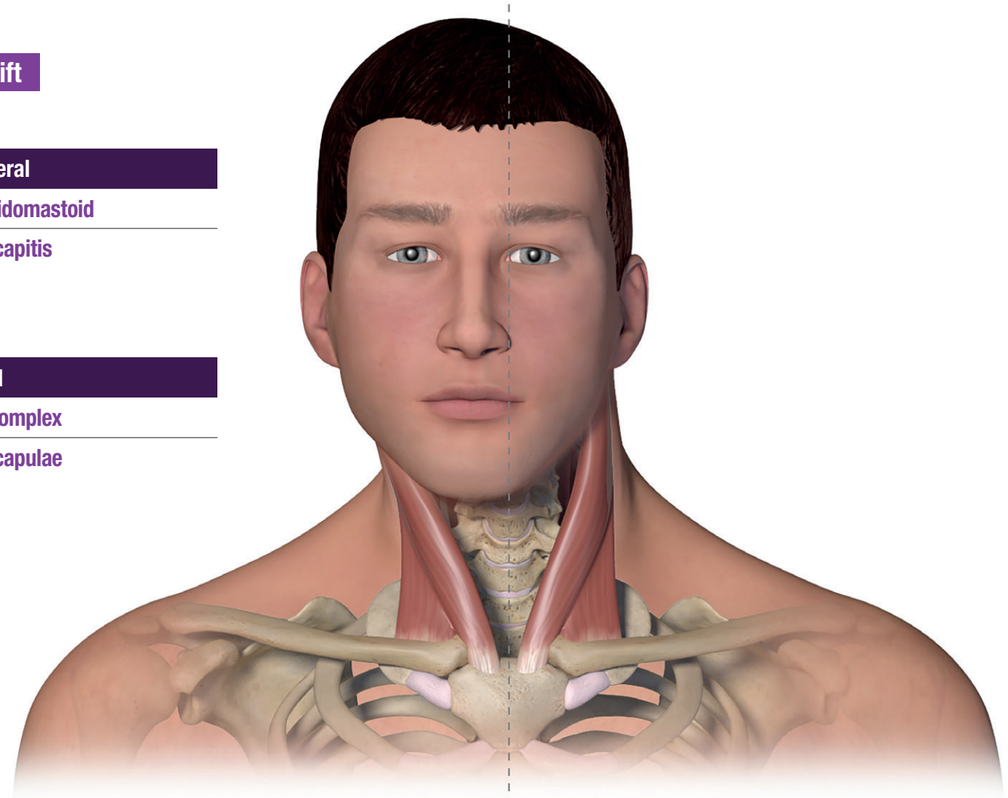
Please see additional Important Safety Information about BOTOX® on following pages.

Clinical presentation of Cervical Dystonia (continued)

Lateral shift

Contralateral
Sternocleidomastoid
Splenius capitis

Ipsilateral
Scalene complex
Levator scapulae



Lateral shift of head.

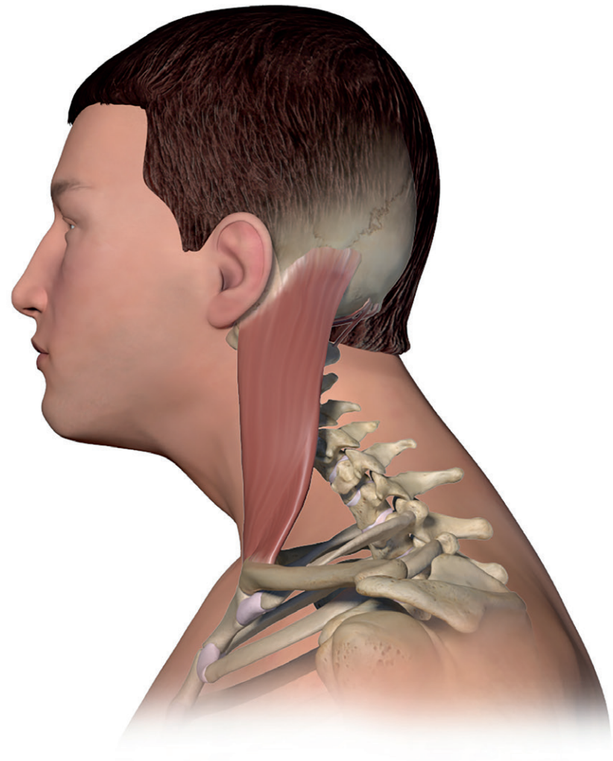
Lateral shift of neck.

Clinical presentation of Cervical Dystonia (continued)

Sagittal shift

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

*For anatomical reference only.



IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS (continued)

Postmarketing Experience (continued)

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 accompanying full Prescribing Information including Boxed Warning and Medication Guide.

Clinical presentation of Cervical Dystonia (continued)

Combination posture: Right torticollis, left laterocollis, shoulder elevation

Contralateral

- Sternocleidomastoid
- Scalene complex

Ipsilateral

- Splenius capitis/cervicis
- Trapezius (upper)
- Levator scapulae

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 about BOTOX® on following pages.

Clinical presentation of Cervical Dystonia (continued)

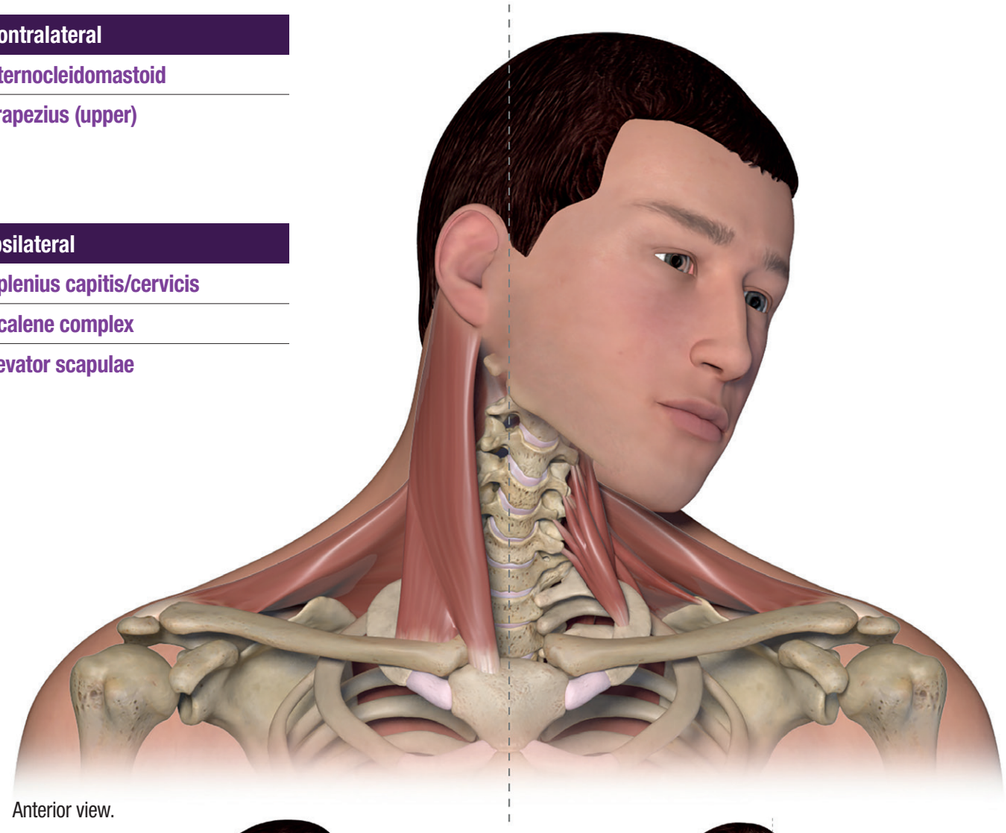
Combination posture: Left torticollis, left laterocollis

Contralateral

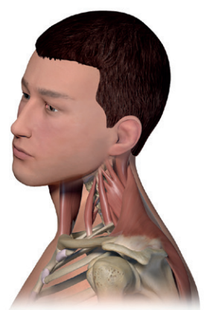
- Sternocleidomastoid
- Trapezius (upper)

Ipsilateral

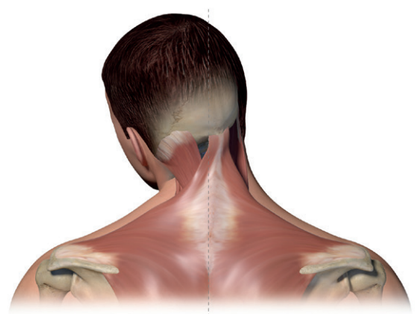
- Splenius capitis/cervicis
- Scalene complex
- Levator scapulae



Anterior view.



Lateral view.



Posterior view.

Clinical presentation of Cervical Dystonia (continued)

Combination posture: Right torticollis, retrocollis

Contralateral

Sternocleidomastoid

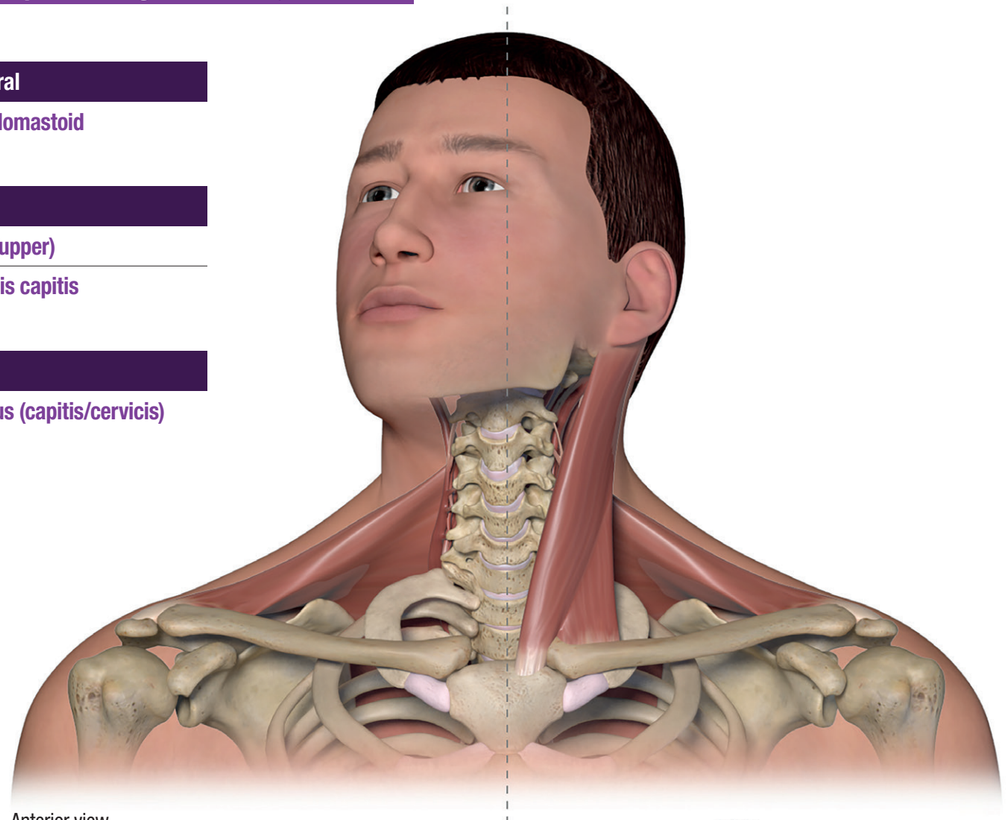
Bilateral

Trapezius (upper)

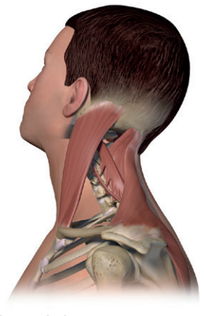
Semispinalis capitis

Pain

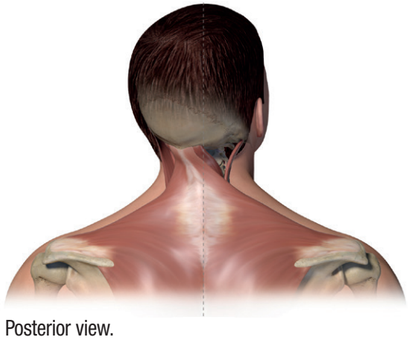
Longissimus (capitis/cervicis)



Anterior view.



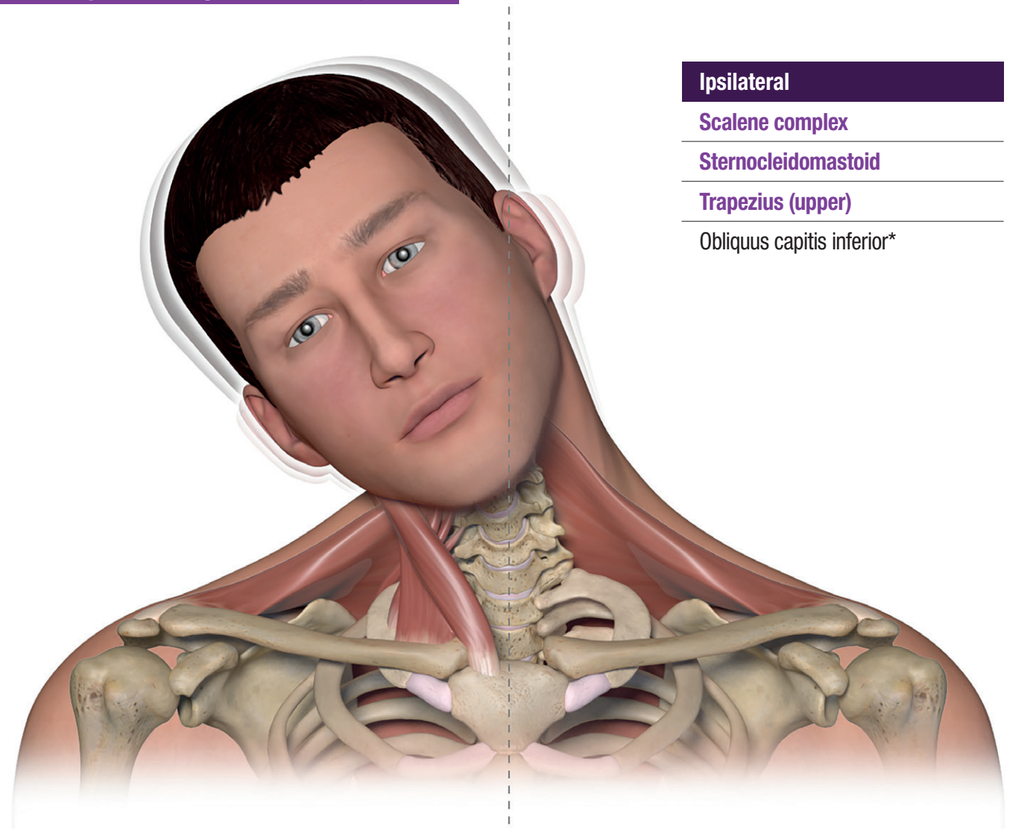
Lateral view.



Posterior view.

Clinical presentation of Cervical Dystonia (continued)

Combination posture: Right laterocollis, tremor



Ipsilateral

Scalene complex

Sternocleidomastoid

Trapezius (upper)

Obliquus capitis inferior*

*For anatomical reference only.

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 about BOTOX® on following pages.

Muscles by posture in Cervical Dystonia

Posture	Muscles		
Single			
Torticollis	**Contralateral**	• Sternocleidomastoid • Anterior scalene • Multifidus*	• Trapezius (upper) • Semispinalis cervicis* • Rotatores muscles*
	Ipsilateral	• Splenius capitis/cervicis • Longissimus (capitis/cervicis) • Obliquus capitis inferior*	• Levator scapulae • Rectus capitis posterior major*
Laterocollis	**Ipsilateral**	• Scalene complex • Splenius capitis/cervicis • Trapezius (upper)	• Sternocleidomastoid • Levator scapulae • Longissimus (capitis/cervicis)
Anterocollis	**Bilateral**	• Anterior/middle scalenes • Rectus capitis anterior*	• Longus capitis/colli*
Retrocollis	**Bilateral**	• Semispinalis capitis • Longissimus (capitis/cervicis) • Trapezius (upper) • Rectus capitis posterior major/minor*	• Splenius capitis/cervicis • Levator scapulae • Semispinalis cervicis* • Obliquus capitis superior*
Lateral shift	**Contralateral**	• Sternocleidomastoid	• Splenius capitis
	Ipsilateral	• Scalene complex	• Levator scapulae
Sagittal shift	**Bilateral**	• Sternocleidomastoid • Obliquus capitis superior*	• Rectus capitis posterior major/minor*
Combination			
Right torticollis, left laterocollis, shoulder elevation	**Contralateral**	• Sternocleidomastoid	• Scalene complex
	Ipsilateral	• Splenius capitis/cervicis • Levator scapulae	• Trapezius (upper)
Left torticollis, left laterocollis	**Contralateral**	• Sternocleidomastoid	• Trapezius (upper)
	Ipsilateral	• Splenius capitis/cervicis • Levator scapulae	• Scalene complex
Right torticollis, retrocollis	**Contralateral**	• Sternocleidomastoid	
	Bilateral	• Trapezius (upper)	• Semispinalis capitis
	Pain	• Longissimus (capitis/cervicis)	
Right laterocollis, tremor	**Ipsilateral**	• Scalene complex • Sternocleidomastoid	• Trapezius (upper) • Obliquus capitis inferior*

*For anatomical reference only.

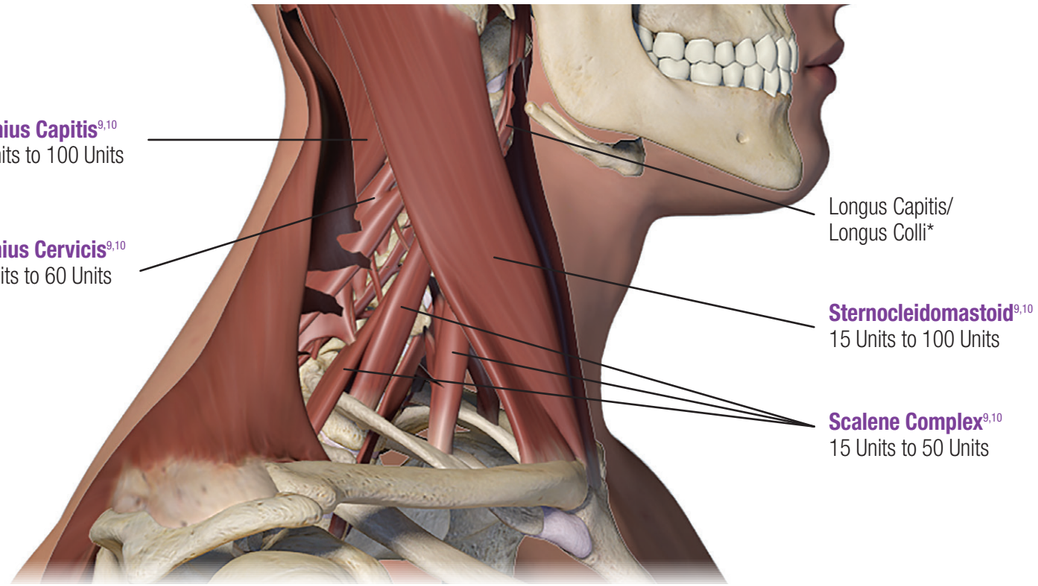
Notes

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 about BOTOX® on following pages.

Main muscles involved in Cervical Dystonia

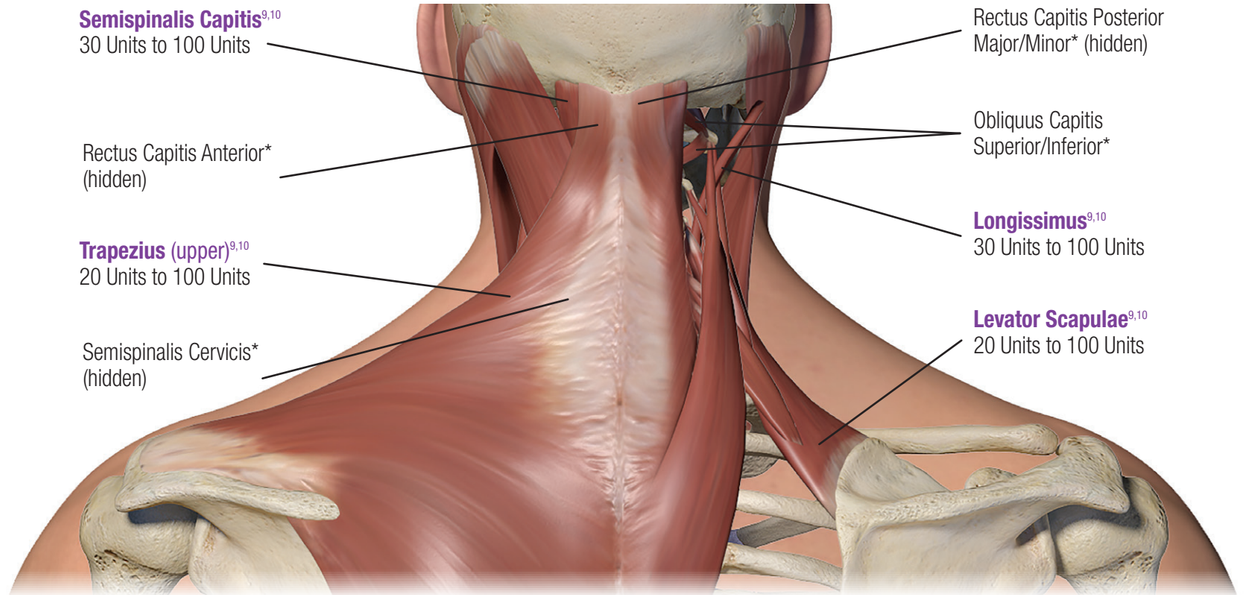
Muscles listed in purple are those approved for BOTOX® injection[9]



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

Main muscles involved in Cervical Dystonia (continued)

Muscles listed in purple are those approved for BOTOX® injection[9]



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

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 pre-existing 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.

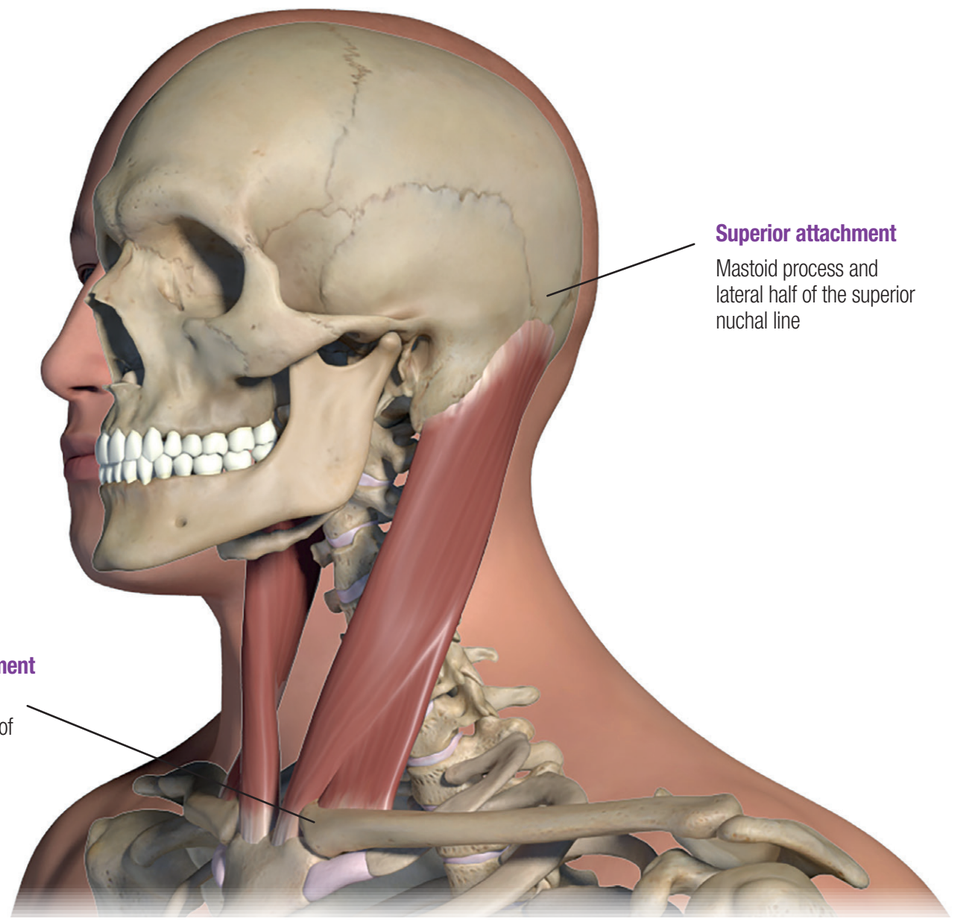
Please see additional Important Safety Information about BOTOX® on following pages.

Sternocleidomastoid

▶ **BOTOX® dose: 15 Units to 100 Units**

Muscle action[11]

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



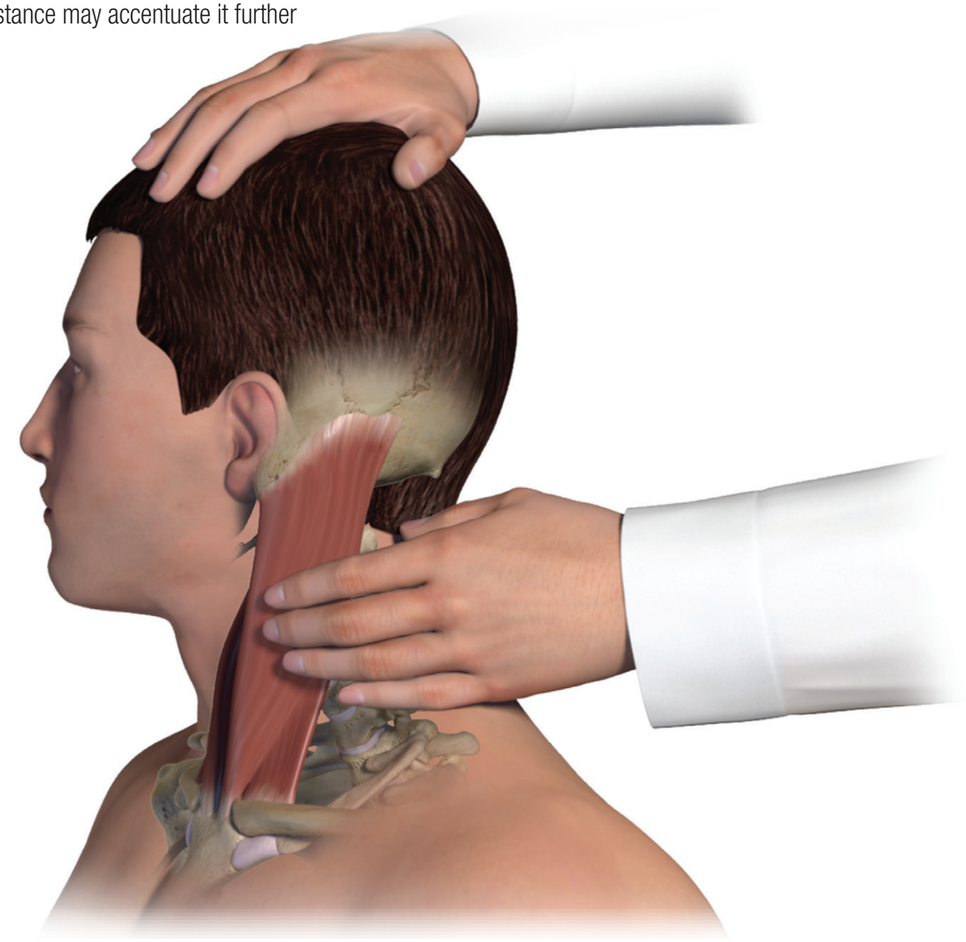
Involved postures[12]

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

Sternocleidomastoid (continued)

Localization[12]

Readily localized with contralateral rotation of the head (may be hypertrophied in contralateral torticollis); providing resistance may accentuate it further

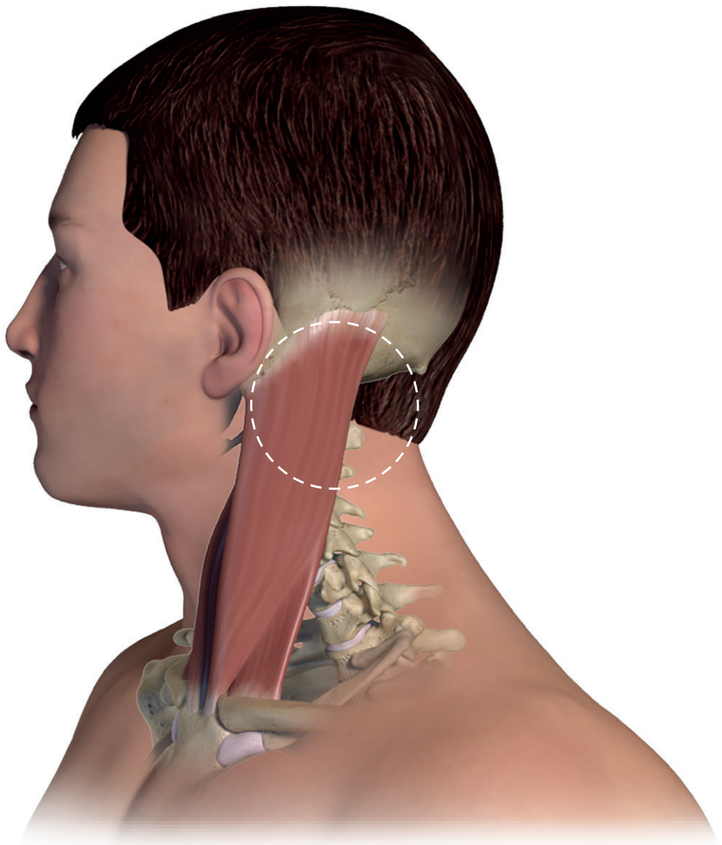


IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Hypersensitivity Reactions
Serious and/or immediate hypersensitivity reactions have been reported. These reactions include anaphylaxis, serum sickness, urticaria, soft-tissue edema, and dyspnea. If such a reaction occurs, further 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 about BOTOX® on following pages.

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

Notes

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Increased Risk of Clinically Significant Effects With Pre-existing 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*).

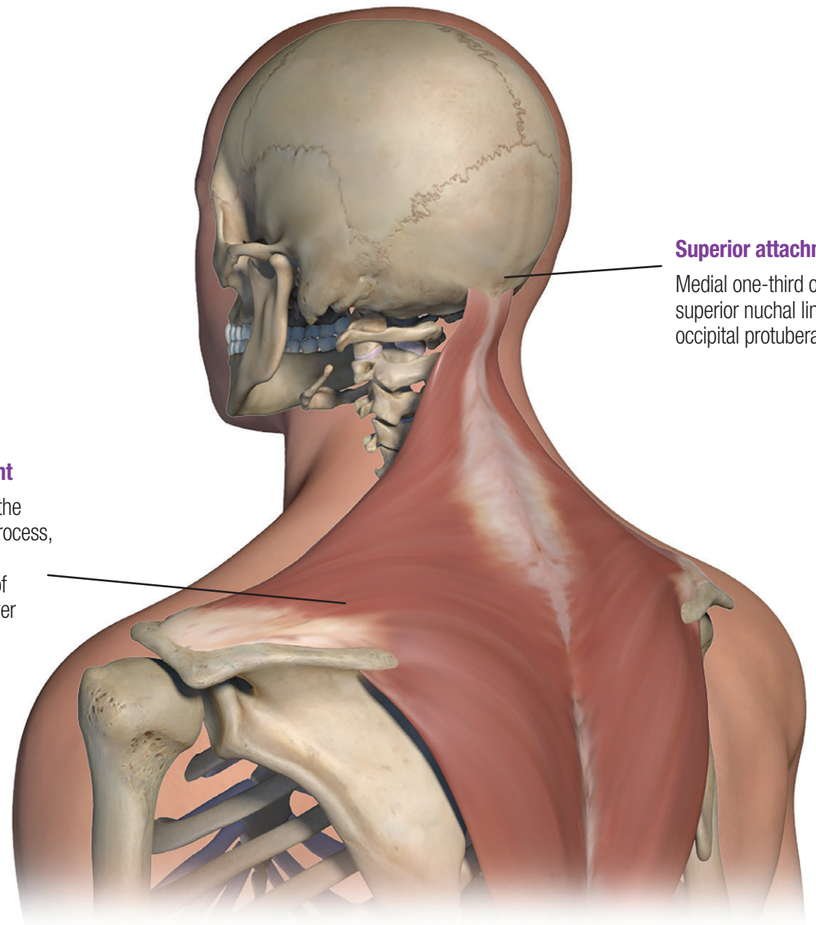
Please see additional Important Safety Information about BOTOX® on following pages.

Trapezius (upper)

▶ **BOTOX® dose: 20 Units to 100 Units**

Muscle action[11,12]

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 occipital protuberance

Inferior attachment

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

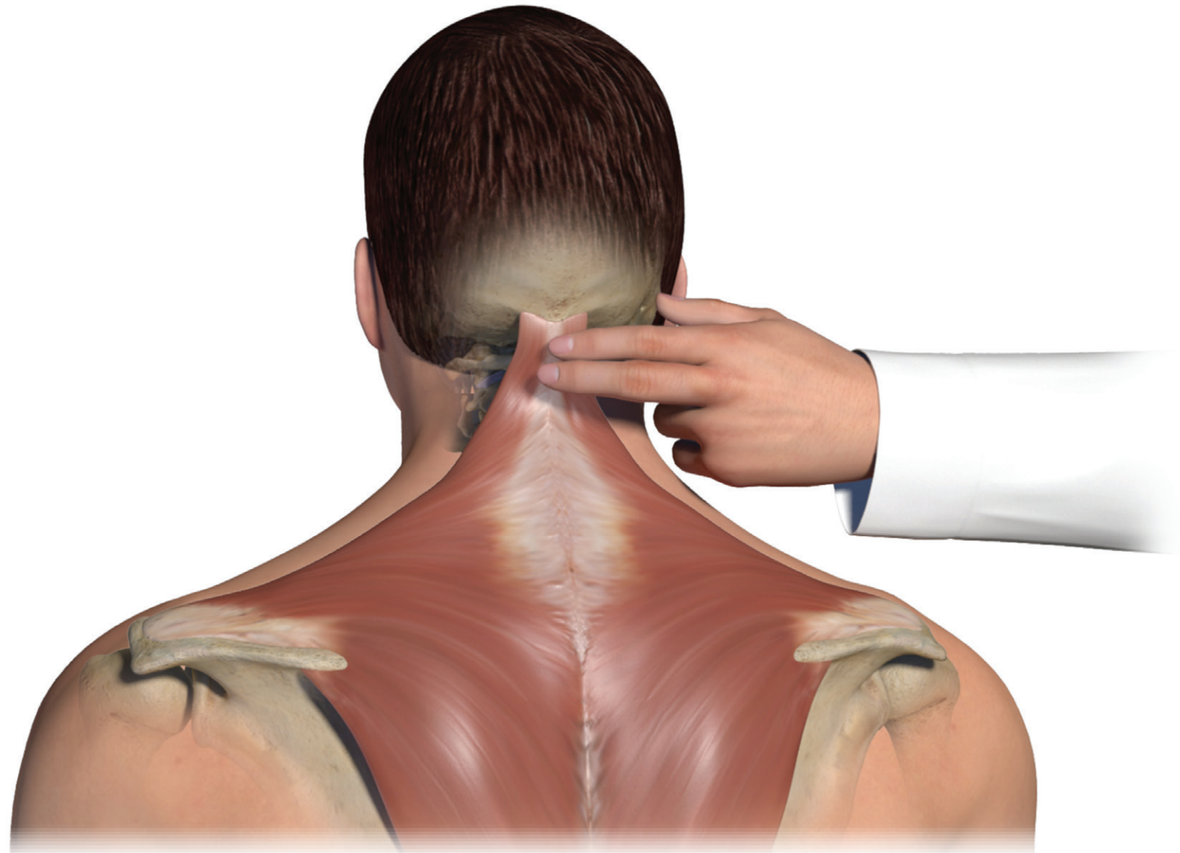
Involved postures[12]

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

Trapezius (upper) (continued)

Localization[12]

Two fingerbreadths below the nuchal line at a depth of 1 cm. However, fibers come together superior to C6



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

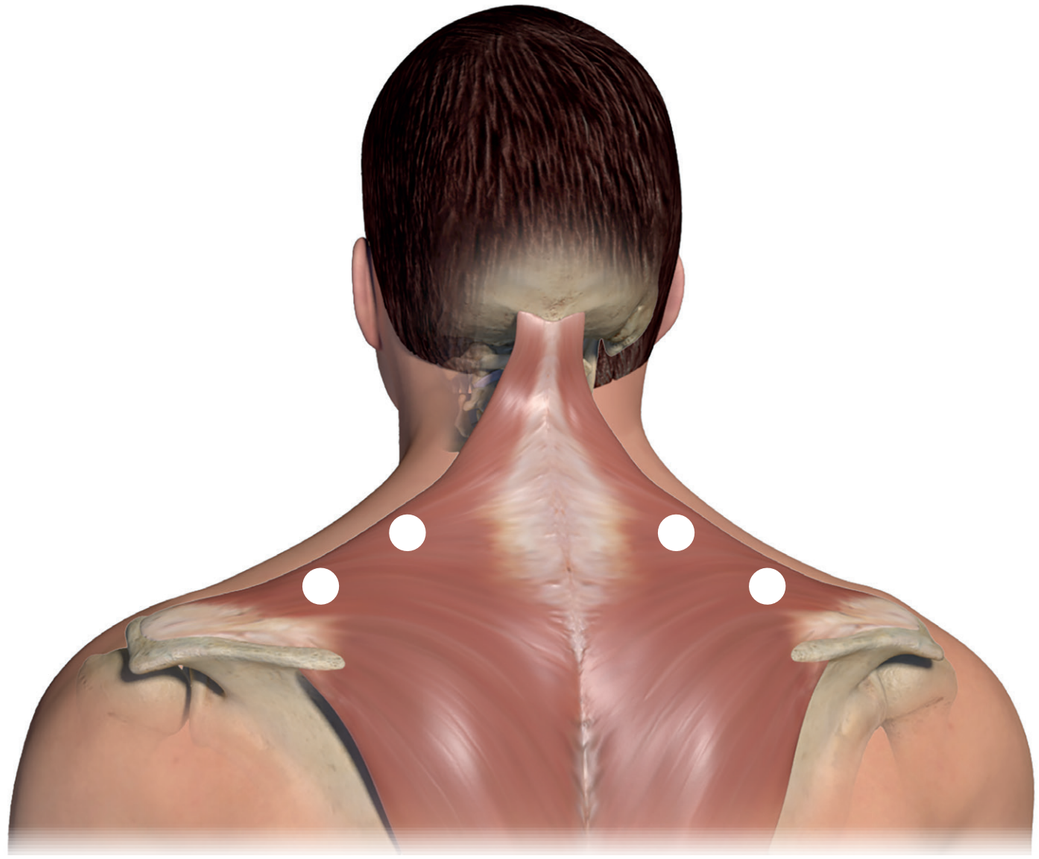
Dysphagia and Breathing Difficulties

Treatment with BOTOX® and other botulinum toxin products can result in swallowing or breathing difficulties. Patients with pre-existing 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 about BOTOX® on following pages.

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
- Consider positioning needle perpendicular to muscle when injecting
- Avoid injecting too deep as this is a very superficial muscle

Notes

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.

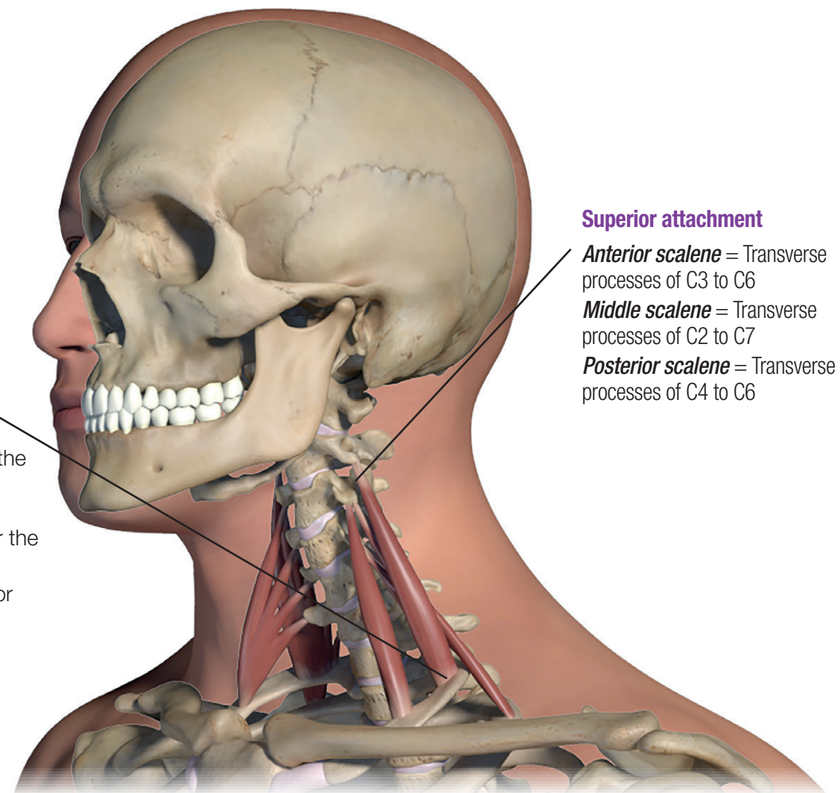
Please see additional Important Safety Information about BOTOX® on following pages.

Scalene complex

▶ **BOTOX® dose:** 15 Units to 50 Units

Muscle action[11,12]

***Anterior scalene* =** Unilaterally bends the neck to the same 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



Superior attachment

Anterior scalene = Transverse processes of C3 to C6
Middle scalene = Transverse processes of C2 to C7
Posterior scalene = Transverse processes of C4 to C6

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

Involved postures[12]

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

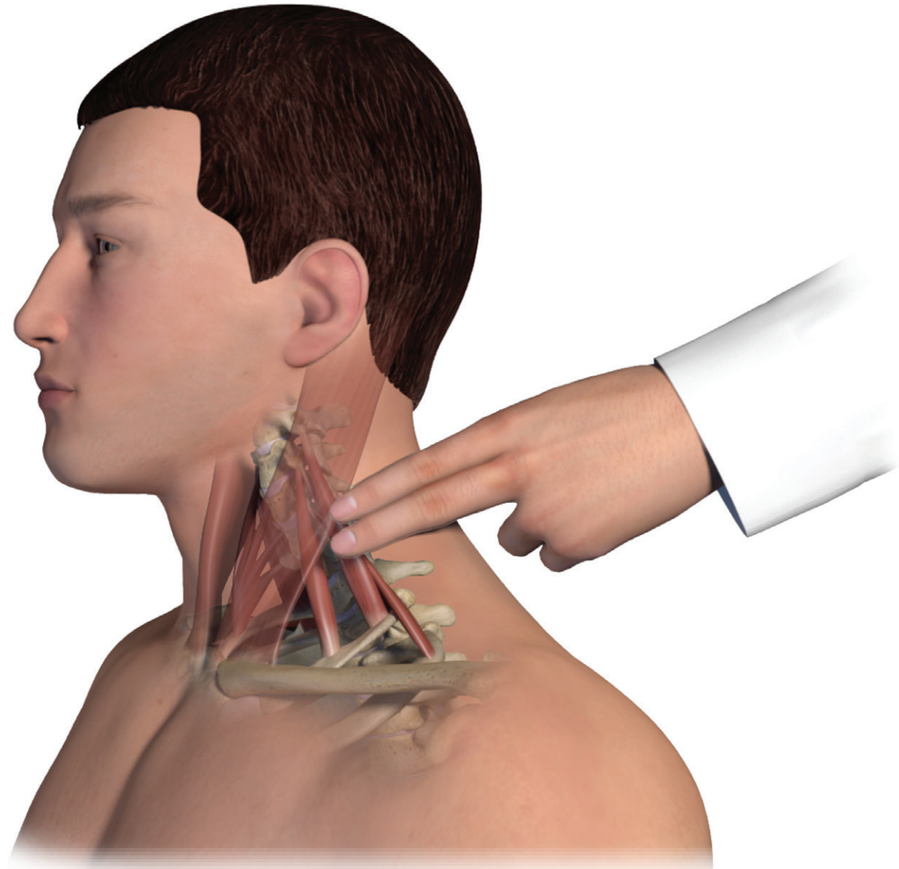
Middle scalene:
- Laterocollis
- Anterocollis
- Lateral shift
- Right torticollis, left laterocollis, shoulder elevation
- Left torticollis, left laterocollis
- Right laterocollis, tremor

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

Scalene complex (continued)

Localization [12]

Two fingerbreadths anterior to the edge of the trapezius. Staying approximately 2 fingerbreadths above the clavicle may lessen the odds of hitting the brachial plexus

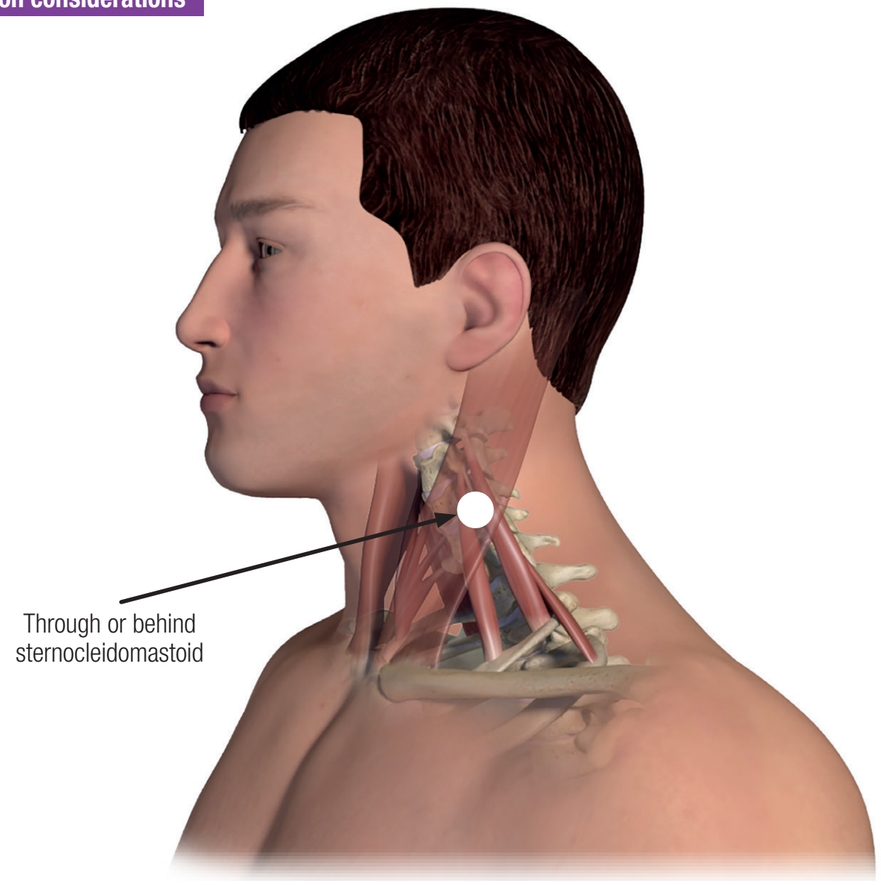


IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Retrobulbar Hemorrhages in Patients Treated With BOTOX® for Strabismus
During the administration of BOTOX® for the treatment of Strabismus, retrobulbar hemorrhages sufficient to compromise retinal circulation have occurred. It is recommended that appropriate instruments to decompress the orbit be accessible.

Please see additional Important Safety Information about BOTOX® on following pages.

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)
- Consider a starting dose at the lower end of the approved range and titrate in 5-Unit increments

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.

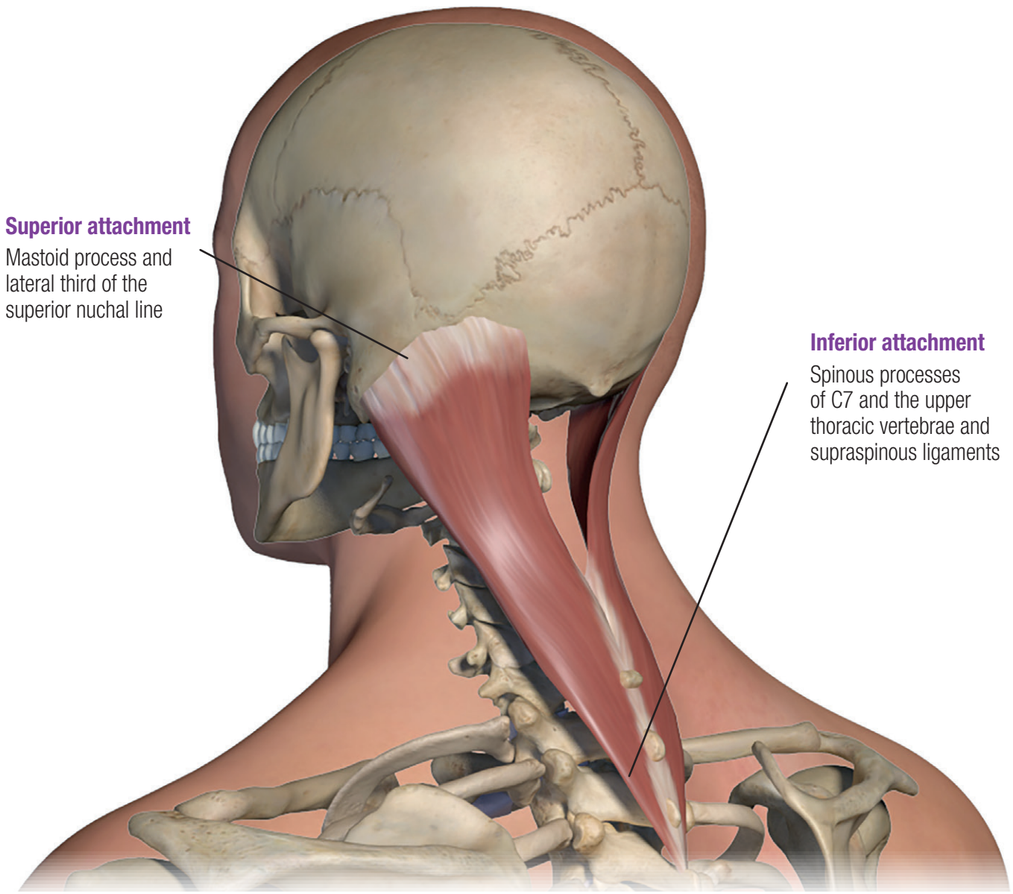
Please see additional Important Safety Information about BOTOX® on following pages.

Splenius capitis

▶ **BOTOX® dose:** 15 Units to 100 Units

Muscle action[11]

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



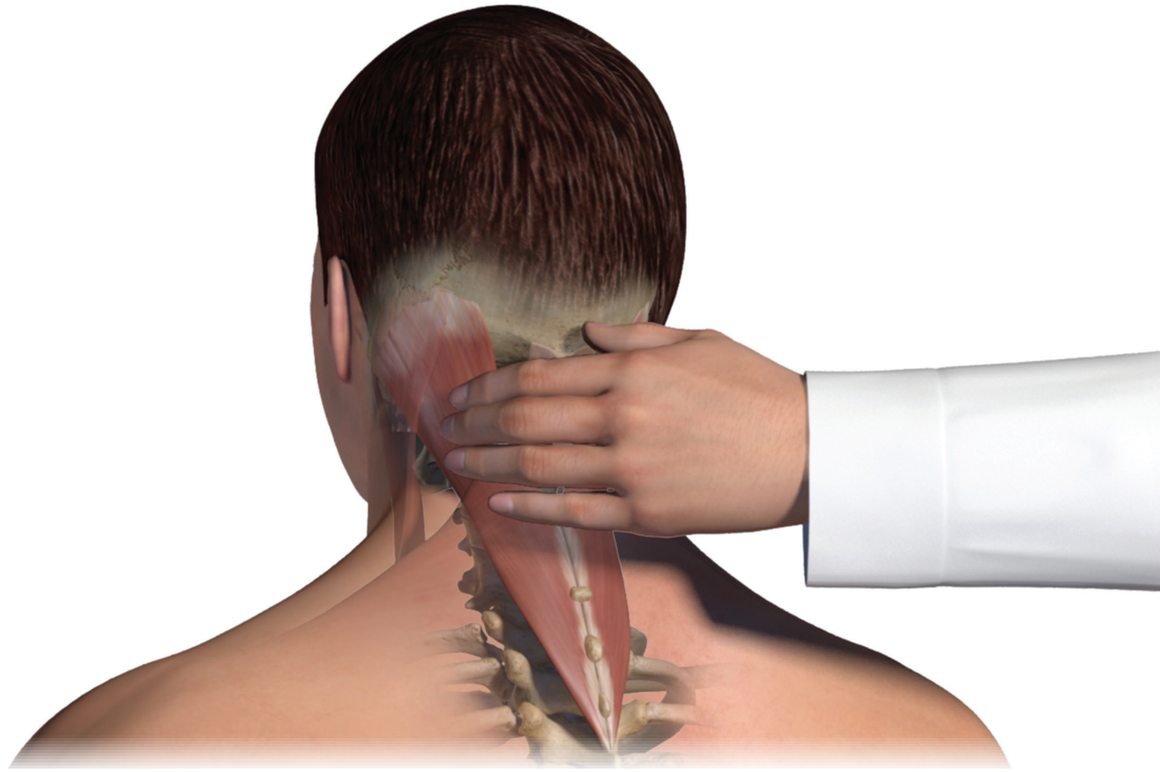
Involved postures[12]

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

Splenius capitis (continued)

Localization[12]

Anterior to the trapezius and posterior to the sternocleidomastoid in the superior portion of the posterior triangle



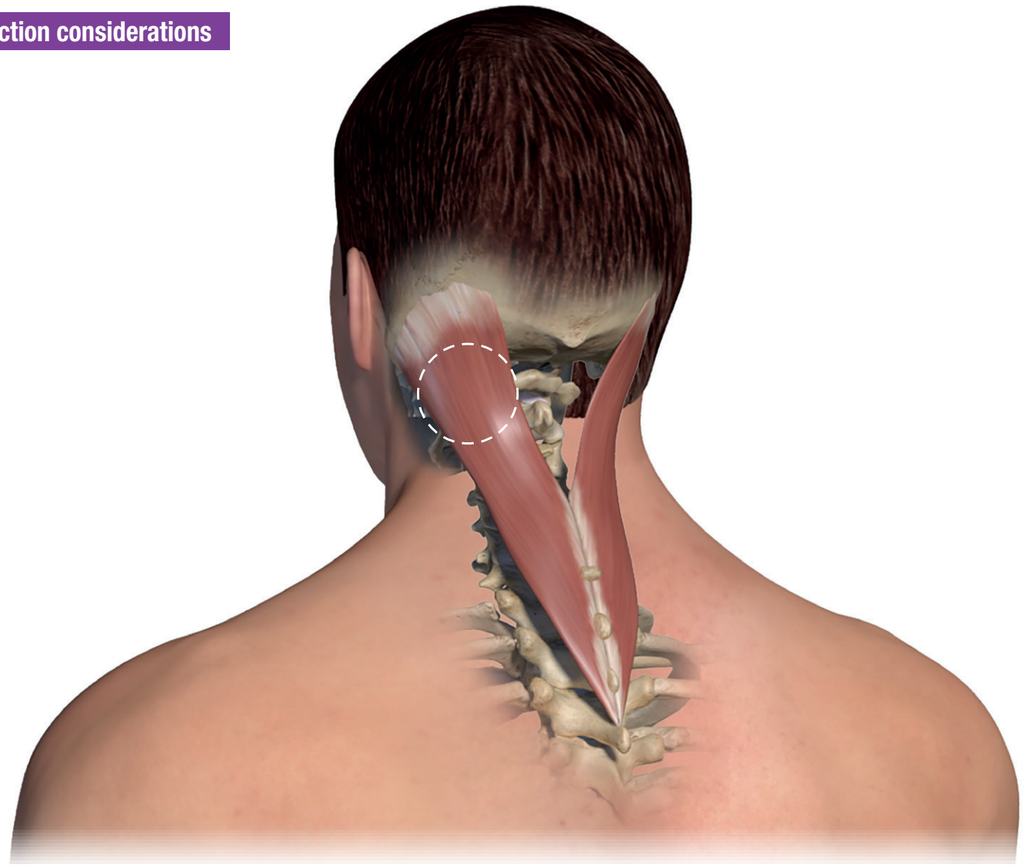
IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS
Adverse reactions to BOTOX® for injection are discussed in greater detail in the following sections: *Boxed Warning*, *Contraindications*, and *Warnings and Precautions*.

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 about BOTOX® on following pages.

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 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 starting in the lower end of approved dosing range and titrate in 5-Unit increments
- Position patient's head in a neutral position during injection, if possible

Notes

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%).

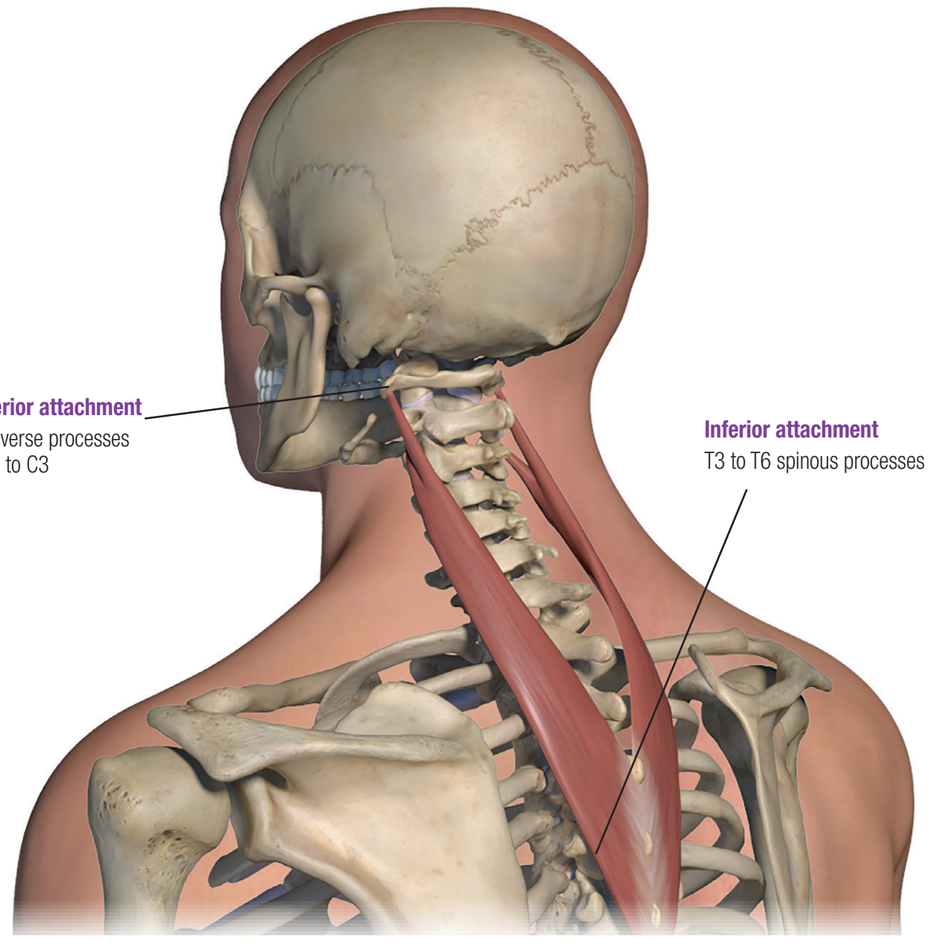
Please see additional Important Safety Information about BOTOX® on following pages.

Splenius cervicis

▶ **BOTOX® dose: 20 Units to 60 Units**

Muscle action[11,12]

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



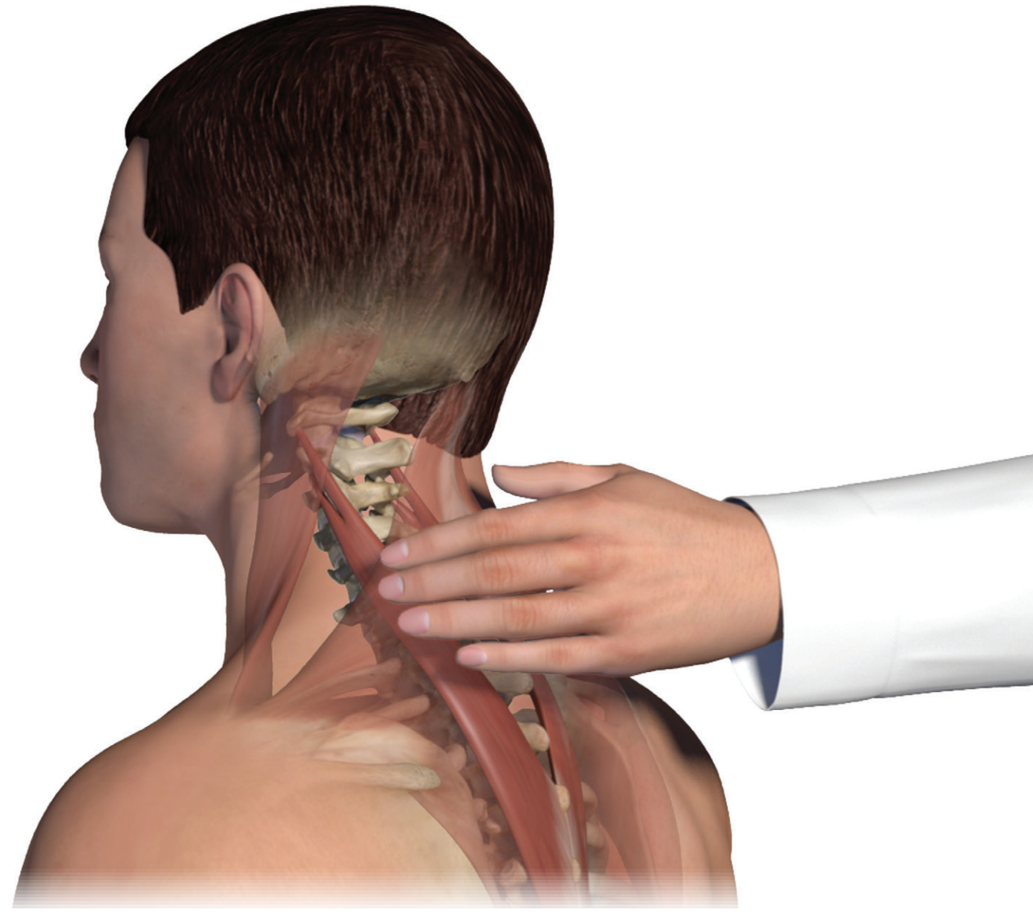
Involved postures[12]

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

Splenius cervicis (continued)

Localization[12]

Anterior to the trapezius, inferior and parallel to the splenius capitis, medial to the levator scapulae

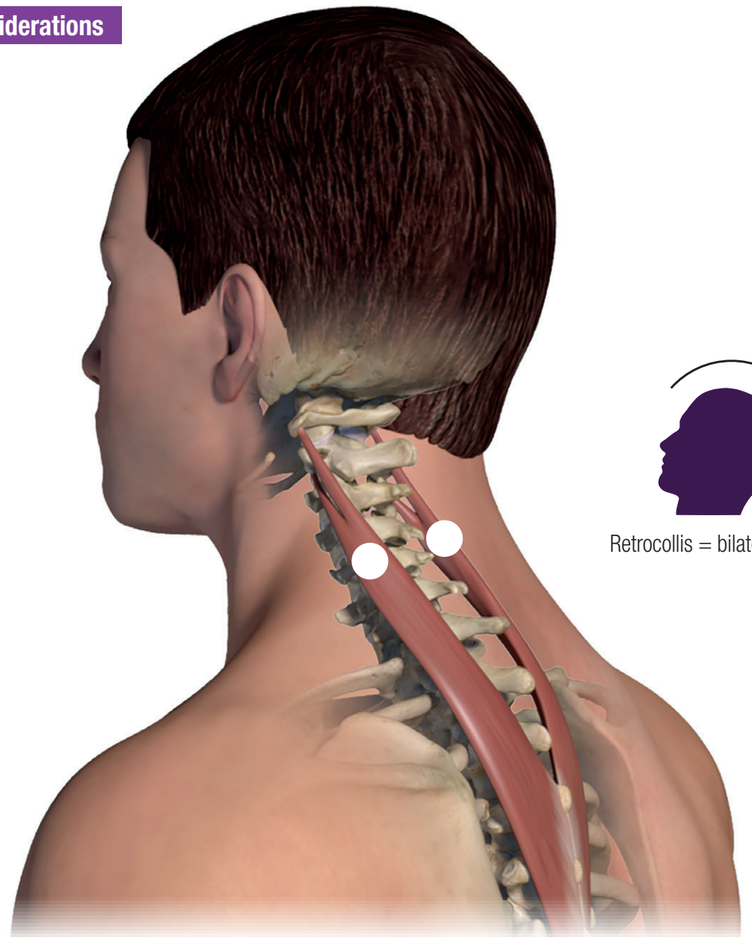


IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Strabismus
The most frequently reported adverse events following injection of BOTOX® for Strabismus include ptosis (15.7%) and vertical deviation (16.9%).

Please see additional Important Safety Information about BOTOX® on following pages.

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 starting in the lower end of approved dosing range and titrate in 10-Unit increments
- Position patient's head in a neutral position during injection, if possible

Notes

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).

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.

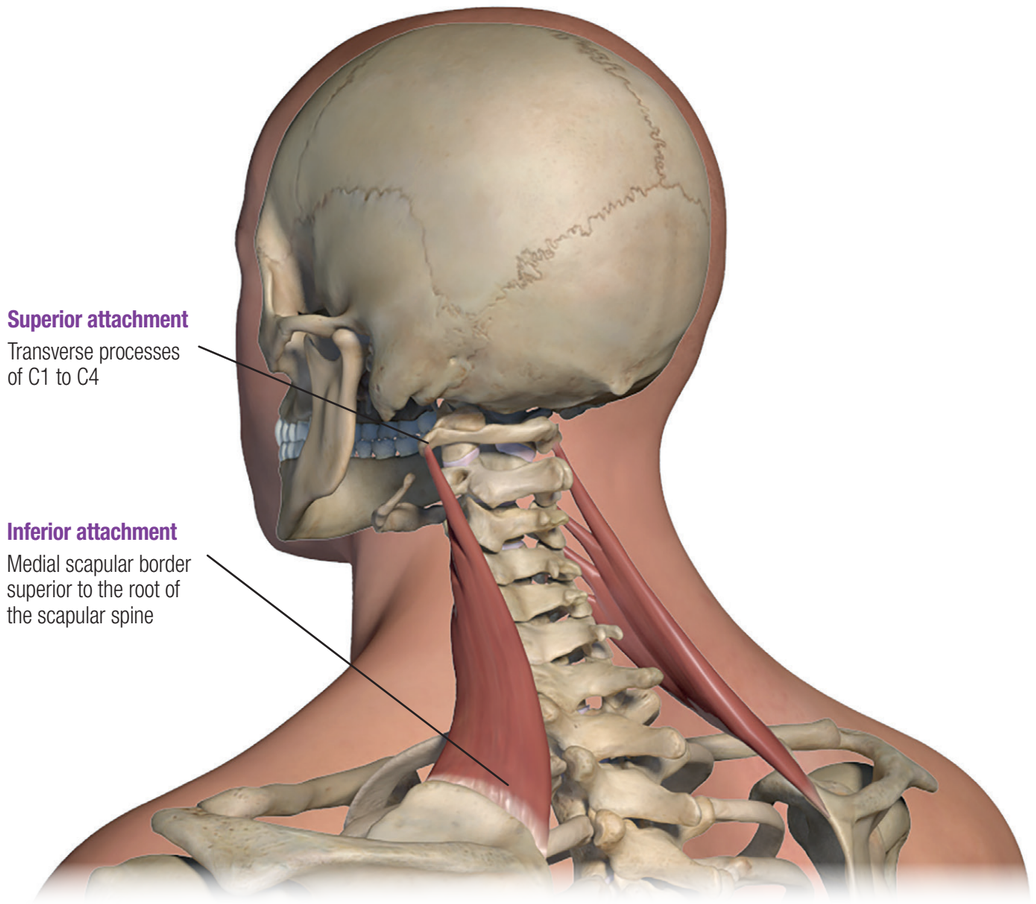
Please see additional Important Safety Information about BOTOX® on following pages.

Levator scapulae

▶ **BOTOX® dose: 20 Units to 100 Units**

Muscle action[11,12]

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



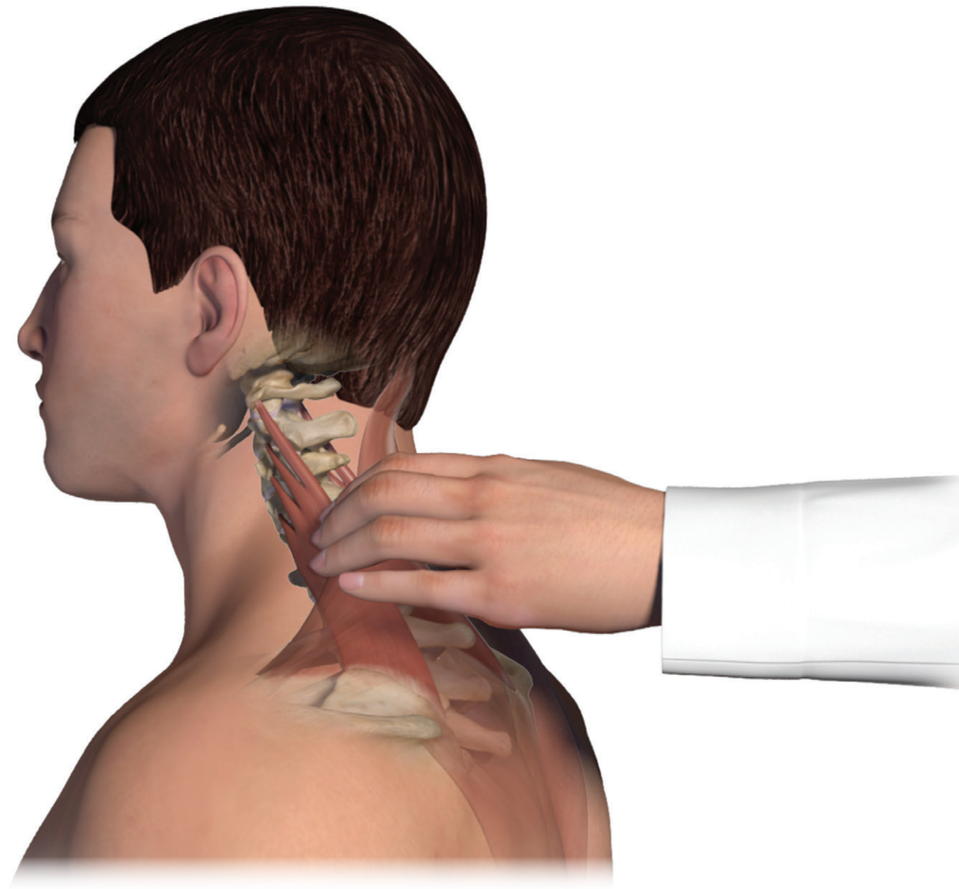
Involved postures[12]

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

Levator scapulae (continued)

Localization[12]

May be palpated immediately anterior to the anterior edge of the trapezius, at the angle of the neck. Although a superficial muscle, the electrically active parts may be at some depth, occasionally up to 3 cm



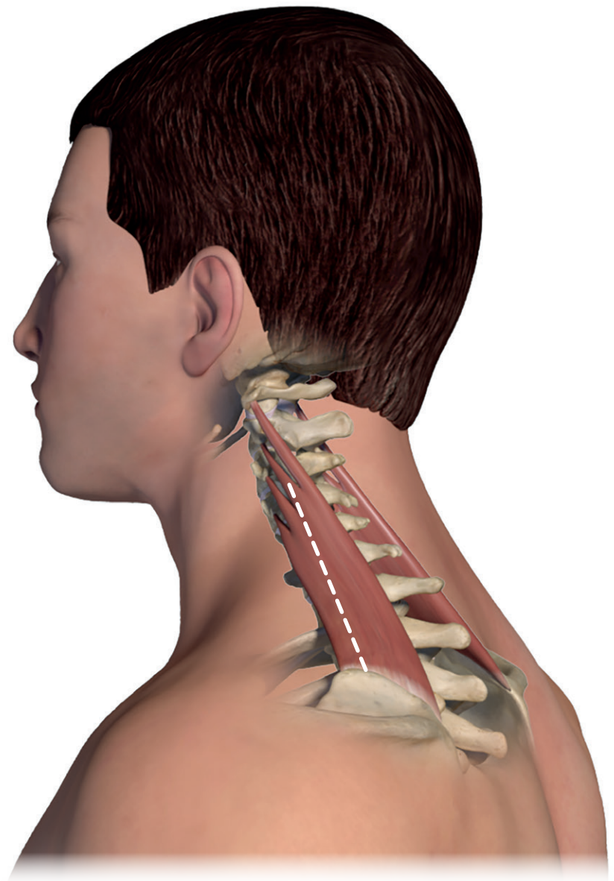
IMPORTANT SAFETY INFORMATION (continued)
DRUG INTERACTIONS

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 accompanying full Prescribing Information including Boxed Warning and Medication Guide.

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
- 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
- Consider a starting dose around 20-25 Units and titrate in 10- to 20-Unit increments

Notes

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.

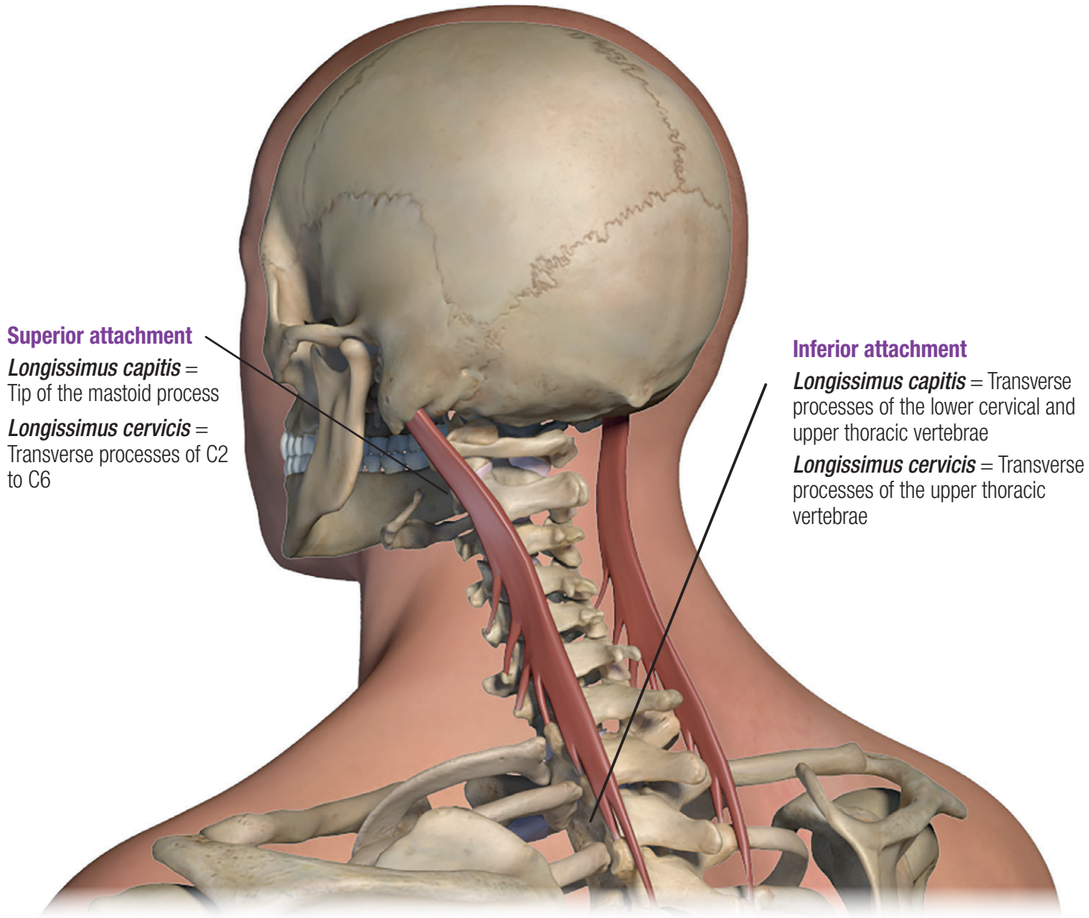
Please see additional Important Safety Information about BOTOX® on following pages.

Longissimus (capitis/cervicis)

▶ **BOTOX® dose: 30 Units to 100 Units**

Muscle action[11,12]

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 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[12]

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

Longissimus (capitis/cervicis) (continued)

Localization[12]

Two fingerbreadths below the lower palpable border of the skull, and 3 fingerbreadths lateral to midline at a depth of 2 cm

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS

Spread of Toxin Effect

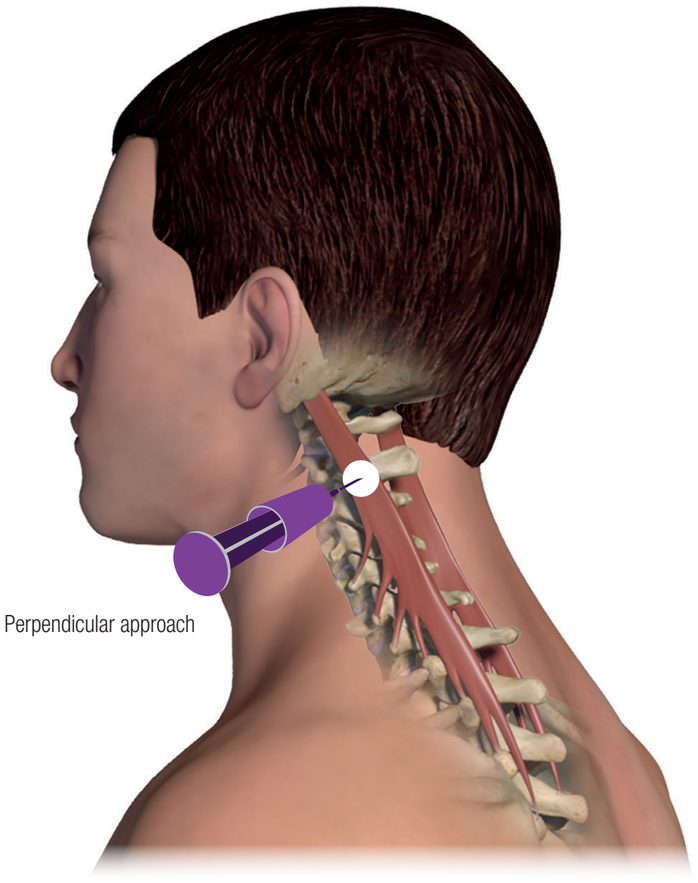
See Boxed Warning.

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 about BOTOX® on following pages.

Longissimus (capitis/cervicis) (continued)

Injection considerations



Perpendicular approach

- 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 1 to 2 fingerbreadths anteriolateral to the spinous process perpendicular to the length of this muscle
- This muscle often responds to smaller doses of BOTOX®, so consider starting in the lower end of the approved dosing range

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.

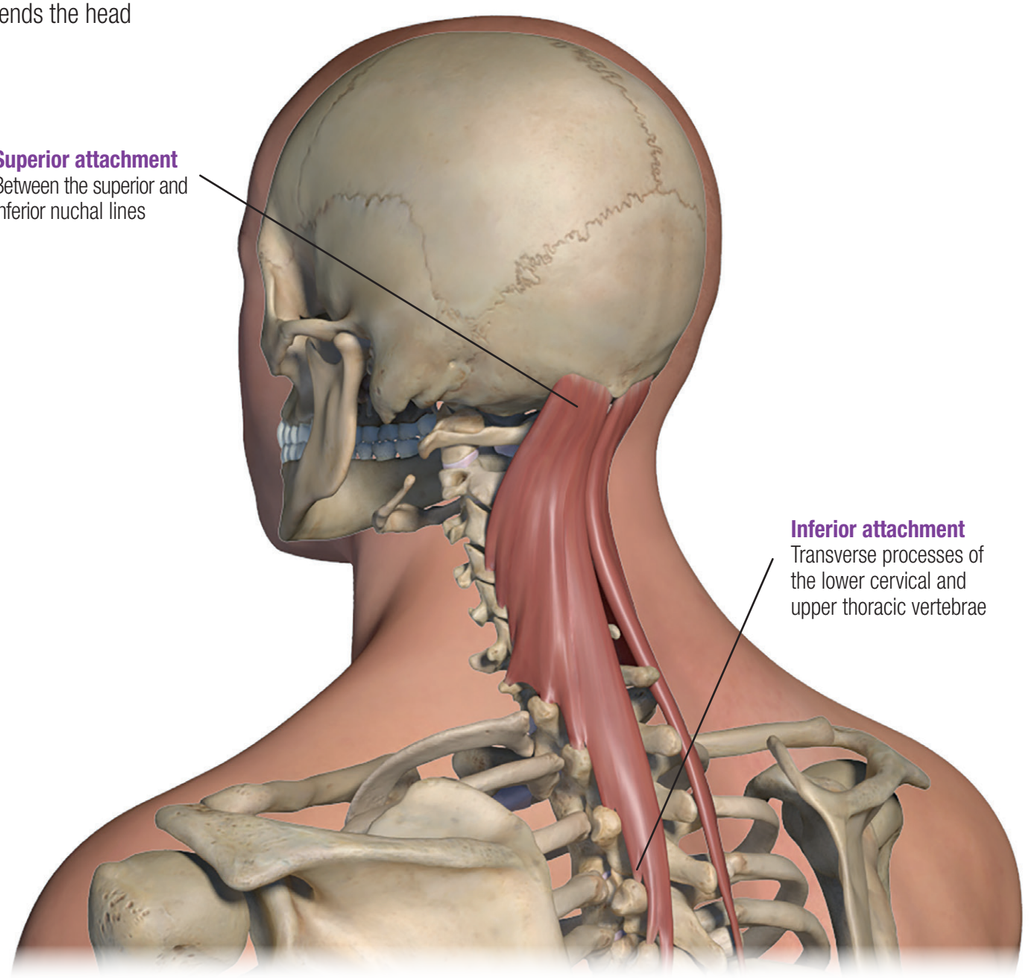
Please see additional Important Safety Information about BOTOX® on following pages.

Semispinalis capitis

▶ **BOTOX® dose:** 30 Units to 100 Units

Muscle action[11]

Extends the head



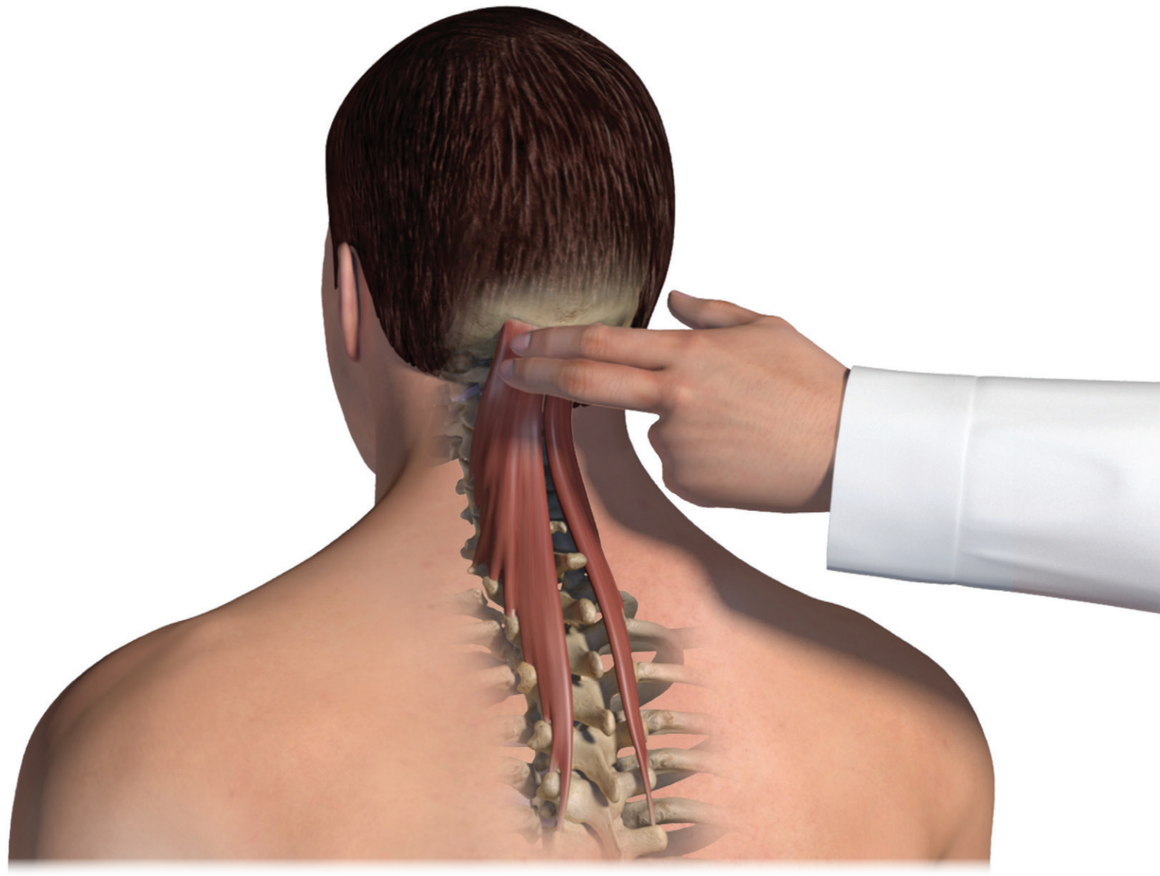
Involved postures[12]

- Retrocollis
- Right torticollis, retrocollis

Semispinalis capitis (continued)

Localization[12]

Two fingerbreadths lateral to the midline, approximately 2 fingerbreadths below the occipital protuberance (posterior to the atlas-C2) at a depth of 3 cm to 4 cm



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 pre-existing 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 about BOTOX® on following pages.

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

Notes

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 about BOTOX® on following pages.

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 two 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

Injection insights and considerations (continued)

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 performing all injections perpendicular to the skin, if possible, to most readily access the involved muscles
  - To optimally target the muscle, consider angulation of the injection needle and 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® Treatment Framework documentation

Utilize the BOTOX® Treatment Framework when evaluating your next Cervical Dystonia patient

The right goals

Patient name: _____

Posture(s): ☐ Torticollis ☐ Laterocollis ☐ Anterocollis ☐ Retrocollis ☐ Lateral shift ☐ Sagittal shift
☐ Right torticollis, left laterocollis, shoulder elevation ☐ Left torticollis, left laterocollis
☐ Right torticollis, retrocollis ☐ Right laterocollis, tremor

- Consider taking photos to document baseline severity

Symptoms: _____

_____

_____

Goals: _____

_____

_____

☐ Repeat goals back to patient

Expectations:

- ☐ BOTOX® is not a cure nor a substitute for usual standard of care
- ☐ Fine needles are used during injections
- ☐ Muscles/dose may need to be adjusted during subsequent injection sessions
- ☐ Patient should return for a 2- to 6-week follow-up evaluation
- ☐ Review insurance plans to determine out-of-pocket costs and use of potential savings programs

Neck pain evaluation:

- ☐ **LOOK** at the patient as they enter the room, when they're relaxing, and during distraction
- ☐ **FEEL** the patient's muscles to assess tenderness, tone, hypertrophy, and range of motion restrictions
- ☐ **LISTEN** to patient's story, if/how neck pain changes during the day, and EMG feedback

BOTOX® Treatment Framework documentation (continued)

Injection 1: Muscles injected/BOTOX® dose

The right muscles/dose

Injected	Approved Muscle[9,10]	BOTOX® Dose
	Levator scapulae (20 Units to 100 Units)	
	Longissimus (30 Units to 100 Units)	
	Scalene complex (15 Units to 50 Units)	
	Semispinalis capitis (30 Units to 100 Units)	
	Splenius capitis (15 Units to 100 Units)	
	Splenius cervicis (20 Units to 60 Units)	
	Sternocleidomastoid (15 Units to 100 Units)	
	Trapezius (20 Units to 100 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 pre-existing 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*).

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 about BOTOX® on following pages.

BOTOX® Treatment Framework documentation (continued)

2- to 6-week follow-up

The right plan

Percentage of goals achieved:

Improvements in head position and neck pain:

Reassess neck pain (LOOK, FEEL, LISTEN) as necessary:

Patient comments:

Potential adjustments in muscles/BOTOX® dose:

☐ Patient scheduled for next treatment session

BOTOX® Treatment Framework documentation (continued)

Injection 2: Muscles injected/BOTOX® dose

The right muscles/dose

Injected	Approved Muscle[9,10]	BOTOX® Dose
	Levator scapulae (20 Units to 100 Units)	
	Longissimus (30 Units to 100 Units)	
	Scalene complex (15 Units to 50 Units)	
	Semispinalis capitis (30 Units to 100 Units)	
	Splenius capitis (15 Units to 100 Units)	
	Splenius cervicis (20 Units to 60 Units)	
	Sternocleidomastoid (15 Units to 100 Units)	
	Trapezius (20 Units to 100 Units)	

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.

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 about BOTOX® on following pages.

Dilution and reconstitution

Follow general dilution instructions for BOTOX® vials (100 Units and 200 Units)[1]

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)

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)
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 (15.7%) and vertical deviation (16.9%).

Please see additional Important Safety Information about BOTOX® on following pages.

Ensure your office is ready for your first BOTOX® injections

- Set up an Allergan® 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

Consider using EMG/E-Stim for BOTOX® injections

- Can be used to help identify individual muscles contributing to the patient's condition[13]
- Assists in localizing approved muscles and ensuring accurate placement of BOTOX®[13]
- Allows the injector to direct BOTOX® into more susceptible parts of the fascicle[13]

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).

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 about BOTOX® on following pages.

Extensive learning opportunities

A broad range of BOTOX® injection training opportunities is available to help you hone your skills

- Several different peer-to-peer programs are available for BOTOX® injection training
  - Expert-On-Demand is a 30- to 45-minute teleconference with an experienced BOTOX® injector who can address specific training needs
- Offers the ability to directly learn from a peer expert
- Many feature live patient injections and case studies

Talk to your Allergan® Representative if you're interested in participating in one of these programs

Injection simulation

- Allows you to simulate hands-on BOTOX® injections
- ELVIS (Electronic Virtual Injection Simulator) is a lifelike, anatomically correct model of the head, neck, and shoulders in adults
- Offers the ability to practice localizing and injecting muscles for Cervical Dystonia treatment using electronic guidance

Talk to your Allergan® Representative if you're interested in practicing with one in your office

BOTOX ACADEMY®

Robust online educational resource that provides:

- Overview of BOTOX® and injection procedures
- Videos and e-lectures on:
  - Injection technique
  - Functional anatomy
  - Muscle localization
  - Reconstitution
- Downloadable patient education and office materials

Register at BOTOXAcademy.com

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 additional Important Safety Information about BOTOX® on following pages.

Resources and support

Reimbursement Business Advisor (RBA)

- Works with practices to identify and focus on operational needs (including reimbursement support) that can facilitate the safe and effective use of BOTOX® treatment
- Provides in-person insights regarding BOTOX® office processes from the time the patient is first identified through retreatment

Ask your Allergan® Representative how an RBA can help

BOTOX® Savings Program

Eligible patients may

PAY as little as $0 for BOTOX® treatments

BOTOX® SAVINGS PROGRAM

Here's how:

- Most insurance plans cover the majority of BOTOX® costs. However some commercially insured patients may still owe a co-pay*
- On average, the out-of-pocket cost for BOTOX® is between $101 and $178 (depending on the indication). There may be additional costs for the procedure, which will vary by healthcare provider and insurance*
- The BOTOX® Savings Program can reimburse eligible patients to help with these remaining costs*

Patients can text† SAVE to 27747
or visit BOTOXSavingsProgram.com to get started.

*Restrictions and maximum savings limits apply. Patient out-of-pocket expense may vary. Offer not valid for patients enrolled in Medicare, Medicaid, or other federal or state healthcare programs. Please see full terms and conditions at BOTOXSavingsProgram.com.

†See Privacy & Terms: BOTOXSavingsProgram.com/eligibility. Message & data rates may apply. Message frequency may vary. Text HELP for help, STOP to end.

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.

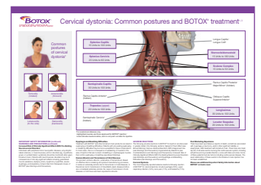
Please see additional Important Safety Information about BOTOX® on following pages.

Resources and support (continued)

Patient education and office materials

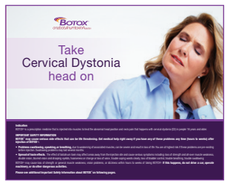
Cervical Dystonia

BOTOXCervicalDystonia.com



Treatment reference sheet

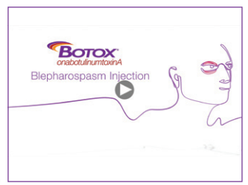
Patient brochure



Patient flipchart

Blepharospasm

BOTOXBlepharospasm.com



Patient injection video

Patient brochure

Materials for practices to help identify and educate patients.

Ask your Allergan® Representative how to get resources for your practice

Find a BOTOX® Specialist tool

Help patients seeking treatment find your practice with this physician locator service.

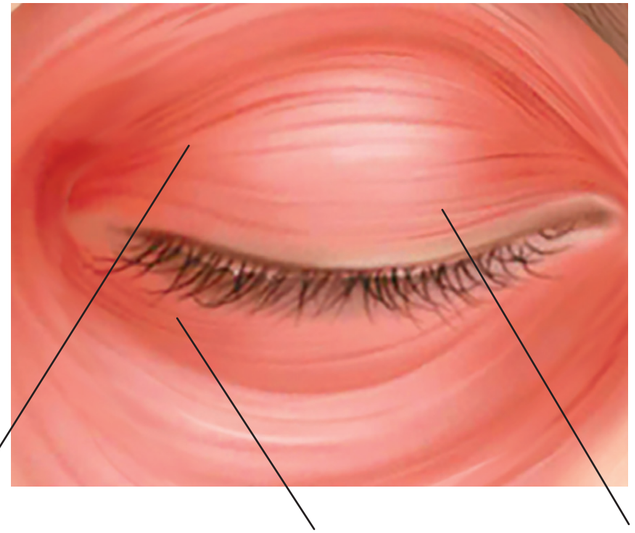
Injectors can customize their profile with multiple options (eg, name and photo, specialty).

Register at BOTOXMedical.com

Understanding BOTOX® treatment for Blepharospasm

A proven first-line option for treating Blepharospasm since 1989

Approved injection sites/dosing[9]



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

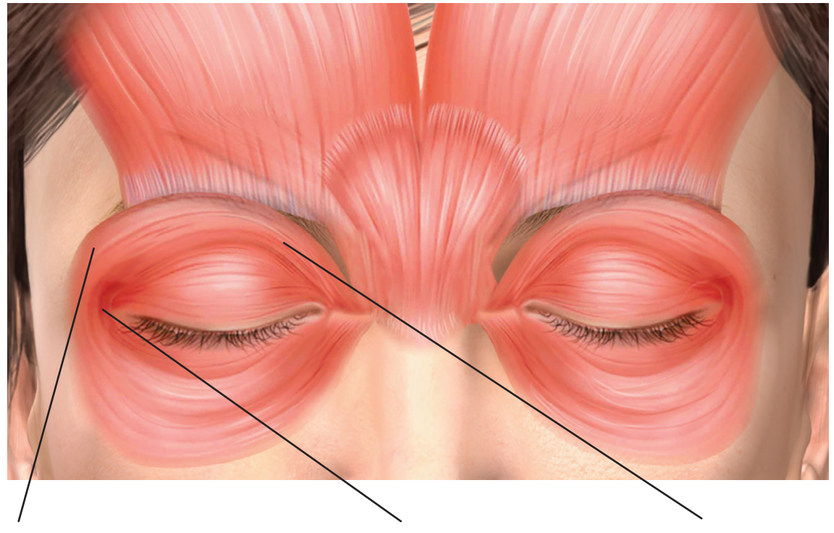
Medial pretarsal orbicularis oculi (upper lid)
1.25 Units to 2.5 Units

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

Orbicularis oculi

Muscle action

Closes eyelids; palpebral part closes lids gently; orbital part closes lids tightly[11]



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

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 about BOTOX® on following pages.

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[9]
- The cumulative dose of BOTOX® treatment for Blepharospasm in a 30-day period should not exceed 200 Units[9]
- Reconstituted BOTOX® is injected using a sterile, 27- to 30-gauge needle without electromyographic guidance[9]
- Avoiding injection near the levator palpebrae superioris may reduce the complication of ptosis[9]
- 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[9]
- Initial effect of the injections is generally seen within 3 days and reaches a peak 1 to 2 weeks post treatment. Each treatment lasts approximately 3 months, following which the procedure can be repeated[9]
- At repeat treatment sessions, the dose may be increased up to twofold 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[9]

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.

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 pre-existing 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 accompanying full Prescribing Information including Boxed Warning and Medication Guide.

BOTOX® Savings Program Terms and Conditions

Program Terms, Conditions, and Eligibility Criteria: 1. This offer is good for use only with a valid prescription for BOTOX® (onabotulinumtoxinA). **2.** Based on insurance coverage, each patient can be reimbursed up to $1000 per treatment with a maximum savings limit of $4000 per year. Patient out-of-pocket expense may vary. **3.** This offer is not valid for use by patients enrolled in Medicare, Medicaid, or other federal or state programs (including any state pharmaceutical assistance programs), or private indemnity or HMO insurance plans that reimburse you for the entire cost of your prescription drugs. Patients may not use this offer if they are Medicare-eligible and enrolled in an employer-sponsored health plan or prescription drug benefit program for retirees. This offer is not valid for cash-paying patients. **4.** This offer is valid for up to 4 treatments over a 12-month period. **5.** Offer is valid only for BOTOX® and BOTOX® treatment-related costs not covered by insurance. **6.** A BOTOX® Savings Program check will be provided upon approval of a claim. The claim must be submitted with treatment details from an Explanation of Benefits (EOB) or a Specialty Pharmacy (SP) receipt. (If the BOTOX® prescription was filled by a Specialty Pharmacy, both EOB and SP details must be provided.) All claims must be submitted within 120 days of treatment date. You may be required to provide a copy of your EOB or SP receipt for your claim to be approved. **7.** A BOTOX® Savings Program check may be sent either directly to you or to your selected healthcare provider who provided treatment. For payment to be made directly to your healthcare provider, you must authorize an assignment of benefit during each claim submission. You are not obligated to assign your BOTOX® Savings Program benefit to your healthcare provider to participate in the program. **8.** Allergan® reserves the right to rescind, revoke, or amend this offer without notice. **9.** Offer good only in the USA, including Puerto Rico, at participating retail locations. **10.** Void where prohibited by law, taxed, or restricted. **11.** This offer is not health insurance. **12. By participating in the BOTOX® Savings Program, you acknowledge that you are an eligible patient and that you understand and agree to comply with the terms and conditions of this offer.**

For questions about this program, please call 1-800-44-BOTOX.

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References: 1. Jankovic J, Leder S, Warner D, Schwartz K. Cervical dystonia: clinical findings and associated movement disorders. *Neurology.* 1991;41(7):1088-1091. **2.** Stacy M. Epidemiology, clinical presentation, and diagnosis of cervical dystonia. *Neurol Clin.* 2008;26(suppl 1):23-42. **3.** Charles PD, Adler CH, Stacy M, et al. Cervical dystonia and pain: characteristics and treatment patterns from CD PROBE. *J Neurol.* 2014;261(7):1309-1319. **4.** Tiderington E, Goodman EM, Rosen AR, et al. How long does it take to diagnose cervical dystonia? *J Neurol Sci.* 2013;335 (1-2):72-74. **5.** Bhidayasiri R, Kaewwilai L, Wannachai N, Brenden N, Truong DD, Devahastin R. Prevalence and diagnostic challenge of dystonia in Thailand: a service-based study in a tertiary university referral centre. *Parkinsonism Relat Disord.* 2011;17(suppl 1):S15-S19. **6.** Consky ES, Lang AE. Clinical assessments of patients with cervical dystonia. In: Jankovic J, Hallett M, eds. *Therapy With Botulinum Toxin.* New York, NY: Marcel Dekker, Inc; 1994:211-237. **7.** Jankovic J. Treatment of cervical dystonia. In: Brin MF, Comella CL, Jankovic J, eds. *Dystonia: Etiology, Clinical Features, and Treatment.* Philadelphia, PA: Lippincott Williams & Wilkins; 2004:159-166. **8.** Saunders-Pullman R, Soto-Valencia J, Costan-Toth C, et al. A new screening tool for cervical dystonia. *Neurology.* 2005;64(12):2046-2049. **9.** BOTOX® Prescribing Information, October 2019. **10.** Charles D, Gill CE. Neurotoxin injection for movement disorders. *Continuum Lifelong Learning Neurol.* 2010;16(1):131-157. **11.** Standring S, ed. *Gray's Anatomy: The Anatomical Basis of Clinical Practice.* 40th ed. London, England: Churchill Livingstone; 2008. **12.** Stacy M. Anatomic principles for botulinum toxin injection. In: Stacy M, ed. *Handbook of Dystonia.* New York, NY: Informa Healthcare USA, Inc; 2007:317-342. **13.** Benecke R, Moore P, Dressler D, Naumann M. Cervical and axial dystonia. In: Moore P, Naumann M, eds. *Handbook of Botulinum Toxin Treatment.* 2nd ed. Malden, MA: Blackwell Science; 2003:158-191.

Helpful phone numbers and websites

BOTOX ACADEMY

ORDERING

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

CUSTOMER SERVICE

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

ALLERGAN MEDICAL INFORMATION LINE

1-800-433-8871

PATIENT FINANCIAL ASSISTANCE

For commercially insured patients: BOTOXSavingsProgram.com

PROFESSIONAL EDUCATION & RESOURCES

For injection training opportunities: Contact your Allergan Representative

For Reimbursement Business Advisors: Contact your Allergan Representative

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

Please see Important Safety Information, including Boxed Warning, inside.

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