BOTOX®
onabotulinumtoxinA injection

Companion App

3D Spasticity

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Injection Workbook for **Adult Spasticity**

Examining Patient Assessment, Advanced Anatomy, and Injection Considerations

INDICATION

Spasticity

BOTOX® (onabotulinumtoxinA) for injection is indicated for the treatment of spasticity in patients 2 years of age and older.

Limitations of Use

BOTOX has not been shown to improve upper extremity functional abilities or range of motion at a joint affected by a fixed contracture.

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

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Introduction

This workbook contains essential information regarding the use of BOTOX® for Adult Spasticity. It is designed to help hone your skills and understanding of the following areas:

- Patient identification and assessment
- Pivotal trial data, including additional insights supporting pattern-based muscle/dose selections and treatment initiation 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*.

Please see additional Important Safety Information throughout.

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Integrate multiple approaches when assessing Adult Spasticity

Upper limb spasticity

Diagnosis technique	Observations
Ask the patient what has impacted post-stroke treatment goals	"Muscle tightness" and "stiffness" are usually mentioned the most
Ask the patient if they have ever taken muscle relaxants	May indicate if another physician had noticed the spasticity
Have the patient stand up	Helps determine the effect of symptoms on balance and exposes the patient's limbs
Shake the patient's hand	Patient must extend 1 arm, allowing you to check for signs and symptoms in both limbs
Have patient raise their arms above their head and/or straight out	Allows you to quickly look for effects of spasticity on elbow, wrist, and fingers

Lower limb spasticity

Ambulatory patients	Nonambulatory patients*
Evaluate all affected joints of ankle and toe in all positions: supine, seated, standing, and moving	Look for potential skin breakdown caused by spasticity
Observe and evaluate patient's gait, including gait cycle, as part of determining severity	Compare positioning when sitting vs lying down
Measure the time it takes for patient to walk a set distance or get up from seated position and walk to a set point	Determine if patient's leg position impedes transfers

*Nonambulatory patients were excluded from the BOTOX® lower limb spasticity clinical trial.

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.

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It may be time to revisit these patients' treatment plans

Do you have Adult Spasticity patients in your practice who...

Are on muscle relaxants and only call in for refills?

Are not meeting treatment goals on current therapy?

Do not follow their treatment regimen?

Have finished PT/OT sessions, but want to continue working on symptoms?

Have contraindications to certain treatment options?

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.

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Latest recommendations from professional organizations regarding Adult Spasticity treatment

AAN Practice Guidelines 2016[1]

For focal manifestations of Adult Spasticity involving the upper limb, BOTOX®, abobotulinumtoxinA, and incobotulinumtoxinA should be offered (Level A) as treatment options.[1]

For focal manifestations of Adult Spasticity involving the lower limb that warrant treatment, BOTOX® and abobotulinumtoxinA should be offered (Level A) as treatment options.[1]

Recommendation Level	Definition
A	**Intervention should be offered**
B	Intervention should be considered
C	Intervention may be considered
U	Insufficient evidence to support or refute intervention

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

Hypersensitivity Reactions
Serious and/or immediate hypersensitivity reactions have been reported.

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.

BOTOX® onabotulinumtoxinA injection

Latest recommendations from professional organizations regarding Adult Spasticity treatment (continued)

AAPM&R CONSENSUS GUIDANCE* 2024

The AAPM&R Spasticity TEP recommends clinicians consider use of botulinum toxin A for management of focal upper and lower limb spasticity (SORT A).[2,*,†]

*This consensus guidance provides clinicians with practical recommendations for Spasticity assessment and management based on the available evidence and expert opinion. Clinical judgment should be exercised, and recommendations tailored to the individual patient.

†BOTOX®, abobotulinumtoxinA, or incobotulinumtoxinA.

The 2024 AAPM&R consensus guidance on Adult Spasticity was developed by the Spasticity Technical Expert Panel (TEP). They graded treatment recommendations using the Strength of Recommendation Taxonomy (SORT), a three-tier system evaluating treatment effectiveness based on evidence quality and patient outcomes.[2]

SORT GRADE Criteria[3]

Recommendation Level	Definition
A	**Recommendation based on consistent and good quality patient-oriented evidence**[‡]
B	Recommendation based on inconsistent and limited quality patient-oriented evidence[‡]
C	Recommendation based on consensus, usual practice, expert opinion, disease-oriented evidence[§], and case series

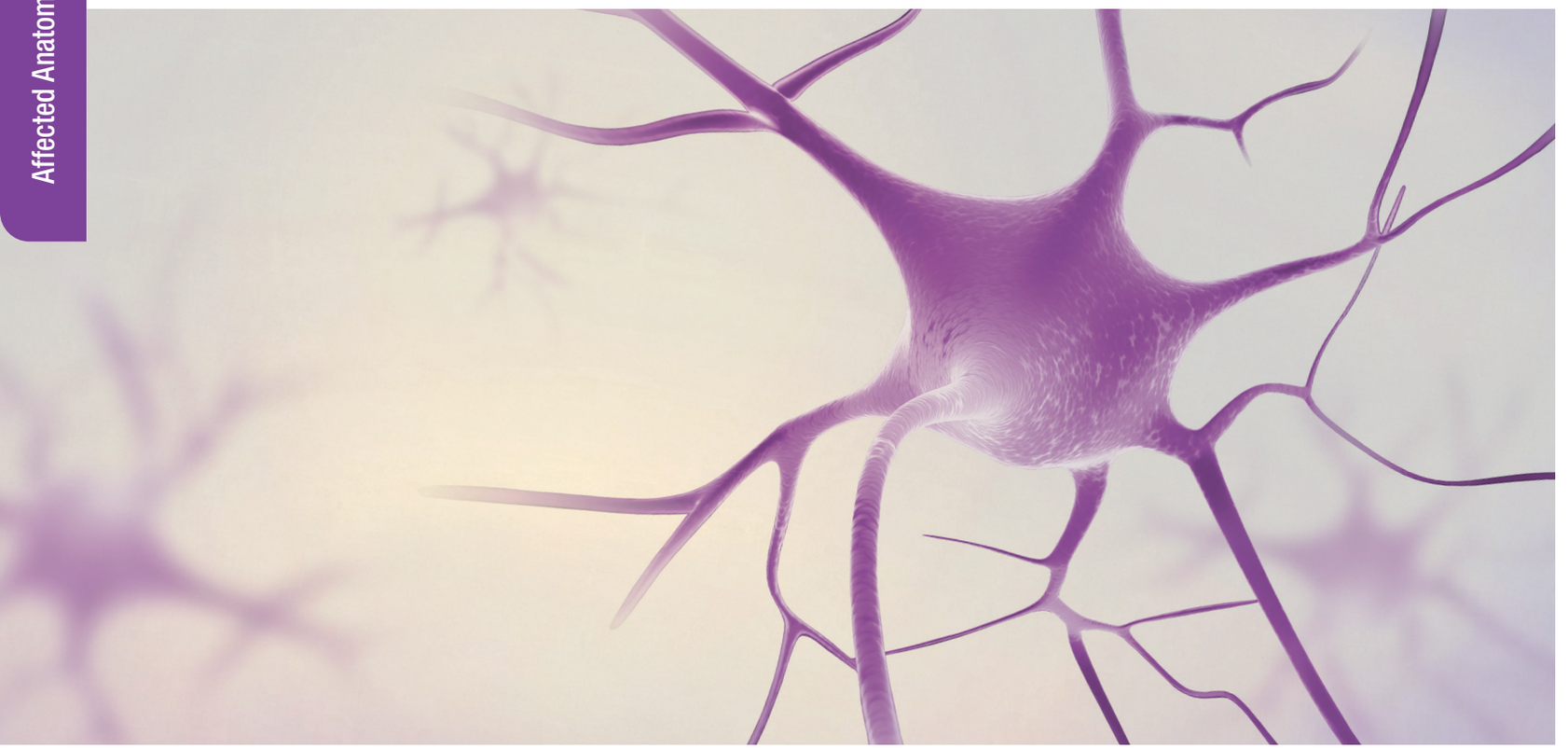
[‡]Patient-oriented evidence measures outcomes that matter to patients.

[§]Disease-orientated evidence measures intermediate, physiologic, or surrogate endpoints that may or may not reflect improvements in patient outcomes.

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



Affected anatomy in Adult Spasticity

- 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 localization and patient assessment in Adult Spasticity
- Combination postures shown in this section reflect those commonly seen in clinical practice
- 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)
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).

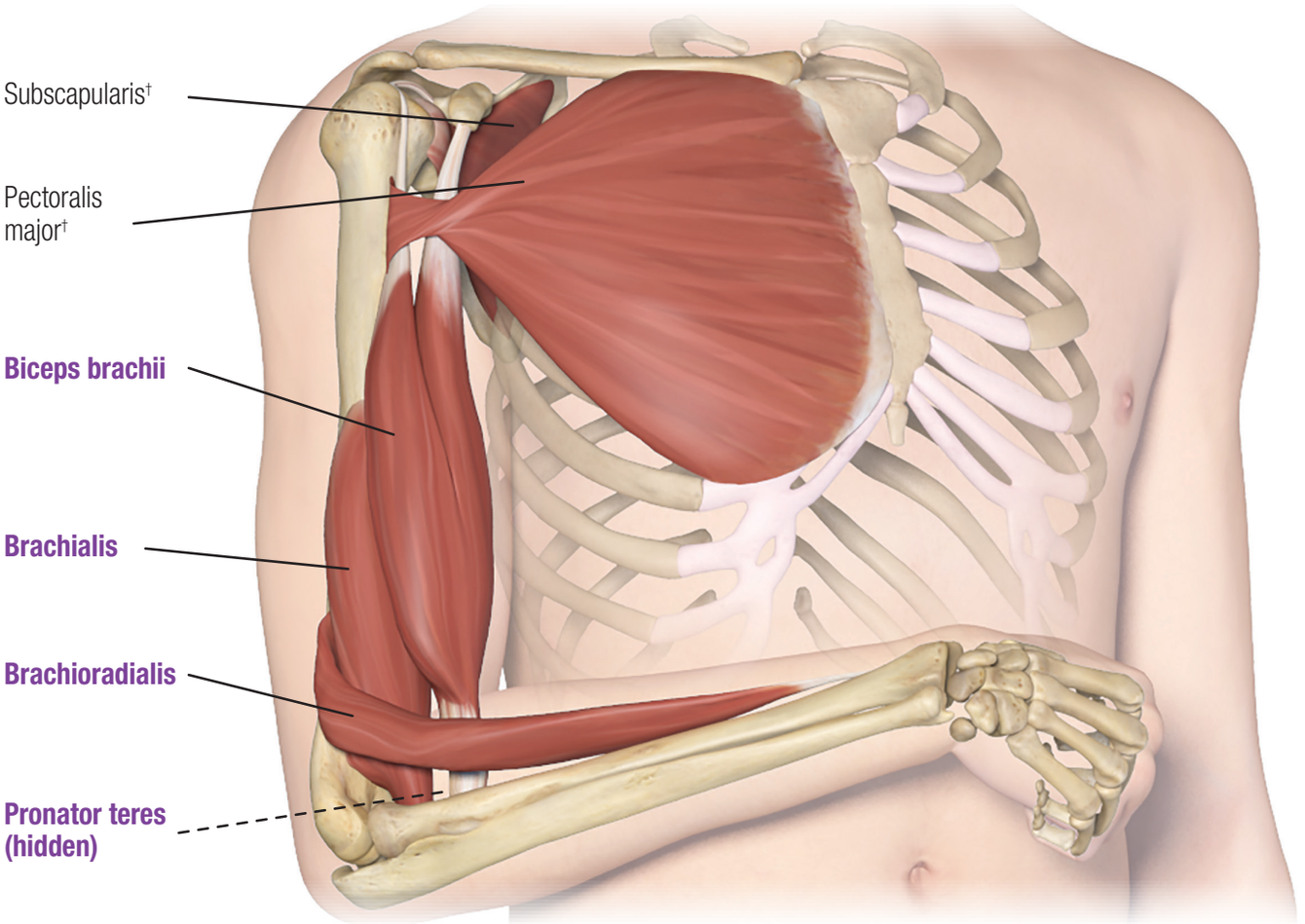
Please see additional Important Safety Information throughout.

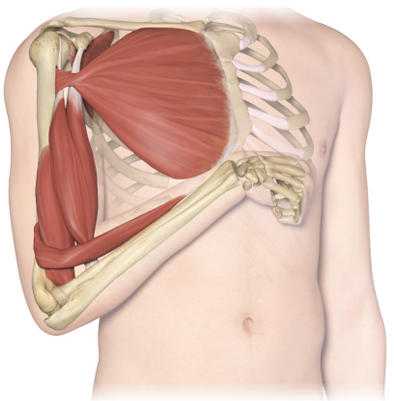
BOTOX® onabotulinumtoxinA injection

Clinical presentation in upper limb

Upper limb posture combination*

Flexed elbow, pronated forearm, flexed wrist, flexed fingers, thumb in palm





*The following muscles contribute to this posture but are not shown as they are more readily identified in the anterior compartment of the forearm, which is not visible here: **pronator quadratus, flexor carpi radialis, flexor carpi ulnaris, flexor digitorum profundus, flexor digitorum superficialis, flexor pollicis longus, flexor pollicis brevis, opponens pollicis, interossei, lumbricals.**

†For anatomical reference only.

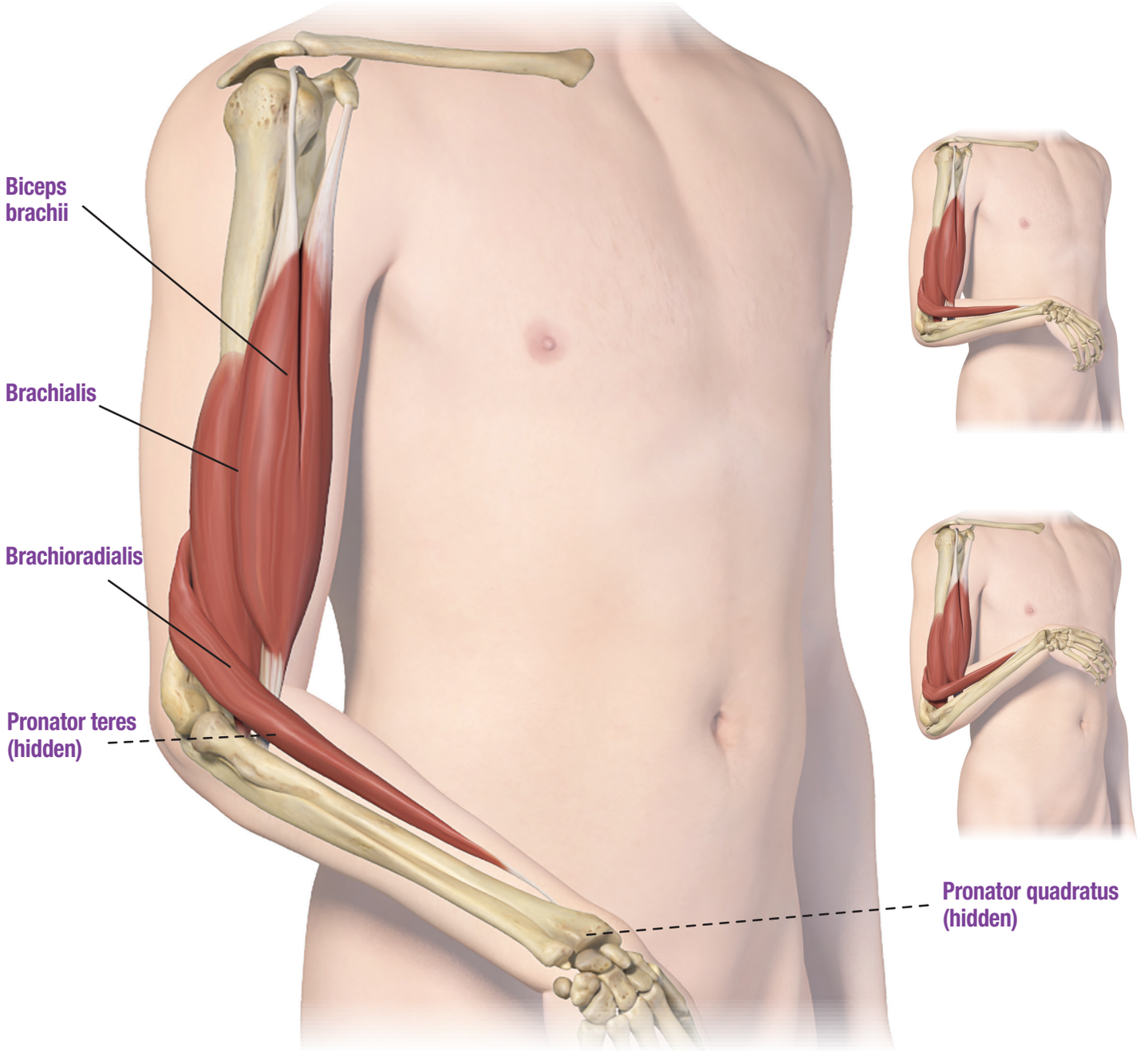
IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Dysphagia and Breathing Difficulties
Treatment with BOTOX and other botulinum toxin products can result in swallowing or breathing difficulties.

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Clinical presentation in upper limb (continued)

Flexed elbow, pronated forearm



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.

Please see additional Important Safety Information throughout.

BOTOX®
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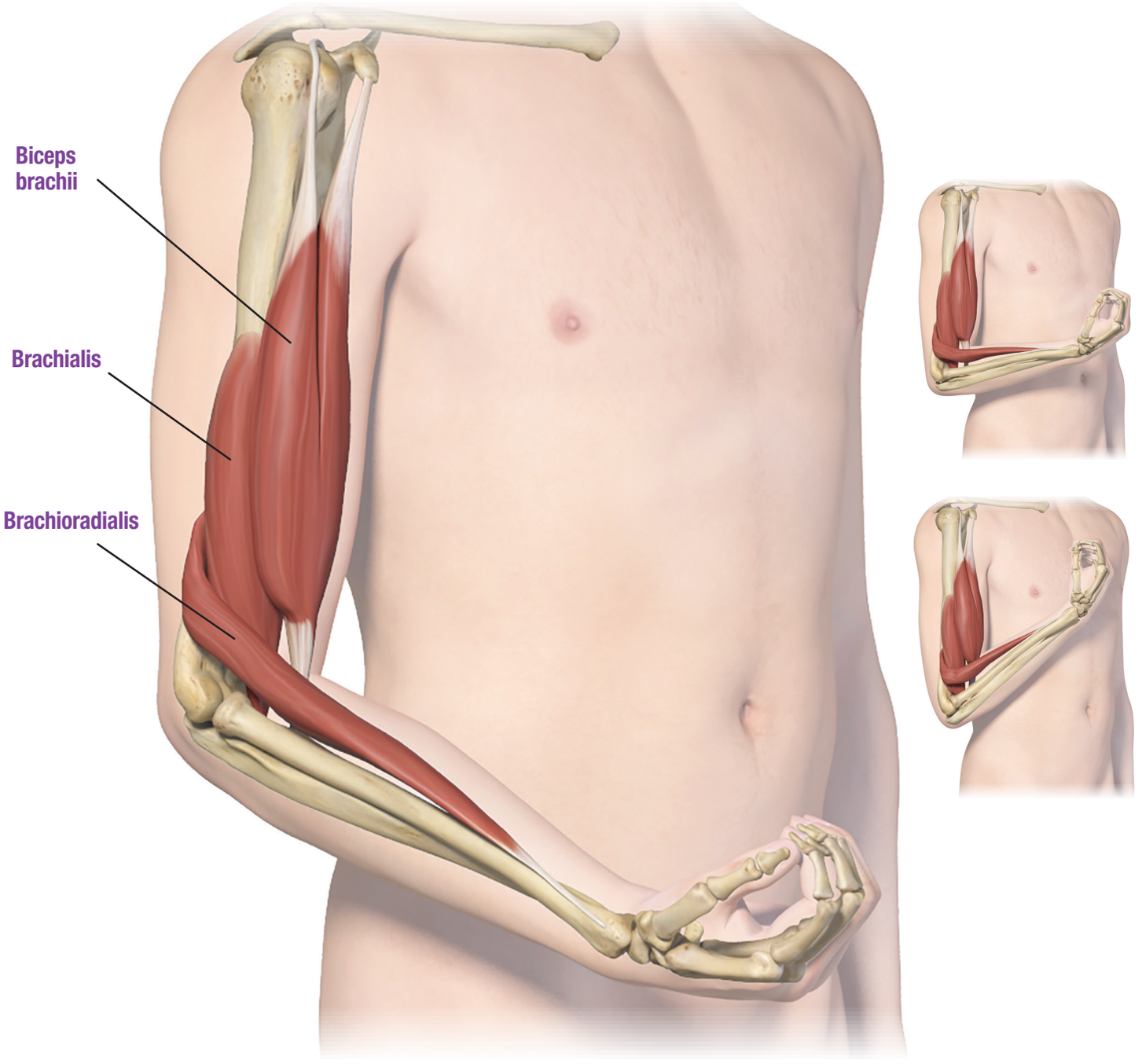
Clinical presentation in upper limb (continued)

Flexed elbow, supinated forearm



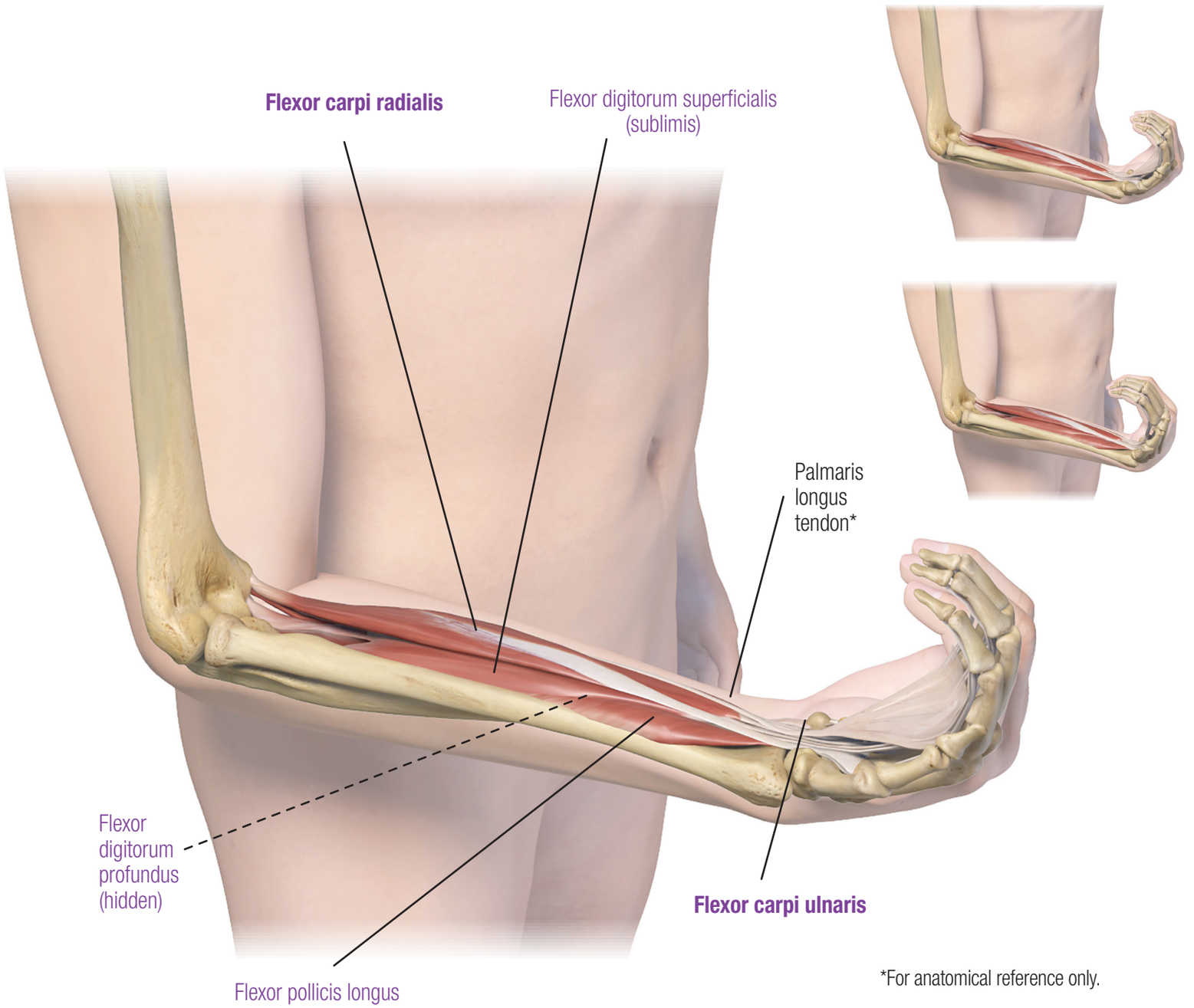
IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Dysphagia and Breathing Difficulties (continued)
In most cases, this is a consequence of weakening of muscles in the area of injection that are involved in breathing or oropharyngeal muscles that control swallowing or breathing (see *Boxed Warning*).

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Clinical presentation in upper limb (continued)

Flexed wrist



*For anatomical reference only.

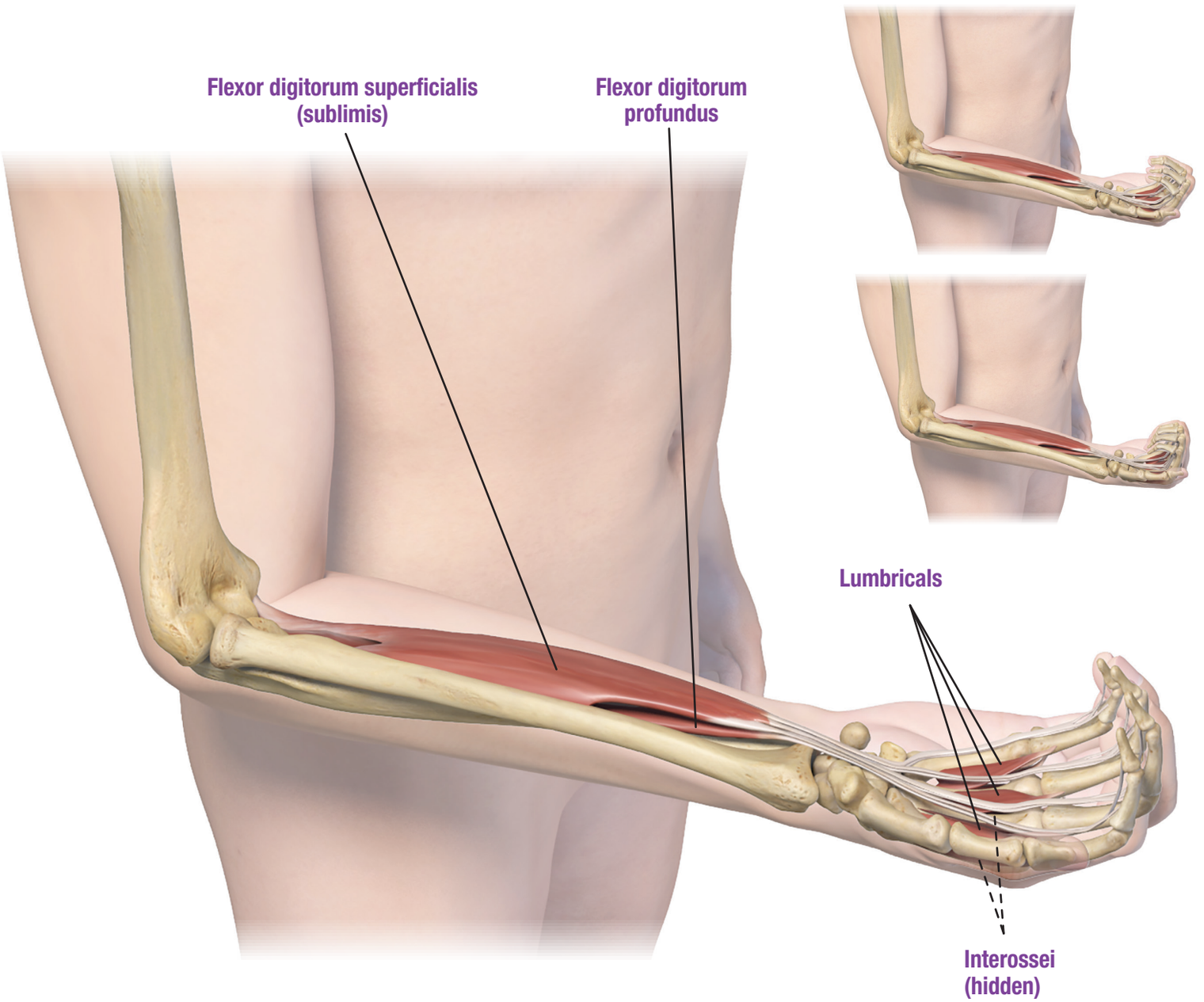
IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Pulmonary Effects of BOTOX in Patients With Compromised Respiratory Status Treated for Spasticity
Patients with compromised respiratory status treated with BOTOX for spasticity should be monitored closely.

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Clinical presentation in upper limb (continued)

Flexed fingers



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

Bronchitis and Upper Respiratory Tract Infections in Patients Treated for Spasticity

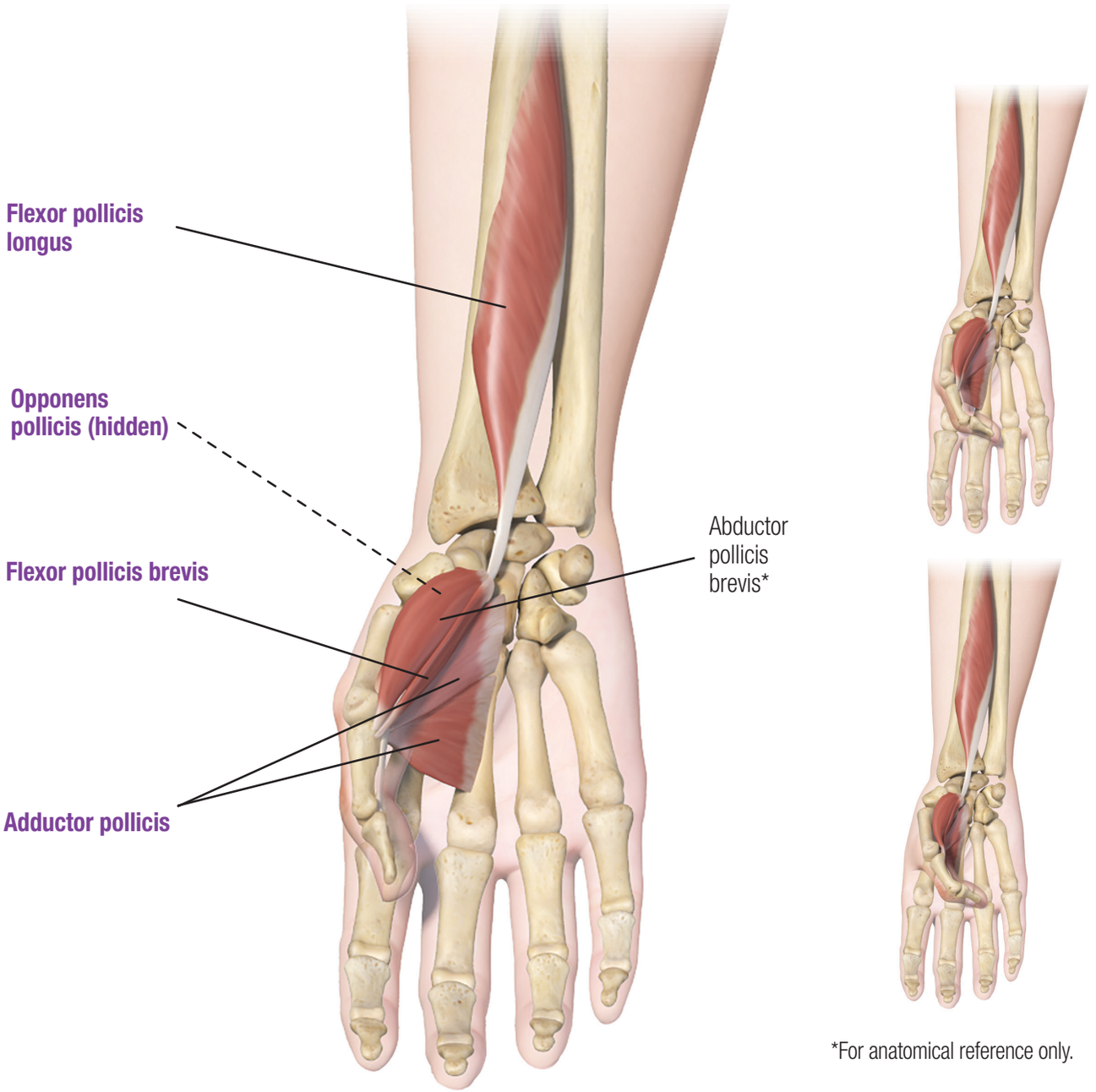
Bronchitis was reported more frequently as an adverse reaction in adult patients treated for upper limb spasticity with BOTOX (3% at 251 Units to 360 Units total dose) compared to placebo (1%). In adult patients with reduced lung function treated for upper limb spasticity, upper respiratory tract infections were also reported more frequently as adverse reactions in patients treated with BOTOX (11% at 360 Units total dose; 8% at 240 Units total dose) compared to placebo (6%).

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Clinical presentation in upper limb (continued)

Thumb in palm



*For anatomical reference only.

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

Bronchitis and Upper Respiratory Tract Infections in Patients Treated for Spasticity (continued)

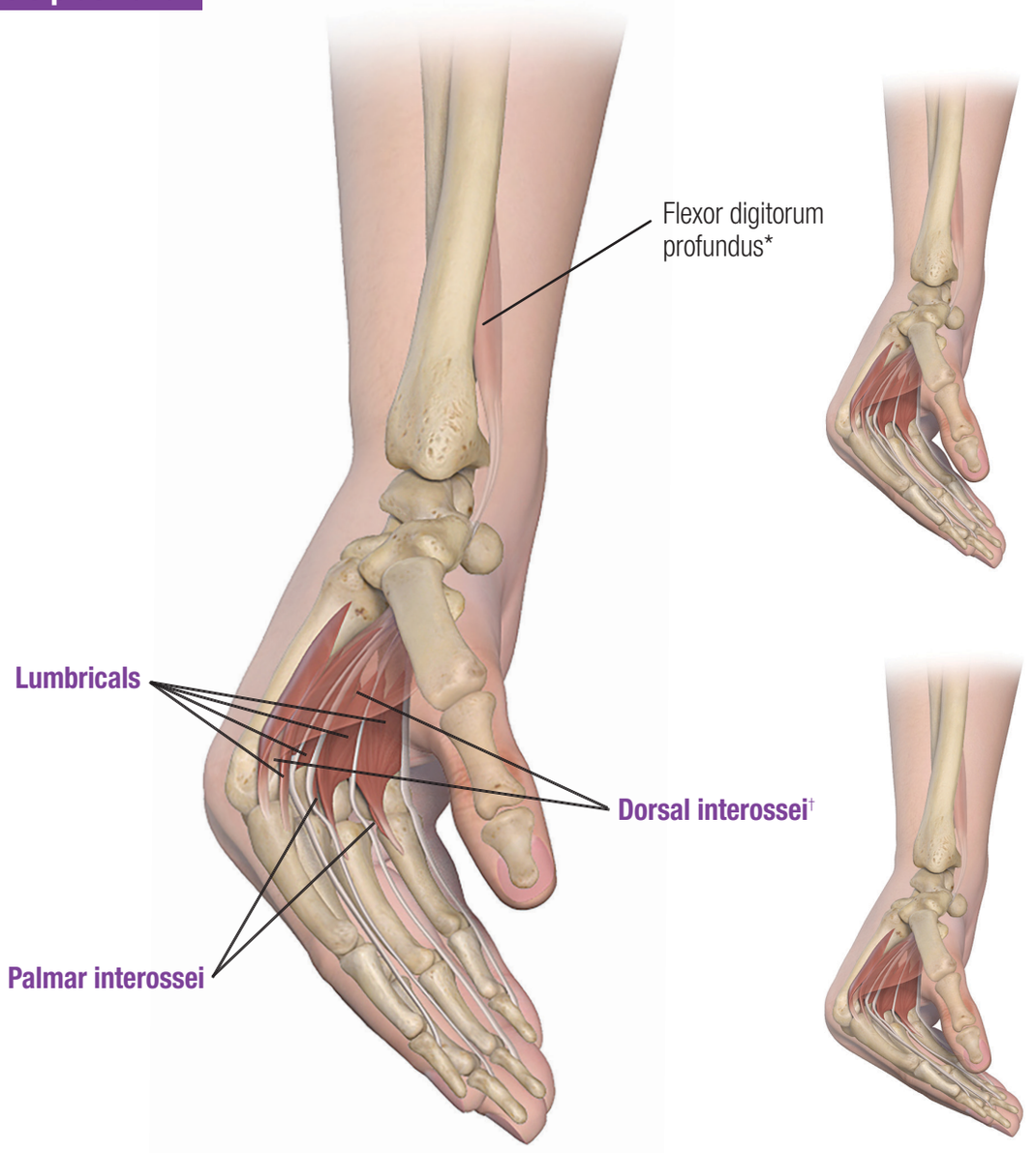
In adult patients treated for lower limb spasticity, upper respiratory tract infections were reported more frequently as an adverse reaction in patients treated with BOTOX (2% at 300 Units to 400 Units total dose) compared to placebo (1%).

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Clinical presentation in upper limb (continued)

Intrinsic plus hand



*The flexor digitorum profundus does not contribute to the intrinsic plus hand posture but has been included for reference as the lumbricals originate from its tendons.

†First dorsal interosseous made transparent to improve visibility of the lumbricals.

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

Human Albumin and Transmission of Viral Diseases

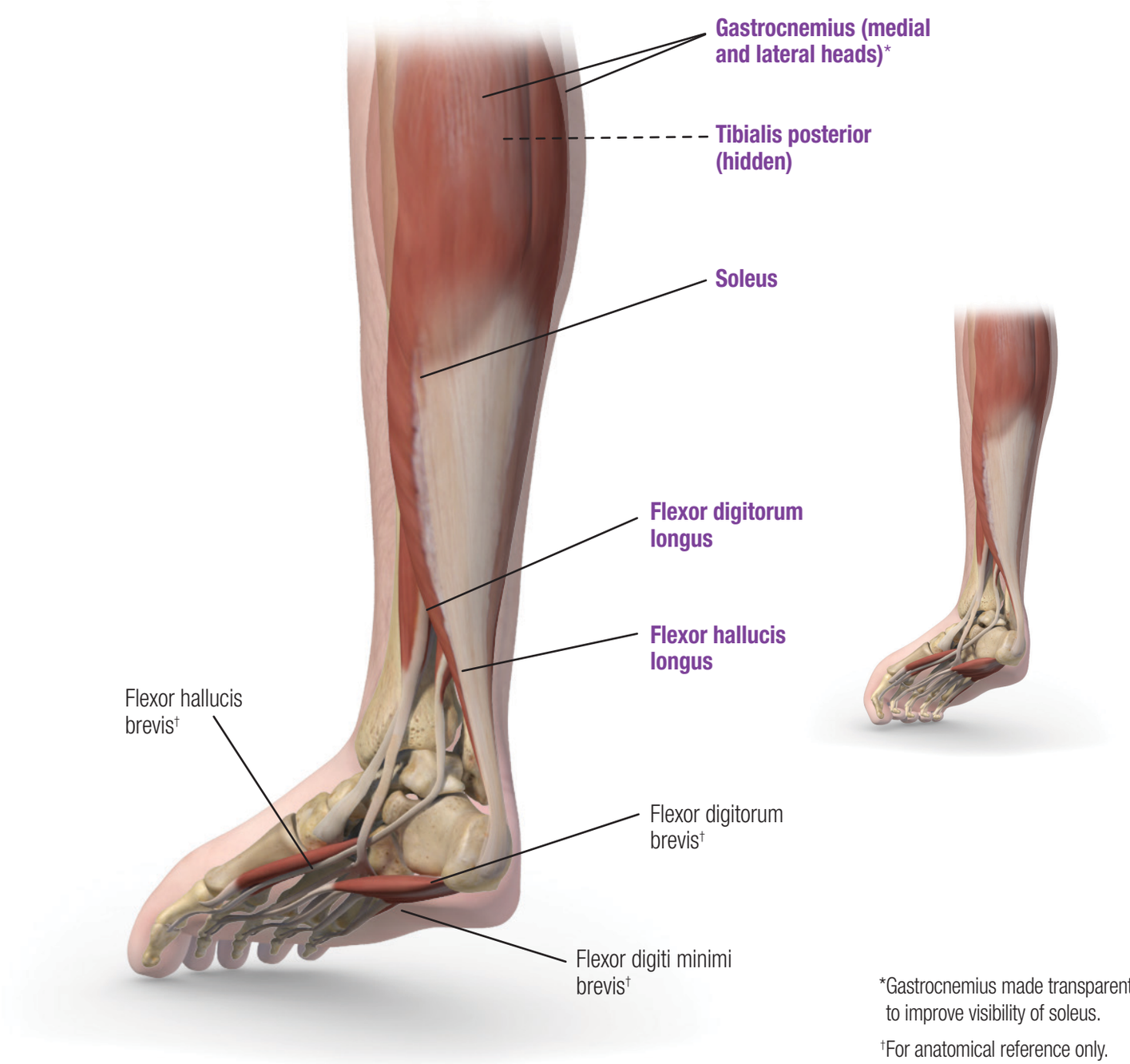
This product contains albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases and variant Creutzfeldt-Jakob disease (vCJD). There is a theoretical risk for transmission of Creutzfeldt-Jakob 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

Clinical presentation in lower limb

Equinovarus foot ± flexed toes



*Gastrocnemius made transparent to improve visibility of soleus.

†For anatomical reference only.

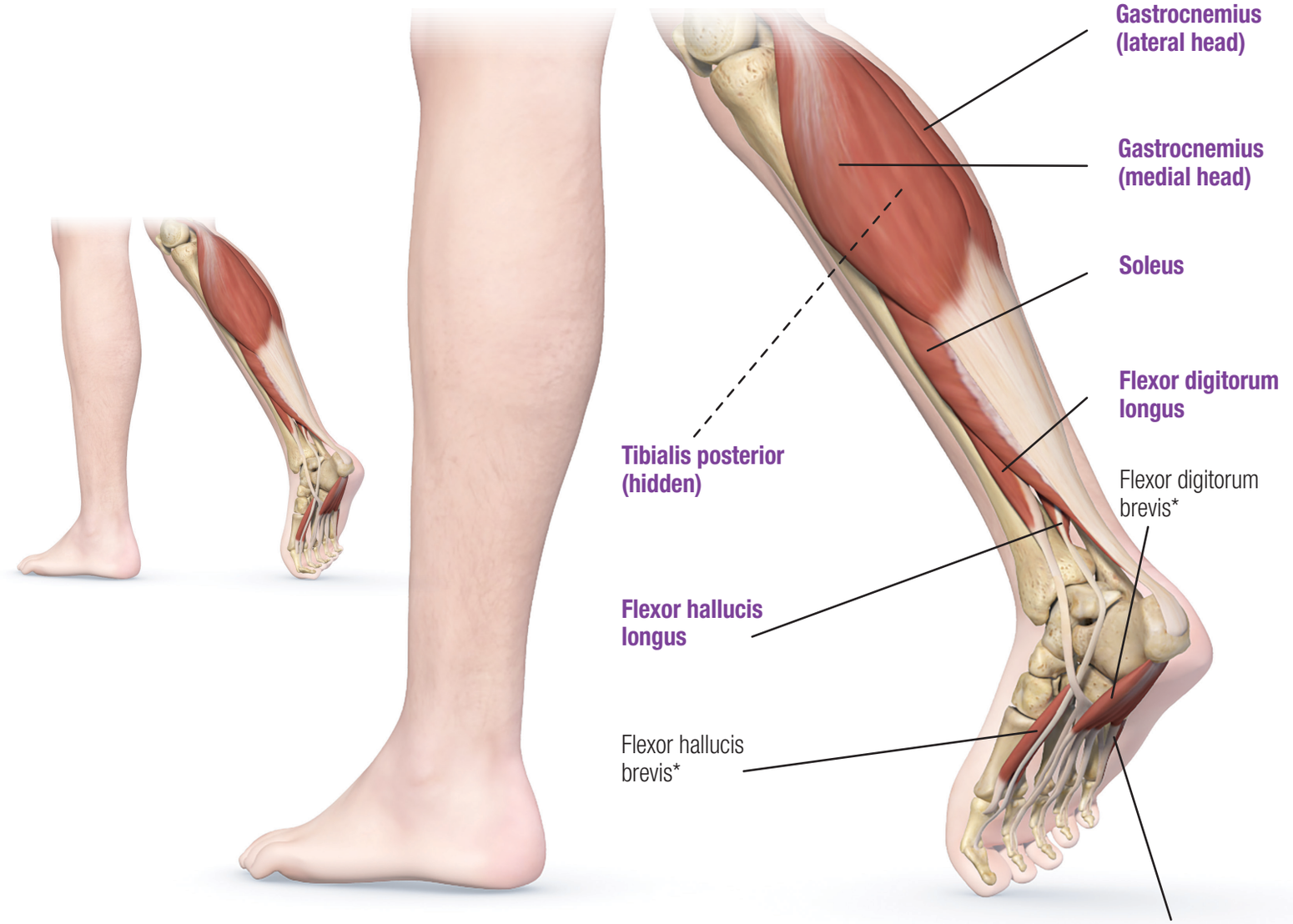
IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS
Adverse reactions to BOTOX for injection are discussed in greater detail in the following sections: *Boxed Warning*, *Contraindications*, and *Warnings and Precautions*.

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Clinical presentation in lower limb (continued)

Flexed ankle, flexed toes



*For anatomical reference only.

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Adult Upper Limb Spasticity
The most frequently reported adverse reactions following injection of BOTOX for upper limb spasticity include pain in extremity, muscular weakness, fatigue, nausea, and bronchitis.

Please see additional Important Safety Information throughout.

BOTOX®
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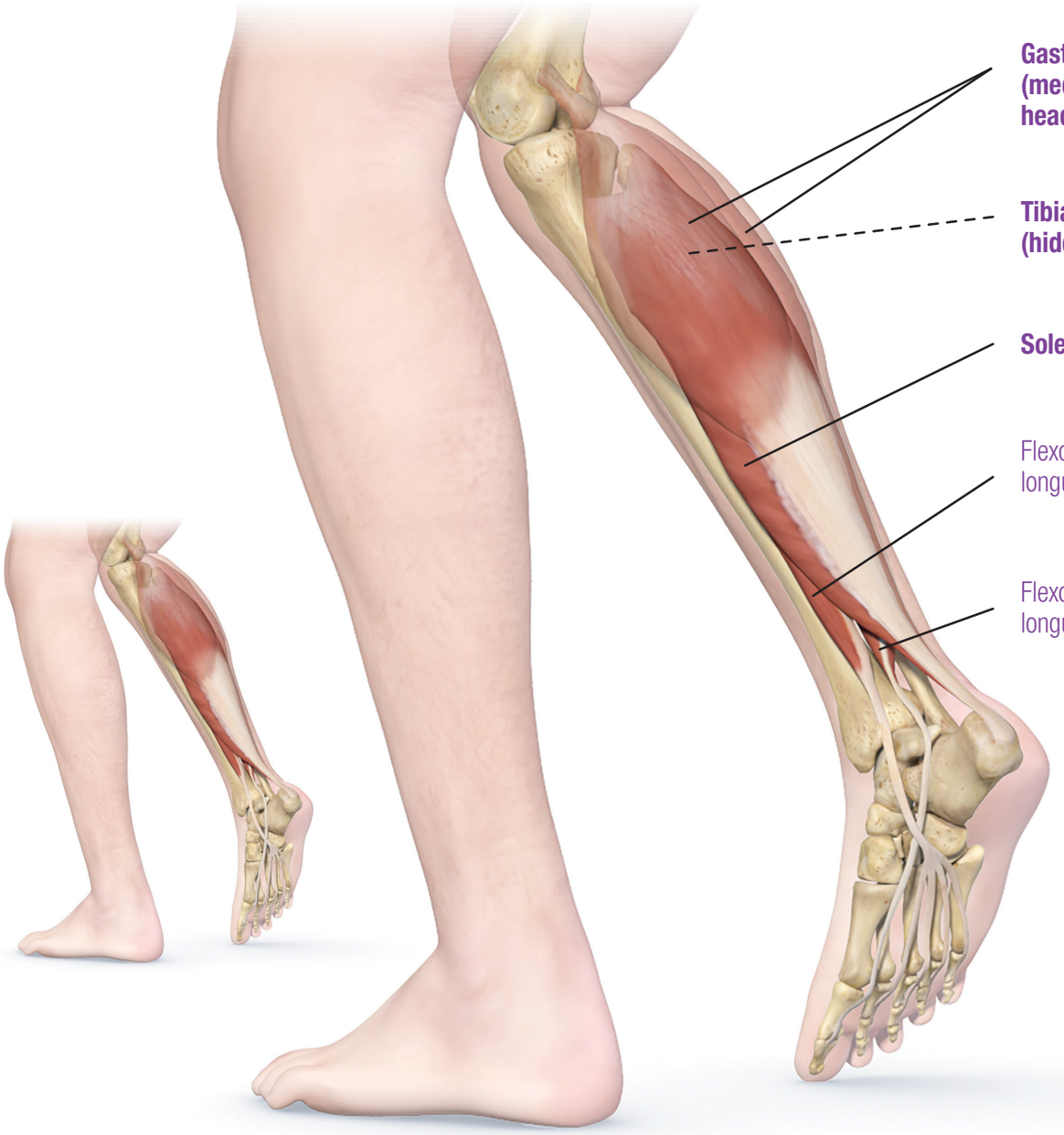
Clinical presentation in lower limb (continued)

Flexed knee*, flexed ankle



*Flexed knee is included for anatomical reference only as this posture is helpful during patient assessment when determining the contribution of the soleus and the gastrocnemius to the observed spasticity in the ankle. BOTOX® is not approved to decrease the severity of increased muscle tone in the knee.

†Gastrocnemius made transparent to improve visibility of soleus.

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)

Adult Lower Limb Spasticity

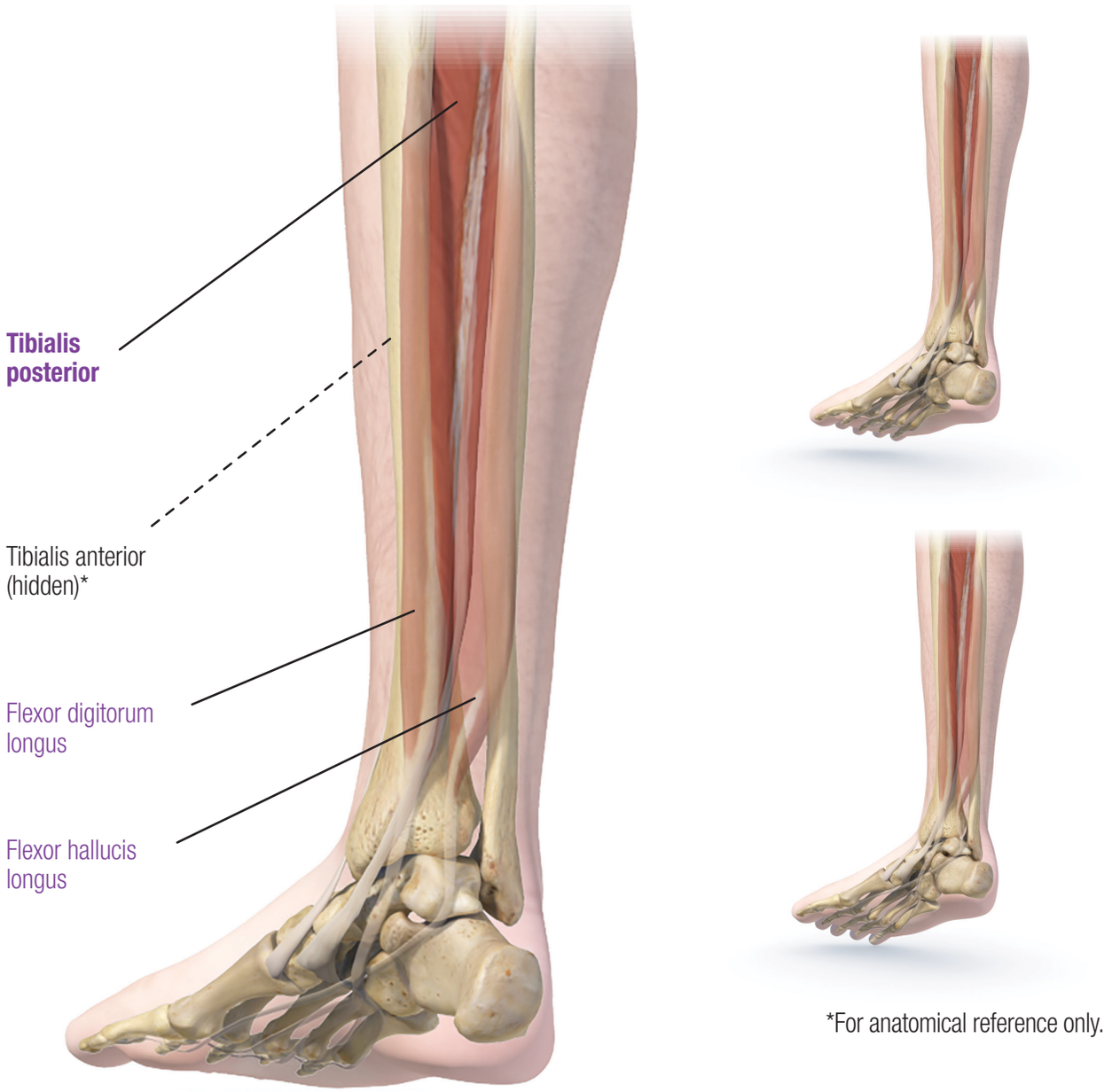
The most frequently reported adverse reactions following injection of BOTOX for lower limb spasticity include arthralgia, back pain, myalgia, upper respiratory tract infection, and injection-site pain.

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Clinical presentation in lower limb (continued)

Inverted/supinated foot



*For anatomical reference only.

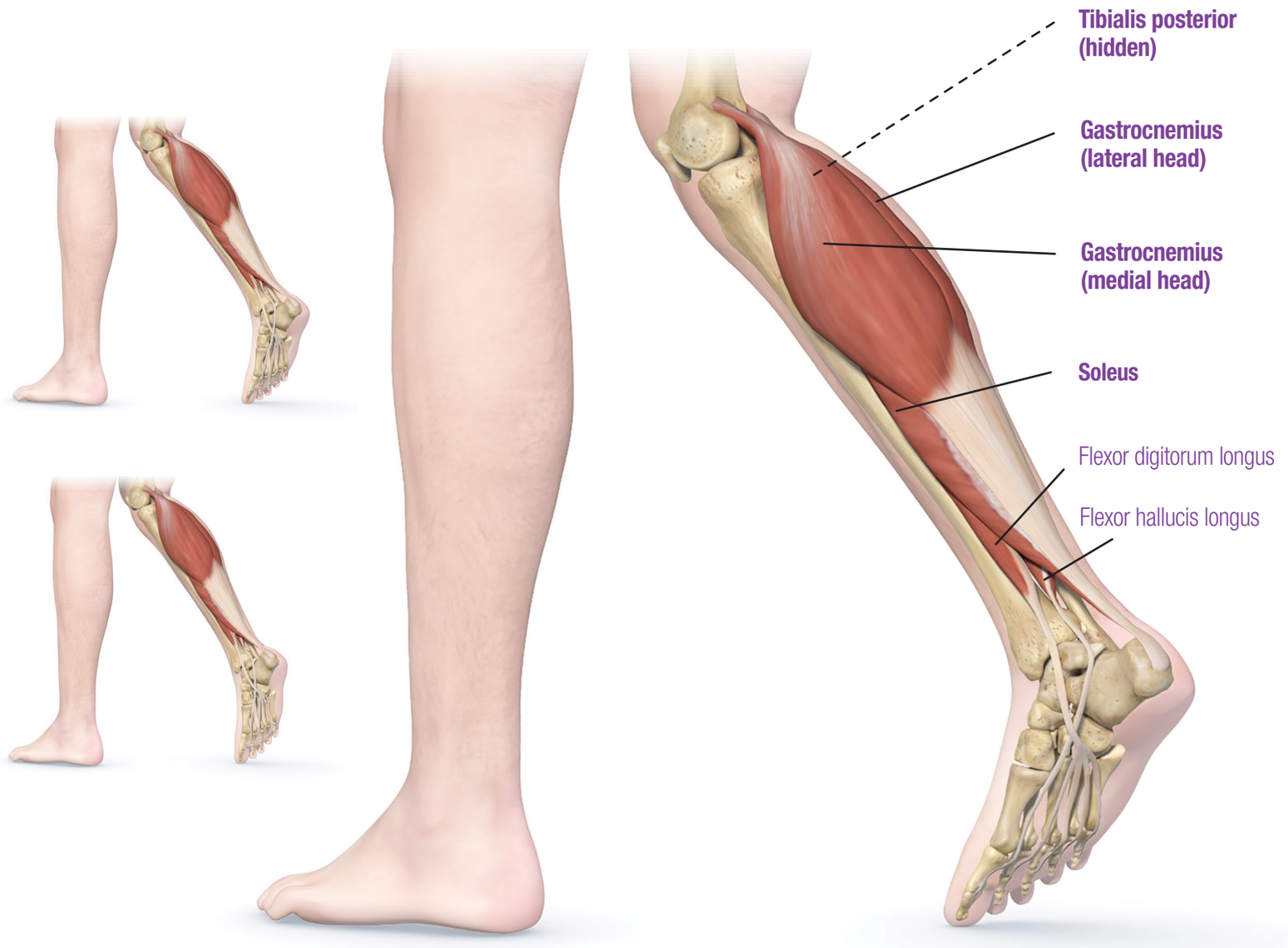
IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Postmarketing Experience
Adverse reactions that have been identified during postapproval use of BOTOX are discussed in greater detail in *Postmarketing Experience* (Section 6.3 of the Prescribing Information).

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Clinical presentation in lower limb (continued)

Flexed ankle

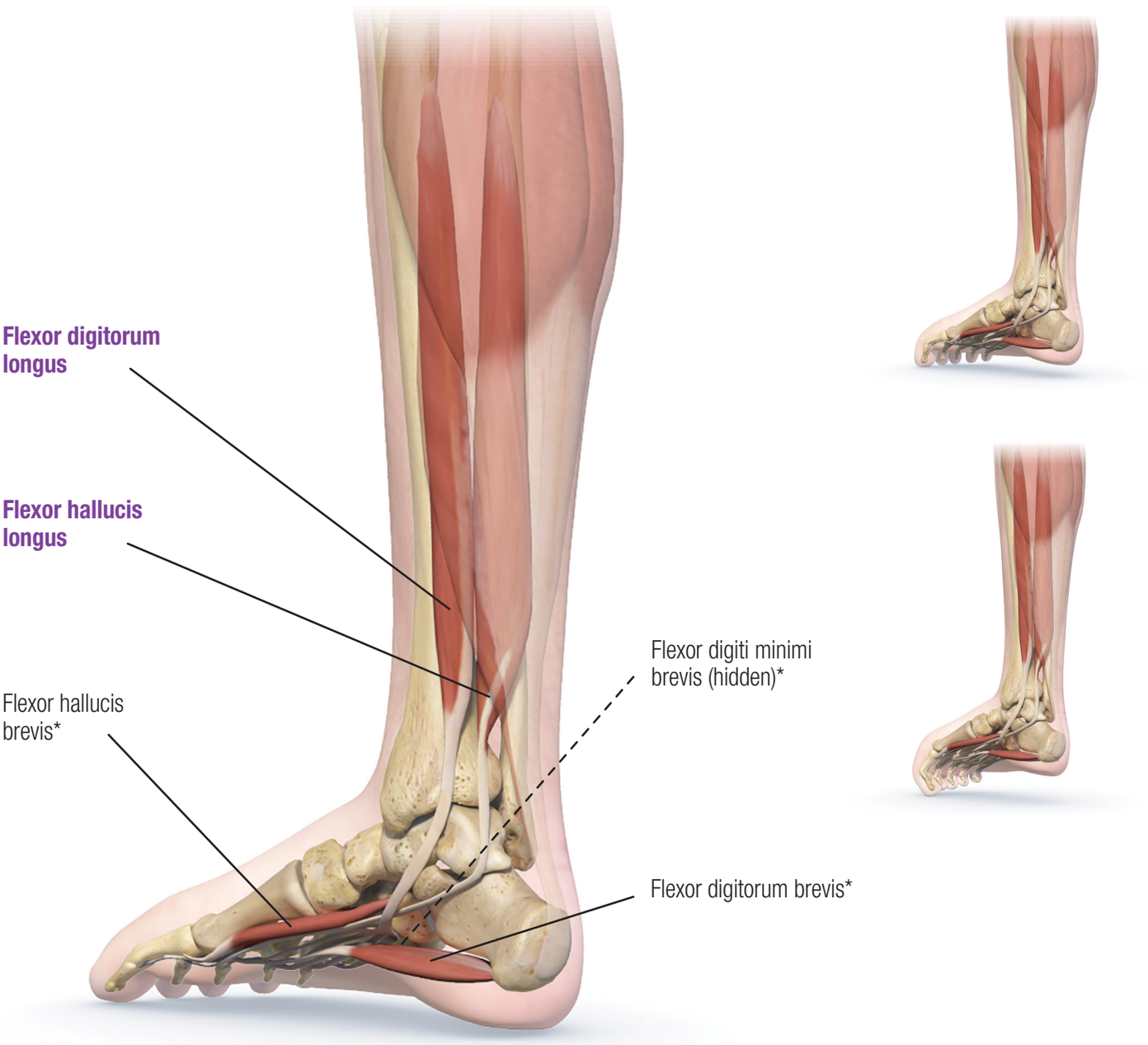


IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Postmarketing Experience (continued)
There have been spontaneous reports of death, sometimes associated with dysphagia, pneumonia, and/or other significant debility or anaphylaxis, after treatment with botulinum toxin.

Please see additional Important Safety Information throughout.

Clinical presentation in lower limb (continued)

Flexed toes



*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.

Please see additional Important Safety Information throughout.

Clinical data summary for BOTOX® in Adult Spasticity

Proven to improve muscle tone and treatment response in Adult Upper and Lower Limb Spasticity[4-7]

Randomized, multicenter, double-blind, placebo-controlled studies in post-stroke adults

Adult ULS				
	Number of patients	**Baseline Ashworth score[a]**	**BOTOX® dosage**	**Labeled endpoints**
Study 1	N = 126 BOTOX® (n = 64) Placebo (n = 62)	Wrist ≥ 3 Finger ≥ 2	200 Units to 240 Units	Median change from baseline in wrist flexor muscle tone (Ashworth Scale)[b]
Study 2	N = 91 BOTOX® (n = 65) Placebo (n = 26)	Elbow ≥ 2 Wrist ≥ 3	360 Units (n = 21) 180 Units (n = 23) 90 Units (n = 21)	Median change from baseline in wrist flexor muscle tone (expanded Ashworth Scale)[b]
Study 3	N = 88 BOTOX® (n = 69) Placebo (n = 19)	Elbow ≥ 2 Wrist and/or Finger ≥ 3	360 Units (n = 23) 180 Units (n = 23) 90 Units (n = 23)	Median change from baseline in elbow and wrist flexor muscle tone (expanded Ashworth Scale)[c]
Study 4	N = 170 BOTOX® (n = 87) Placebo (n = 83)	Wrist ≥ 3 Finger ≥ 2	20 Units in the adductor pollicis 20 Units in the flexor pollicis longus	Median change from baseline in thumb flexor muscle tone (modified Ashworth Scale [MAS])[d]
Study 5	N = 109 BOTOX® (n = 72) Placebo (n = 37)	Wrist ≥ 3 Finger ≥ 2 Thumb ≥ 2	Low-dose group (n = 14) 15 Units into the adductor pollicis 15 Units into the flexor pollicis longus High-dose group (n = 43) 20 Units into the adductor pollicis 20 Units into the flexor pollicis longus	Median change from baseline in thumb flexor muscle tone (MAS)[e] and Clinical Global Impression (CGI)[d]
Study 6	N = 124 BOTOX® (n = 61) BOTOX® + placebo (n = 63)	Elbow ≥ 3 Finger or Wrist ≥ 2	400 Units (n = 61) 240 Units (n = 63)	Mean change from baseline in elbow flexor muscle tone (MAS)[b]
Study participants received BOTOX® 240 Units in the wrist and finger flexors plus either placebo (n = 63) or an additional 160 Units of BOTOX® (400 Units total; n = 61) in the elbow flexors (biceps brachii, brachioradialis, and brachialis).				

[a]Includes original, expanded, and modified Ashworth Scales. [b]Primary endpoint at Week 6. [c]Primary endpoint at Week 4. [d]Secondary endpoint at Week 6. [e]Other endpoint at Week 6.

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®
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Clinical data summary for BOTOX® in Adult Spasticity (continued)

Adult LLS				
	Number of patients	**Baseline MAS**	**BOTOX® dosage**	**Labeled endpoints**
Study 7	N = 468 BOTOX® (n = 233) Placebo (n = 235)	Ankle ≥ 3	300 Units to 400 Units	Mean change from baseline in ankle flexor score (modified Ashworth Scale)[a] Mean Physician Global Assessment of Response (CGI)[a]

[a]Co-primary endpoint: Average of scores at Weeks 4 and 6.

BOTOX® provided significant improvements in muscle tone in Adult Spasticity[4]

0.5- to 2-point change from baseline in Ashworth Scale* score vs 0 to 1 point for placebo

See pages 28-43 for additional data and insights on BOTOX® for Adult Spasticity

*Includes original, expanded, and modified Ashworth Scales.

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

Clinical data summary for BOTOX® in Adult Spasticity (continued)

Established and well-characterized safety profile[4]

Adverse reactions reported by ≥ 2% of BOTOX® treated patients and more frequent than in placebo-treated patients in Adult Spasticity double-blind, placebo-controlled clinical trials.

Adult ULS (Studies 1-6)[4]				
Adverse reactions	**BOTOX® 251-360 Units (N = 115) %**	**BOTOX® 150-250 Units (N = 188) %**	**BOTOX® < 150 Units (N = 54) %**	**Placebo (N = 182) %**
Gastrointestinal disorder				
Nausea	3	2	2	1
General disorders and administration site conditions				
Fatigue	3	2	2	0
Infections and infestations				
Bronchitis	3	2	0	1
Musculoskeletal and connective tissue disorders				
Pain in extremity	6	5	9	4
Muscular weakness	0	4	2	1

For Adult ULS, 22 adult patients enrolled in double-blind, placebo-controlled studies and received ≥ 400 Units of BOTOX® for treatment of ULS. In addition, 44 adults received ≥ 400 Units of BOTOX® for 4 consecutive treatments over ≈ 1 year for treatment of ULS. The type and frequency of adverse reactions observed in patients treated with 400 Units of BOTOX® were similar to those reported in patients treated for ULS with 360 Units of BOTOX®. The discontinuation rate due to adverse events was 0.3% (n = 362) for BOTOX® vs 0.5% (n = 182) for placebo.[4,8]

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 data summary for BOTOX® in Adult Spasticity (continued)

Adult LLS (Study 7)[4]		
Adverse reactions	**BOTOX® (N = 231) %**	**Placebo (N = 233) %**
Musculoskeletal and connective tissue disorders		
Arthralgia	3	1
Back pain	3	2
Myalgia	2	1
Infections and infestations		
Upper respiratory tract infection	2	1
General disorders and administration site conditions		
Injection-site pain	2	1

For Adult LLS, 231 patients enrolled in a double-blind, placebo-controlled study, received 300-400 Units of BOTOX®, and were compared with 233 patients who received placebo. Patients were followed for an average of 91 days after injection.

BOTOX® is the most studied neurotoxin in the world

23,000
Patients studied[9,*]

3,300
Published papers[10,†]

20
Muscles
Approved for Adult Spasticity[4,‡]

*Across indications.

†Across therapeutic indications.

‡BOTOX® is approved for 15 muscles in Upper Limb Spasticity and 5 muscles in Lower Limb Spasticity.

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

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Guiding principles for effective BOTOX® treatment planning

PATTERN-BASED MUSCLE/DOSE SELECTION

Select muscle/dose combinations clinically proven to help treat common postures in Adult Spasticity

- Identify the patient's posture(s)
- Determine appropriate treatment goals and set expectations
- Choose muscles and doses aimed at helping meet goals and manage postures

Consider additional factors to help optimize muscle/dose selection

- Time since stroke
- Spasticity severity
- Caregiver input/perspective
- Additional clinical data insights (see pages 28-43)

SETTING PROPER GOALS AND TREATMENT EXPECTATIONS

Set specific and realistic goals related to key patient characteristics

- Primary symptoms/complaints
- Impact of condition on patient and exacerbating factors
- Time frame within which the patient hopes to achieve their goals

Share important details about BOTOX® treatment plan with patients/caregivers

- BOTOX® is not a cure. It helps reduce the severity of muscle stiffness and tightness in the arms and legs due to Adult Spasticity
- Multiple injection sessions may be needed
- It's important to return for a 4- to 6-week follow-up evaluation

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

Guiding principles for effective BOTOX® treatment planning (continued)

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

Explore additional clinical trial data on the following pages as part of your approach to BOTOX® treatment

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.

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

Pattern-based muscle/dose selections in Adult ULS

Study 6 evaluated BOTOX® 400 Units vs 240 Units in Adult ULS[11]

STUDY 6
MAS

Subjects
- N = 124
- Diagnosed with ULS in elbow, wrist, fingers, and thumb
- ≥ 3 months post-stroke

BOTOX® 400 UNITS (n = 61)

240 Units in the wrist, finger, and thumb flexors
+
160 Units in the elbow flexors

BOTOX® 240 UNITS (n = 63)

240 Units in the wrist, finger, and thumb flexors
+
Placebo in the elbow flexors

Week 0 — Week 2 — Week 4 — Week 6 — Week 12

PRIMARY ENDPOINT

Mean change from baseline in elbow flexor MAS score at Week 6[11]

OPEN-LABEL EXTENSION PHASE

Up to 3 repeat BOTOX® treatments (400 Units each) through 48 weeks[11]

Note: The efficacy data from Study 6, presented here and in the BOTOX® label, is not related to the open-label portion of the study

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

Increased Risk of Clinically Significant Effects With Preexisting Neuromuscular Disorders

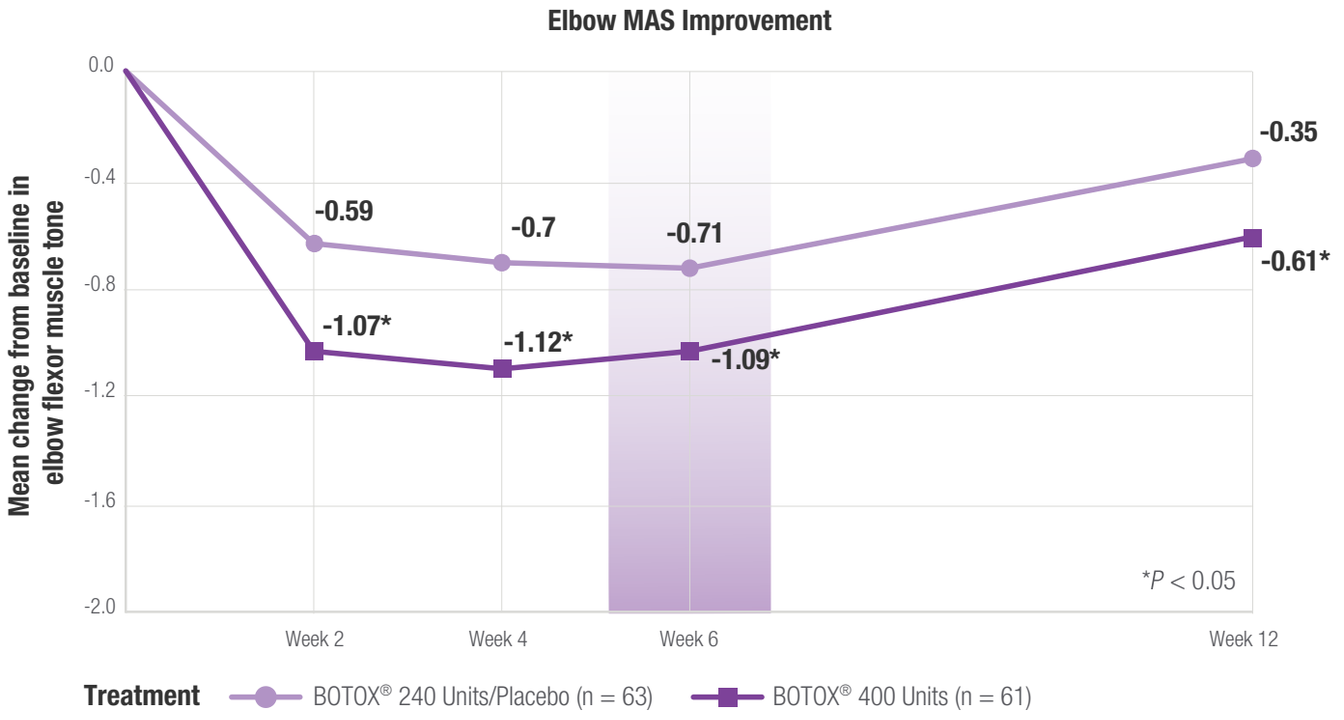
Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis (ALS), or neuromuscular junction disorders (eg, myasthenia gravis or Lambert-Eaton syndrome) should be monitored when given botulinum toxin. Patients with known or unrecognized neuromuscular disorders or neuromuscular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

Pattern-based muscle/dose selections in Adult ULS (continued)

STUDY 6 MAS

In Study 6, BOTOX® 400 Units demonstrated significant MAS reductions vs 240 Units[7,11]



Greater elbow MAS reductions were seen across Weeks 2, 4, 6, and 12 in patients receiving BOTOX® 400 Units vs patients receiving BOTOX® 240 Units + placebo[11]

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*).

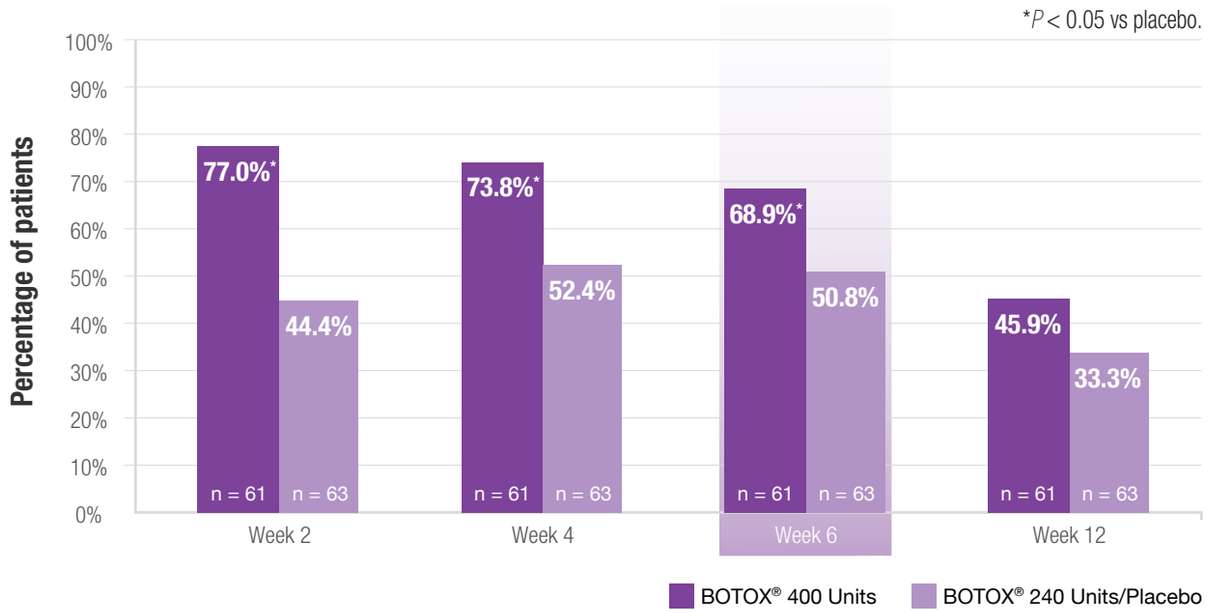
Please see additional Important Safety Information throughout.

Pattern-based muscle/dose selections in Adult ULS (continued)

STUDY 6 MAS

In Study 6, BOTOX® 400 Units demonstrated significant MAS reductions vs 240 Units[7]

Percentage of Patients Who Had a MAS Reduction (≥ 1 from Baseline) in Elbow Flexors



The responder rate analysis supports the statistically significant change from baseline in elbow flexor MAS score at Week 6. In the clinical study report, the responder rate analysis at Week 6 for elbow flexors is the primary endpoint, while change from baseline in MAS score in elbow flexors is a secondary endpoint. In the final labeling, however, mean change from baseline in elbow MAS score at Week 6 is the primary endpoint.

No new safety signals were seen in Study 6[11]

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Pulmonary Effects of BOTOX in Patients With Compromised Respiratory Status Treated for Spasticity
Patients with compromised respiratory status treated with BOTOX for spasticity should be monitored closely.

Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Notes

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

Bronchitis and Upper Respiratory Tract Infections in Patients Treated for Spasticity

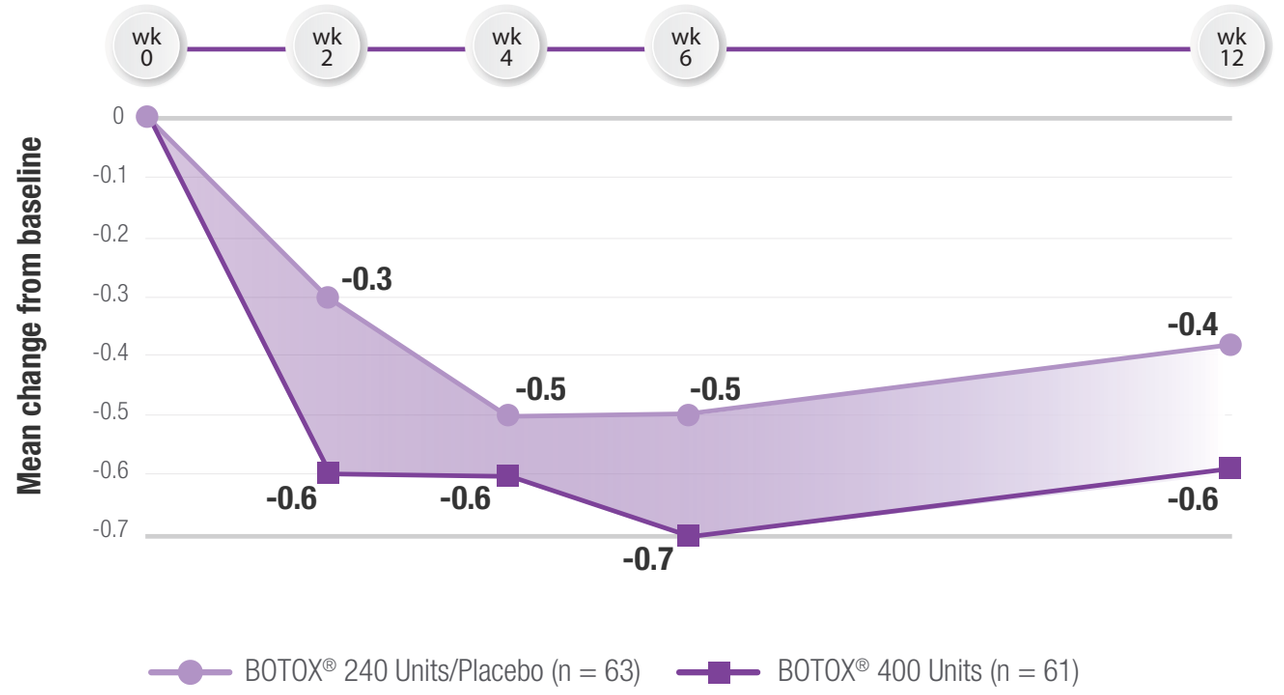
Bronchitis was reported more frequently as an adverse reaction in adult patients treated for upper limb spasticity with BOTOX (3% at 251 Units to 360 Units total dose) compared to placebo (1%). In adult patients with reduced lung function treated for upper limb spasticity, upper respiratory tract infections were also reported more frequently as adverse reactions in patients treated with BOTOX (11% at 360 Units total dose; 8% at 240 Units total dose) compared to placebo (6%). In adult patients treated for lower limb spasticity, upper respiratory tract infections were reported more frequently as an adverse reaction in patients treated with BOTOX (2% at 300 Units to 400 Units total dose) compared to placebo (1%).

Please see additional Important Safety Information throughout.

The impact of BOTOX® was studied using the Disability Assessment Scale (DAS) in Study 6[7,11]

Change in DAS Principal Therapeutic Target Rating

STUDY 6 DAS



STUDY DESIGN[11]

Study 6 was a phase 3, multicenter, randomized, double-blind placebo-controlled clinical trial for Adult ULS in patients who were ≥ 3 months post-stroke (n = 124). Patients received 240 units of BOTOX® in the wrist, finger, and thumb flexors plus either an additional 160 units of BOTOX® (400 Units total; n = 61) or placebo (240 Units total; n = 63) in the elbow flexors. The primary endpoint was the mean change from baseline in elbow flexor MAS at Week 6. Patients were followed for 12 weeks during the double-blind phase.

LIMITATIONS[7,11]

The DAS principal therapeutic target was a ranked secondary endpoint. Other DAS domains were prespecified, nonranked, exploratory endpoints and not adjusted for multiplicity. Therefore, treatment difference cannot be regarded as statistically significant.

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

The Disability Assessment Scale is a measure of functional impairment that encompasses 4 domains[7]

Hygiene

Extent of maceration, ulceration, and/or palmar infection; palm and hand cleanliness; ease of cleanliness, nail trimming; degree of interference cause by hygiene-related disability

Pain Associated With Spasticity

Intensity of pain or discomfort related to upper limb spasticity and the degree of related interference in the patient's daily life

Dressing

Difficulty/ease in putting on clothing; degree of interference caused by dressing-related disability

Limb Position

Degree of physical, psychological, and/or social interference due to limb position-related disability in the patient's daily life

Scale

0 – No functional disability
1 – Mild disability; noticeable, but does not interfere significantly with normal activities
2 – Moderate disability; normal activities require increased effort/assistance
3 – Severe disability; normal activities are limited

Principal Therapeutic Target:
One DAS domain was selected as the primary focus for evaluation throughout the study period as agreed upon by the HCP and patient prior to the study treatment start.[7,11]

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*.

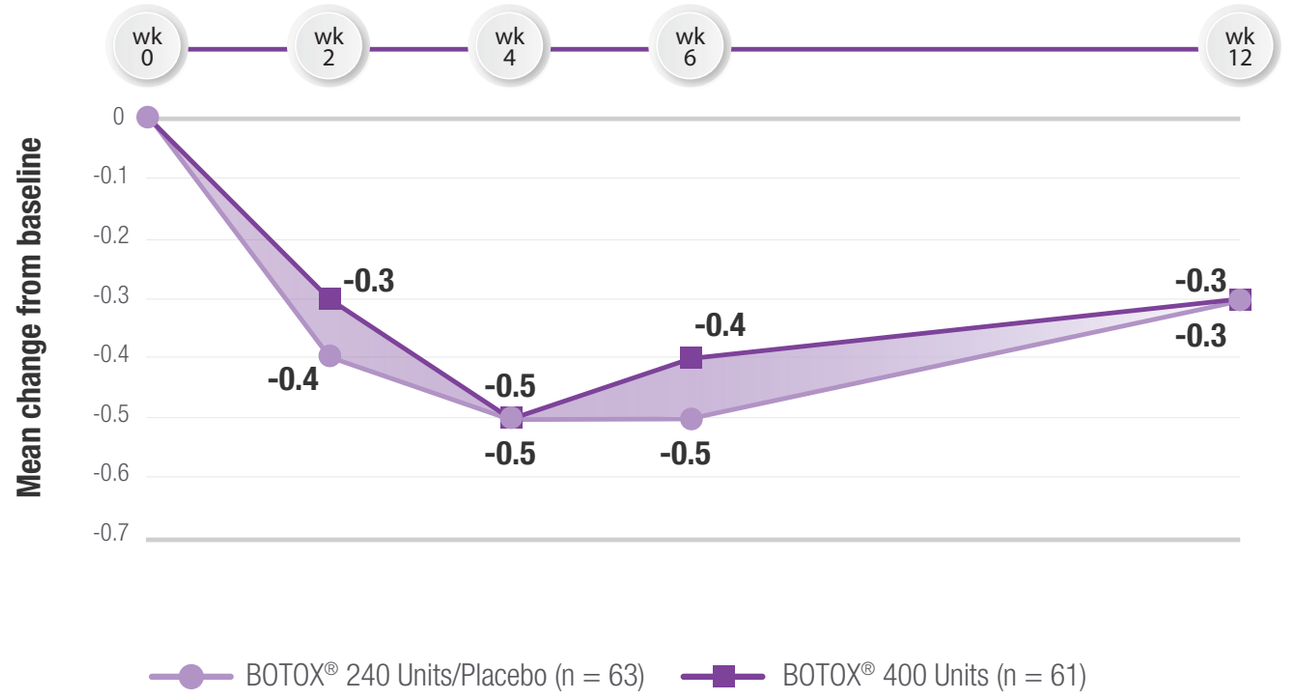
Please see additional Important Safety Information throughout.

The impact of BOTOX® was studied using the Disability Assessment Scale (DAS) in Study 6 (continued)[7,11]

Exploratory Endpoint

Change in DAS Hygiene Subscale Rating

STUDY 6 DAS



STUDY DESIGN[11]

Study 6 was a phase 3, multicenter, randomized, double-blind placebo-controlled clinical trial for Adult ULS in patients who were ≥ 3 months post-stroke (n = 124). Patients received 240 units of BOTOX® in the wrist, finger, and thumb flexors plus either an additional 160 units of BOTOX® (400 Units total; n = 61) or placebo (240 Units total; n = 63) in the elbow flexors. The primary endpoint was the mean change from baseline in elbow flexor MAS at Week 6. Patients were followed for 12 weeks during the double-blind phase.

LIMITATIONS[7,11]

The DAS principal therapeutic target was a ranked secondary endpoint. Other DAS domains were prespecified, nonranked, exploratory endpoints and not adjusted for multiplicity. Therefore, treatment difference cannot be regarded as statistically significant.

IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS (continued)

Adult Upper Limb Spasticity

The most frequently reported adverse reactions following injection of BOTOX for upper limb spasticity include pain in extremity, muscular weakness, fatigue, nausea, and bronchitis.

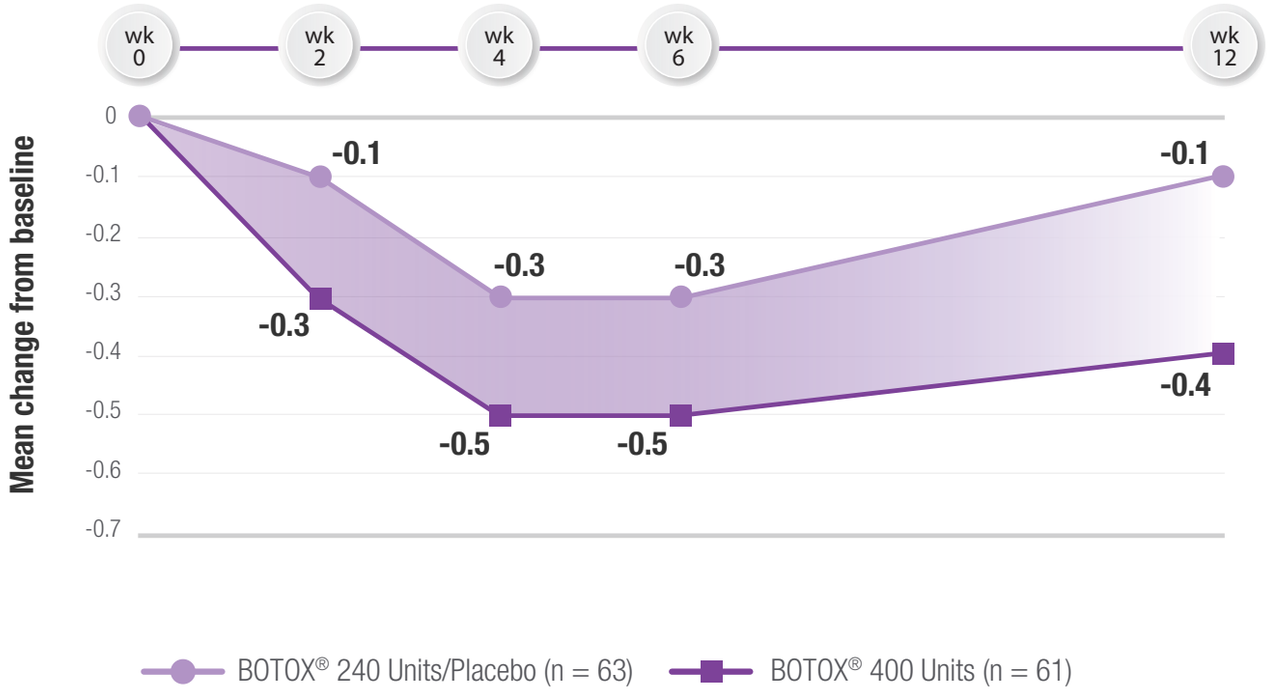
Please see additional Important Safety Information throughout.

The impact of BOTOX® was studied using the Disability Assessment Scale (DAS) in Study 6 (continued)[7,11]

Exploratory Endpoint

Change in DAS Pain Subscale Rating

STUDY 6 DAS



STUDY DESIGN[11]

Study 6 was a phase 3, multicenter, randomized, double-blind placebo-controlled clinical trial for Adult ULS in patients who were ≥ 3 months post-stroke (n = 124). Patients received 240 units of BOTOX® in the wrist, finger, and thumb flexors plus either an additional 160 units of BOTOX® (400 Units total; n = 61) or placebo (240 Units total; n = 63) in the elbow flexors. The primary endpoint was the mean change from baseline in elbow flexor MAS at Week 6. Patients were followed for 12 weeks during the double-blind phase.

LIMITATIONS[7,11]

The DAS principal therapeutic target was a ranked secondary endpoint. Other DAS domains were prespecified, nonranked, exploratory endpoints and not adjusted for multiplicity. Therefore, treatment difference cannot be regarded as statistically significant.

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Adult Lower Limb Spasticity
The most frequently reported adverse reactions following injection of BOTOX for lower limb spasticity include arthralgia, back pain, myalgia, upper respiratory tract infection, and injection-site pain

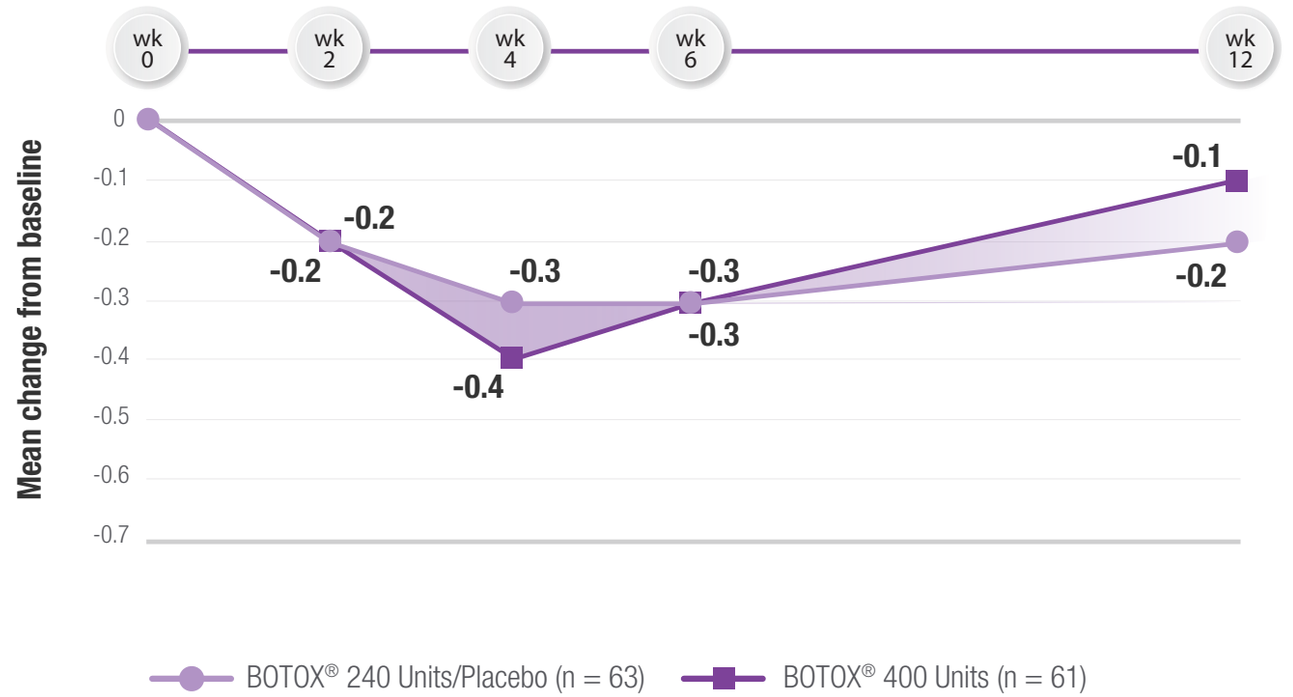
Please see additional Important Safety Information throughout.

The impact of BOTOX® was studied using the Disability Assessment Scale (DAS) in Study 6 (continued)[7,11]

Exploratory Endpoint

Change in DAS Dressing Subscale Rating

STUDY 6 DAS



STUDY DESIGN[11]

Study 6 was a phase 3, multicenter, randomized, double-blind placebo-controlled clinical trial for Adult ULS in patients who were ≥ 3 months post-stroke (n = 124). Patients received 240 units of BOTOX® in the wrist, finger, and thumb flexors plus either an additional 160 units of BOTOX® (400 Units total; n = 61) or placebo (240 Units total; n = 63) in the elbow flexors. The primary endpoint was the mean change from baseline in elbow flexor MAS at Week 6. Patients were followed for 12 weeks during the double-blind phase.

LIMITATIONS[7,11]

The DAS principal therapeutic target was a ranked secondary endpoint. Other DAS domains were prespecified, nonranked, exploratory endpoints and not adjusted for multiplicity. Therefore, treatment difference cannot be regarded as statistically significant.

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).

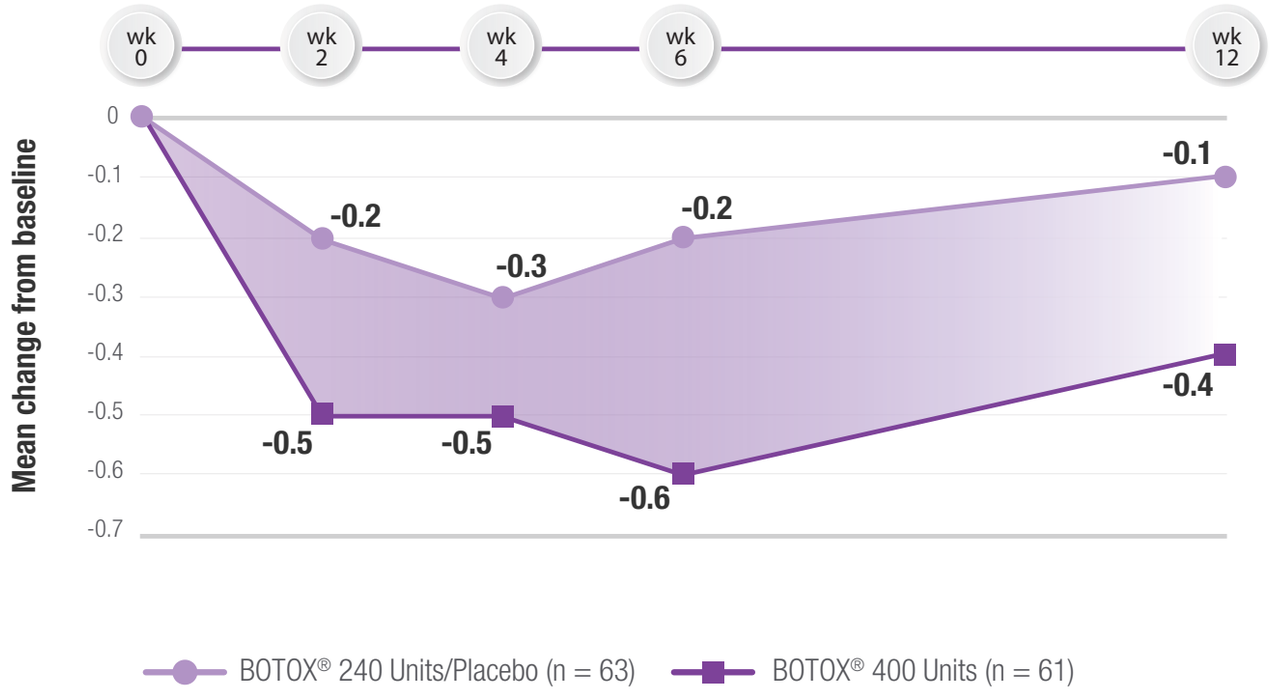
Please see additional Important Safety Information throughout.

The impact of BOTOX® was studied using the Disability Assessment Scale (DAS) in Study 6 (continued)[7,11]

Exploratory Endpoint

Change in DAS Limb Position Subscale Rating

STUDY 6 DAS



STUDY DESIGN[11]

Study 6 was a phase 3, multicenter, randomized, double-blind placebo-controlled clinical trial for Adult ULS in patients who were ≥ 3 months post-stroke (n = 124). Patients received 240 units of BOTOX® in the wrist, finger, and thumb flexors plus either an additional 160 units of BOTOX® (400 Units total; n = 61) or placebo (240 Units total; n = 63) in the elbow flexors. The primary endpoint was the mean change from baseline in elbow flexor MAS at Week 6. Patients were followed for 12 weeks during the double-blind phase.

LIMITATIONS[7,11]

The DAS principal therapeutic target was a ranked secondary endpoint. Other DAS domains were prespecified, nonranked, exploratory endpoints and not adjusted for multiplicity. Therefore, treatment difference cannot be regarded as statistically significant.

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

Notes

BOTOX®
onabotulinumtoxinA injection

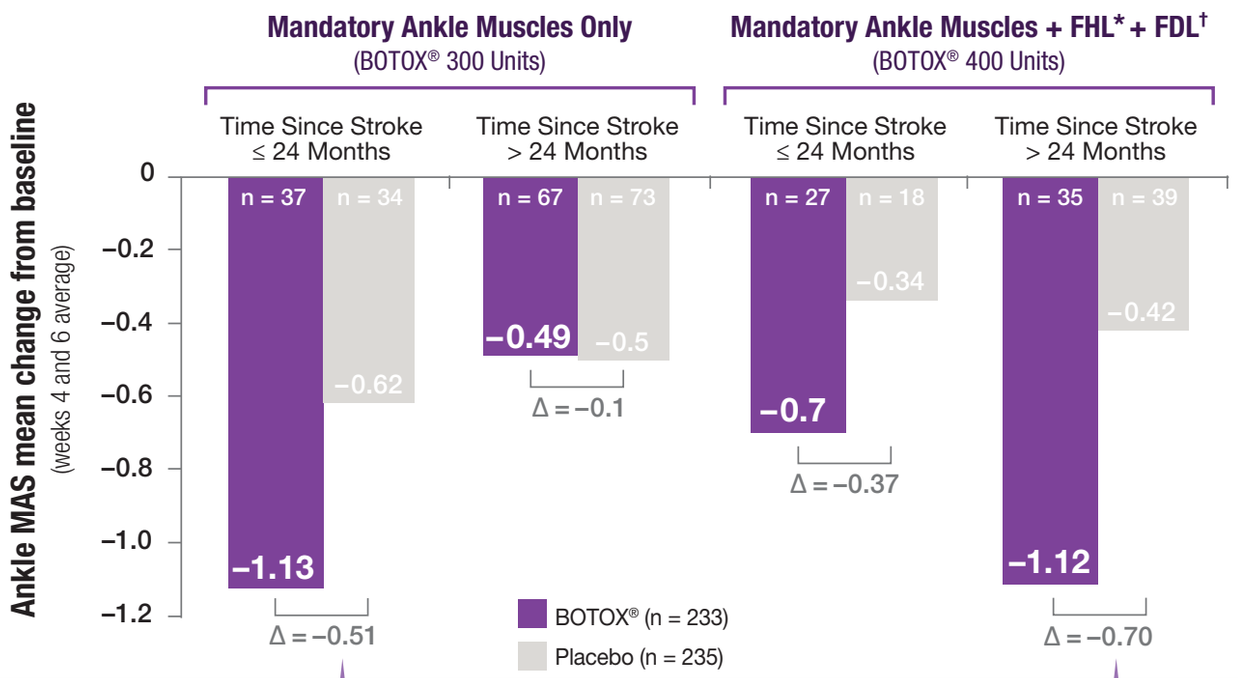
Notes

BOTOX® onabotulinumtoxinA injection

Pattern-based muscle/dose selections in Adult LLS

STUDY 7
POST-HOC ANALYSIS

In a post-hoc subgroup analysis, Adult LLS patients 2+ years post-stroke saw ankle MAS reduction from BOTOX® treatment when injected in both ankle and toe flexors[12]



*FHL = Flexor hallucis longus.
†FDL = Flexor digitorum longus.

BOTOX® injections (300 Units) into the ankle flexors alone in patients ≤ 2 years post-stroke was sufficient to provide ankle MAS reduction[12]

BOTOX® injections (400 Units) into both ankle and toe flexors in patients > 2 years post-stroke provided ankle MAS reduction[12]

STUDY DESIGN[12]

- Post-hoc analysis of the double-blind phase of the BOTOX® pivotal study for Adult LLS (REFLEX, Study 7)
- Subgroup analyses were performed on patients stratified by muscle selection (total BOTOX® dose/muscles injected) and time since stroke (≤ 2 years or > 2 years)
- Assessed impact of muscle selection patterns and time since stroke on ankle MAS and physician-assessed CGI based on change from baseline to average of Weeks 4/6 vs placebo

LIMITATIONS[12]

- It is unclear whether the results shown were due to the additional muscles injected or the increase in total BOTOX® dose administered
- The dilution of BOTOX® used in this study (4 mL of preservative-free saline per 100-Unit vial) was higher than the dilution recommended in the BOTOX® label (2 mL of preservative-free saline per 100-Unit vial). It is unknown whether this difference in dilution would have had any effect on outcomes through diffusion

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

Pattern-based muscle/dose selections in Adult LLS (continued)

Safety results from post-hoc analysis of REFLEX[12]

STUDY 7
POST-HOC ANALYSIS

Adverse Events (AEs)	BOTOX® (n = 231)[a]	Placebo (n = 233)[a]
Pain in extremity	4.8%	4.7%
Nasopharyngitis	3.5%	3.0%
Fall	2.6%	3.9%
Back pain	2.6%	1.7%
Arthralgia	3.5%	0.9%
Injection-site pain	2.2%	0.9%

[a]Two patients from each group discontinued before treatment and, therefore, were not included in the safety population.

- Treatment-emergent AEs were reported in 42% (97/231) of BOTOX®-treated patients vs 35.2% (82/233) of placebo-treated patients
  - The majority were mild or moderate and not considered to be related to study treatment
- Serious AEs occurred in 4.3% (10/231) of BOTOX®-treated patients vs 3.9% (9/233) of placebo-treated patients
  - 1 treatment-related serious AE occurred with placebo
- Discontinuations due to an AE occurred in 5 BOTOX®-treated patients vs 2 placebo-treated patients[12]

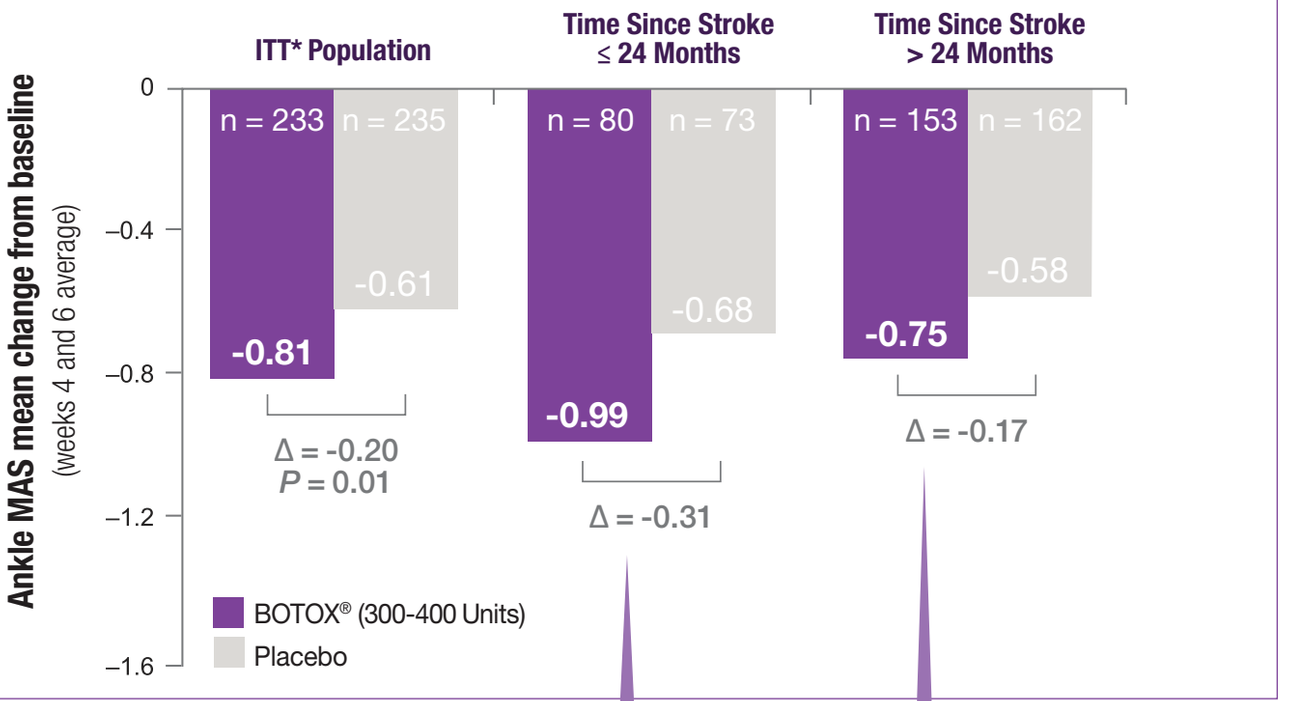
IMPORTANT SAFETY INFORMATION (continued)
DRUG INTERACTIONS (continued)
Use of anticholinergic drugs after administration of BOTOX may potentiate systemic anticholinergic effects. The effect of administering different botulinum neurotoxin products at the same time or within several months of each other 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

Evidence-based treatment initiation strategies for Adult LLS

STUDY 7 POST-HOC ANALYSIS

In another post-hoc subgroup analysis, Adult LLS patients treated with BOTOX® within 2 years post-stroke saw ankle MAS reduction[13]



*ITT = Intent-to-treat.

Early BOTOX® treatment (≤ 2 years post-stroke) provided greater ankle MAS reduction (vs placebo)[13]

Later BOTOX® treatment (> 2 years post-stroke) showed numerical differences in ankle MAS reduction (vs placebo)[13]

STUDY DESIGN[13]

- Post-hoc analysis of the BOTOX® pivotal study for Adult LLS (REFLEX, Study 7)
- Based on subgroup data from patients stratified by time since stroke (≤ 2 years or > 2 years)
- Assessed impact of time to BOTOX® treatment initiation following stroke on ankle MAS and physician-assessed CGI based on change from baseline to average of Weeks 4 and 6 vs placebo

LIMITATIONS[13]

- The early/late post-stroke treatment stratification used in this post-hoc analysis (≤ 2 years or > 2 years) differed from the time points prespecified and prospectively analyzed in the original REFLEX study protocol (≤ 4 years vs > 4 years). This may be a potential limitation to this study
- The 2 patient subgroups studied in this analysis differed markedly in size and mean baseline time since stroke, representing 2 potentially very different patient populations
  - Size: n = 153 (≤ 2 years post-stroke) vs n = 315 (> 2 years post-stroke)
  - Baseline time since stroke (mean): 1.1 years (≤ 2 years post-stroke) vs 7.5 years (> 2 years post-stroke)

IMPORTANT SAFETY INFORMATION (continued)

CONTRAINDICATIONS

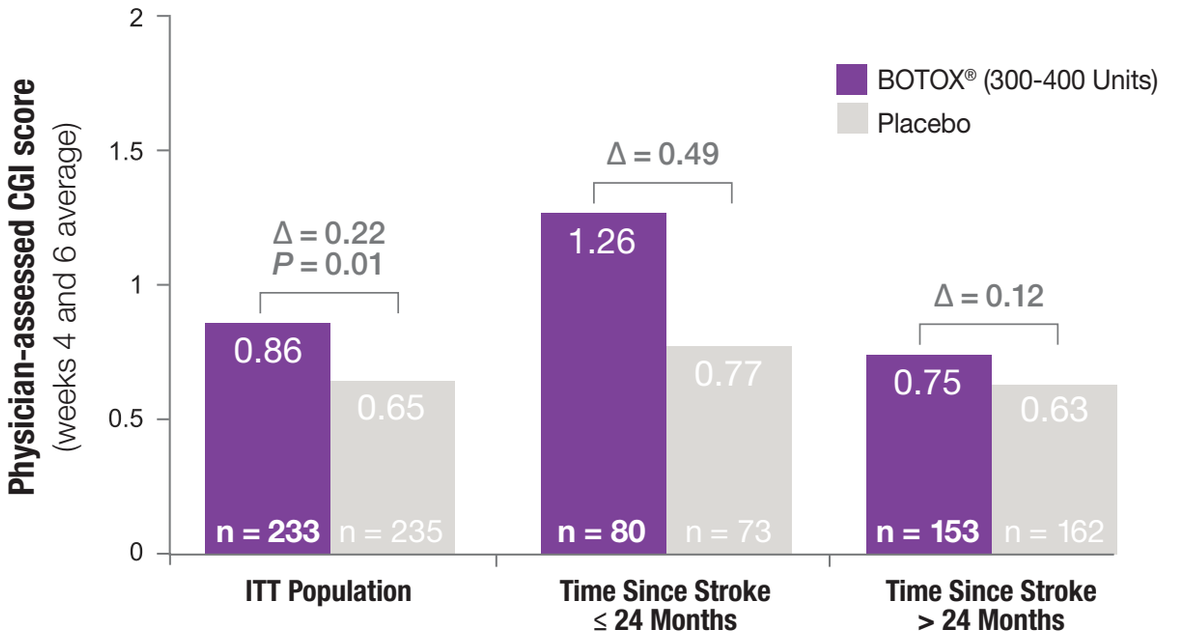
BOTOX is contraindicated in the presence of infection at the proposed injection site(s) and in patients who are hypersensitive to any botulinum toxin product or to any of the components in the formulation.

Please see additional Important Safety Information throughout.

Evidence-based treatment initiation strategies for Adult LLS (continued)

In the same study, earlier BOTOX® intervention also provided higher CGI scores[13]

STUDY 7
POST-HOC ANALYSIS



Early BOTOX® treatment (≤ 2 years post-stroke) provided increased CGI scores (vs placebo)[13]

Later BOTOX® treatment (> 2 years post-stroke) showed numerical differences in CGI scores (vs placebo)[13]

LIMITATIONS[13] (continued)

- Statistically significant between-group differences (ie, between time-since-stroke subgroups) could not be determined because the REFLEX study was not designed to be statistically powered for the current subgroup analysis
  - Note: This post-hoc analysis compared BOTOX® to placebo within the ankle MAS and CGI endpoints. It did not assess outcomes among the subgroups (≤ 2 years vs > 2 years post-stroke)

BOTOX® onabotulinumtoxinA injection

Muscles by posture in Adult Spasticity

Posture	Muscles	
	Upper limb spasticity[4, 14, 15]	
Flexed elbow	• Biceps brachii • Brachialis	• Brachioradialis • Pronator teres
Pronated/supinated forearm	• Biceps brachii (supination) • Supinator (supination)*	• Pronator teres (pronation) • Pronator quadratus (pronation)
Flexed wrist	• Flexor carpi radialis • Flexor carpi ulnaris • Flexor digitorum superficialis (sublimis)	• Flexor digitorum profundus • Flexor pollicis longus[14] • Palmaris longus*
Flexed fingers	• Flexor digitorum superficialis (sublimis) • Flexor digitorum profundus	• Lumbricals • Interossei
Thumb in palm	• Flexor pollicis longus • Flexor pollicis brevis • Opponens pollicis	• Adductor pollicis • Abductor pollicis brevis*
Intrinsic plus hand	• Lumbricals • Interossei	• Abductor digiti minimi* • Flexor digiti minimi*
	Lower limb spasticity[4, 14, 16, 17]	
Equinovarus foot	• Gastrocnemius • Soleus	• Tibialis posterior
Flexed ankle	• Gastrocnemius • Soleus • Tibialis posterior[13]	• Flexor hallucis longus • Flexor digitorum longus • Fibularis longus*
Flexed toes	• Flexor hallucis longus • Flexor hallucis brevis* • Flexor digitorum longus	• Flexor digitorum brevis* • Flexor digiti minimi brevis*
Inverted/supinated foot	• Tibialis posterior • Tibialis anterior*	• Flexor hallucis longus[16] • Flexor digitorum longus[16]

*For anatomical reference only.

Prioritize which muscles/dose to inject based on the established treatment goals

BOTOX®
onabotulinumtoxinA injection

Notes

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Lack of Interchangeability Between Botulinum Toxin Products
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

Injection insights and considerations

GENERAL CONSIDERATIONS

- The recommended dilution rate for Adult Spasticity is 2:1, meaning put:
  - 4 mL of saline into a 200-Unit vial or
  - 2 mL of saline into a 100-Unit vial
- Evaluate the anatomy, including relevant function and the effects of treatment on these muscles (eg, reducing tone), when considering muscle and dose selection
- Recognize the impact of spasticity on the anatomy, as no 2 patients are alike; muscles may be hypertrophied or atrophied, so thorough assessment of the spastic muscles is critical at each injection cycle
- 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

Utilize guidance techniques to help ensure proper needle placement

Ultrasound

EMG/E-Stim

- Accurate needle guidance is necessary to ensure proper muscle selection
- When using E-Stim on hyperflexed muscles, passively extend the muscle to allow for flexion

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.

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Injection insights and considerations (continued)

BEFORE INJECTION

- Examine the patient to identify the muscles contributing to the posture(s) and spasticity
  - Isolate the involved muscles using a clinical exam as well as guidance techniques
- 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 using cold spray to numb the injection site(s) with your patients
- Explain that some injection sites may be more sensitive than others so the pain level can vary with each injection

DURING INJECTION

- An assistant may be helpful to position the patient's spastic limb 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 1 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 muscles involved
  - To optimally target the muscle, consider angulation of the injection needle and patient's limb 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.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Serious Adverse Reactions With Unapproved Use (continued)
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.

Please see additional Important Safety Information throughout.

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 (saline)
  - Alcohol swabs for cleaning the rubber stoppers on the saline and BOTOX® vials
  - Adhesive bandages
  - Muscle localization guidance 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)
Serious Adverse Reactions With Unapproved Use (continued)
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.

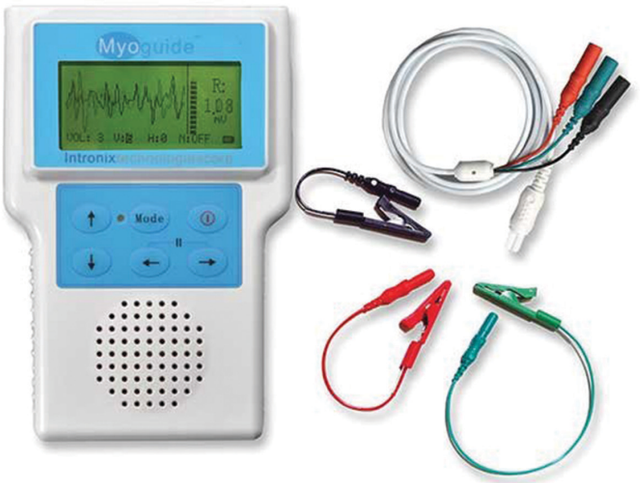
Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Consider using guidance techniques for BOTOX® injections

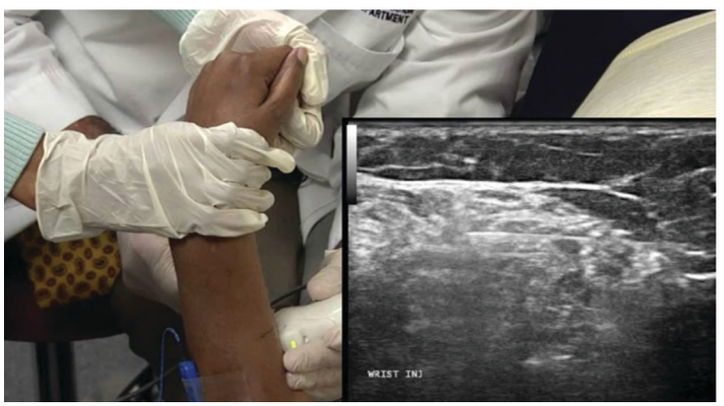
EMG/E-Stim[18]

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



Ultrasound[19]

- Enhanced precision when determining approved muscle position, depth, and size
- Continuous visualization of injection needle and local spread within the approved muscle
- Direct identification of non-targeted muscles and vulnerable structures to be avoided



IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Hypersensitivity Reactions
Serious and/or immediate hypersensitivity reactions have been reported.

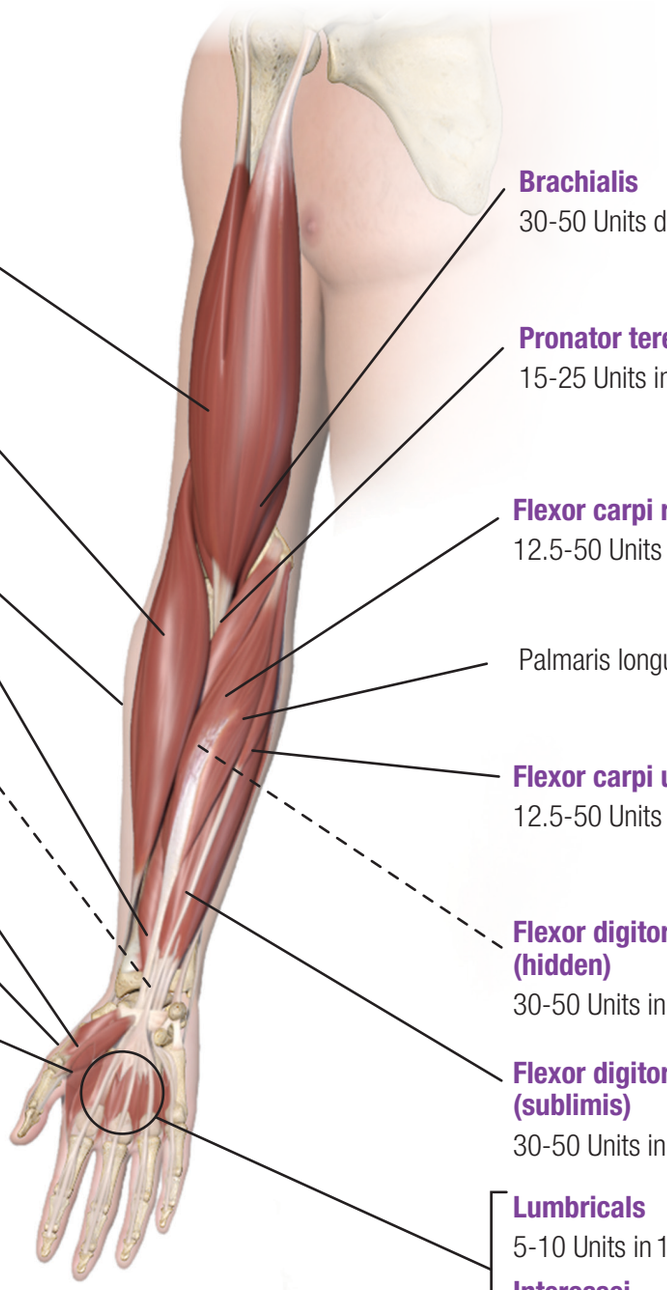
Please see additional Important Safety Information throughout.

BOTOX®
onabotulinumtoxinA injection

Main muscles involved in Adult Upper Limb Spasticity

Muscles listed in purple are those approved for BOTOX® injection[4]

Anterior view



Biceps brachii
60-200 Units
divided in 2-4 sites

Brachioradialis
45-75 Units divided
in 1-2 sites

Extensor carpi
Radialis longus*

Flexor pollicis longus
20 Units in 1 site

Pronator quadratus (hidden)
10-50 Units in 1 site

Opponens pollicis
5-25 Units in 1 site

Flexor pollicis brevis
5-25 Units in 1 site

Adductor pollicis
20 Units in 1 site

Brachialis
30-50 Units divided in 1-2 sites

Pronator teres
15-25 Units in 1 site

Flexor carpi radialis
12.5-50 Units in 1 site

Palmaris longus*

Flexor carpi ulnaris
12.5-50 Units in 1 site

Flexor digitorum profundus (hidden)
30-50 Units in 1 site

Flexor digitorum superficialis (sublimis)
30-50 Units in 1 site

Lumbricals
5-10 Units in 1 site per muscle

Interossei
5-10 Units in 1 site per muscle

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

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.

Approved Muscles Involved in Common Postures

Elbow flexors
Biceps brachii
Brachialis
Brachioradialis

Forearm pronators
Pronator teres
Pronator quadratus

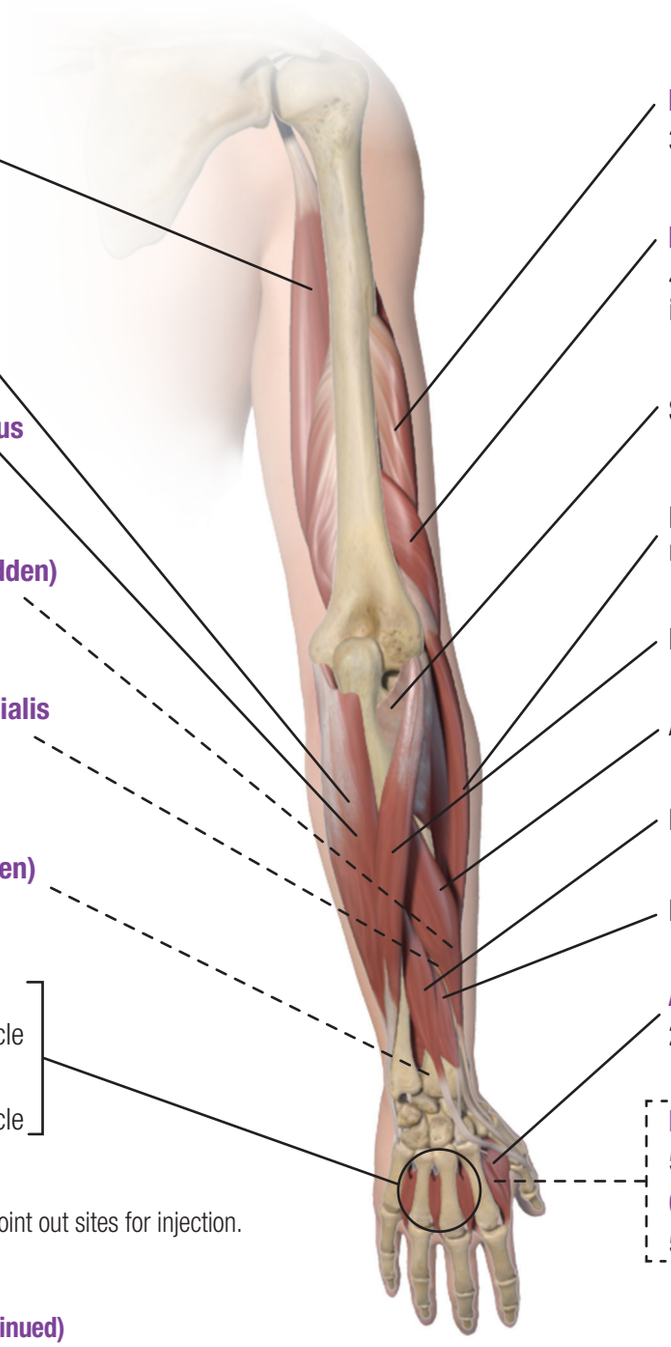
Wrist flexors
Flexor carpi radialis
Flexor carpi ulnaris

Finger flexors
Flexor digitorum profundus
Flexor digitorum superficialis (sublimis)
Lumbricals
Interossei

Finger adductors/abductors
Interossei (palmar/dorsal)

Thumb flexors
Adductor pollicis
Flexor pollicis longus
Flexor pollicis brevis
Opponens pollicis

Posterior view



Biceps brachii
60-200 Units divided in 2-4 sites

Flexor carpi ulnaris
12.5-50 Units in 1 site

Flexor digitorum profundus
30-50 Units in 1 site

Flexor pollicis longus (hidden)
20 Units in 1 site

Flexor digitorum superficialis (sublimis) (hidden)
30-50 Units in 1 site

Pronator quadratus (hidden)
10-50 Units in 1 site

Lumbricals
5-10 Units in 1 site per muscle

Interossei
5-10 Units in 1 site per muscle

Brachialis
30-50 Units divided in 1-2 sites

Brachioradialis
45-75 Units divided in 1-2 sites

Supinator*

Extensor carpi radialis longus*

Extensor carpi ulnaris*

Abductor pollicis longus*

Extensor pollicis longus*

Extensor pollicis brevis*

Adductor pollicis
20 Units in 1 site

Flexor pollicis brevis (hidden)
5-25 Units in 1 site

Opponens pollicis (hidden)
5-25 Units in 1 site

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

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.

Biceps brachii

▶ BOTOX® dose: 60 Units to 200 Units divided in 2-4 sites

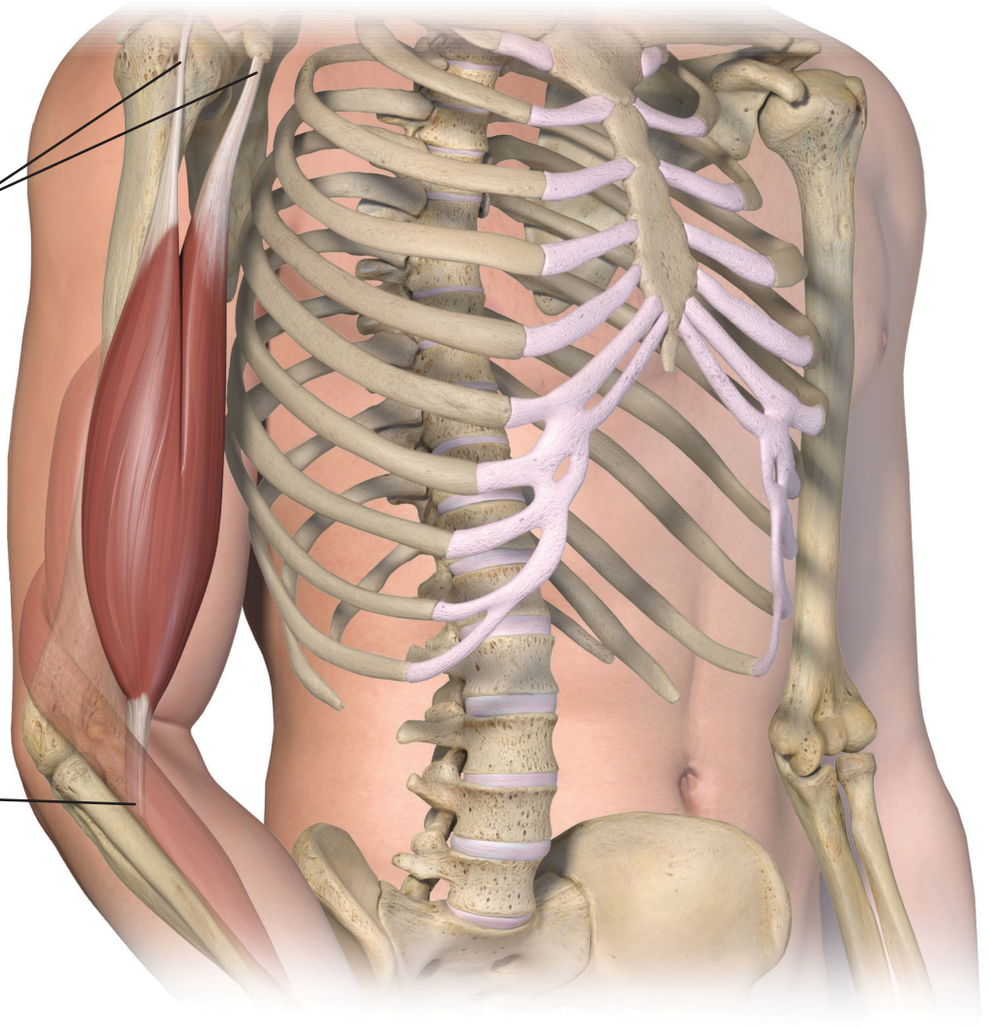
Muscle action[14]

Supinates the forearm and flexes the elbow

Proximal attachments

Long head arises from the supraglenoid tubercle of the scapula

Short head arises from the coracoid process of the scapula



Distal attachment

Radial tuberosity

Other muscles involved in elbow flexion/forearm supination

- Brachialis (flexion only)
- Supinator (supination only)*
- Brachioradialis (flexion only)
- Pronator teres (flexion only)

*For anatomical reference only.

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

Biceps brachii (continued)

Localization[20]

The biceps brachii is located in the anterior surface of the midarm.

Cross-sectional anatomy: upper arm

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Pulmonary Effects of BOTOX in Patients With Compromised Respiratory Status Treated for Spasticity
Patients with compromised respiratory status treated with BOTOX for spasticity should be monitored closely.

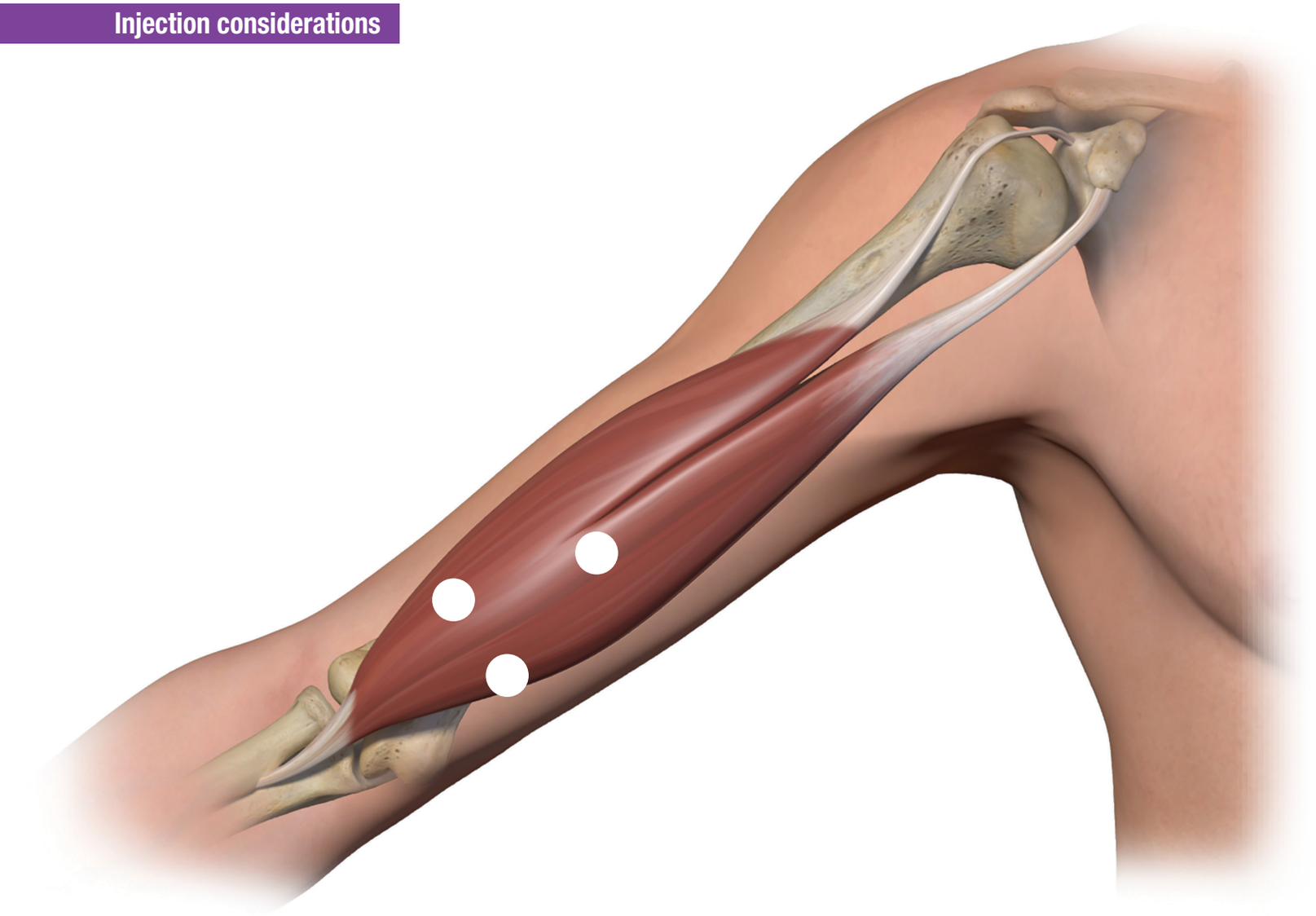
Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Biceps brachii (continued)

Ultrasound EMG/E-Stim

Injection considerations



Dots represent injection sites.

- Extend the forearm, if possible, and approach the muscle through the anterior aspect of the biceps to avoid the vascular areas
- Consider using an inverted *V* pattern at the junction of the middle and lower third of the muscle
- Biceps muscles may be thinner in some individuals

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

Bronchitis and Upper Respiratory Tract Infections in Patients Treated for Spasticity

Bronchitis was reported more frequently as an adverse reaction in adult patients treated for upper limb spasticity with BOTOX (3% at 251 Units to 360 Units total dose) compared to placebo (1%).

Please see additional Important Safety Information throughout.

Digital Resource Library
Scan the QR code with your mobile device to access interactive anatomy resources and multimedia content for this section.

Or visit BOTOXDigitalTools.com

Notes

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Bronchitis and Upper Respiratory Tract Infections in Patients Treated for Spasticity (continued)
In adult patients with reduced lung function treated for upper limb spasticity, upper respiratory tract infections were also reported more frequently as adverse reactions in patients treated with BOTOX (11% at 360 Units total dose; 8% at 240 Units total dose) compared to placebo (6%). In adult patients treated for lower limb spasticity, upper respiratory tract infections were reported more frequently as an adverse reaction in patients treated with BOTOX (2% at 300 Units to 400 Units total dose) compared to placebo (1%).

Please see additional Important Safety Information throughout.

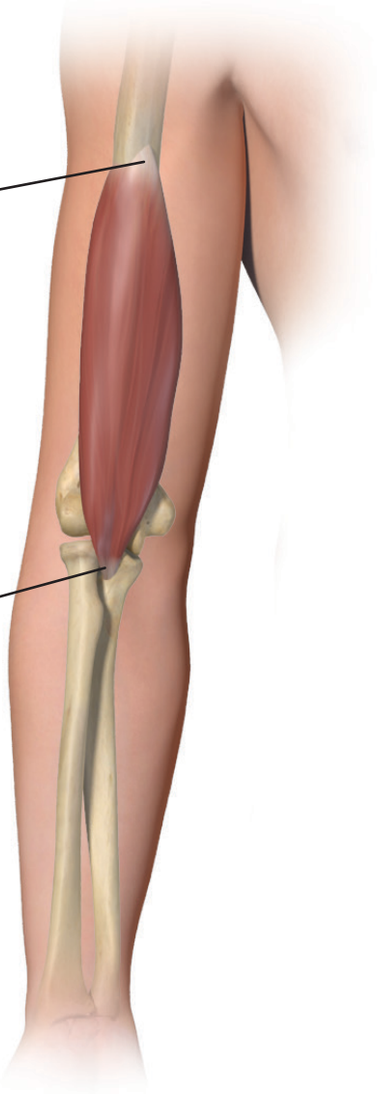
BOTOX® onabotulinumtoxinA injection

Brachialis

▶ BOTOX® dose: 30 Units to 50 Units divided in 1-2 sites

Muscle action[14]

Flexes the elbow



Proximal attachment

Anterior surface of the distal half of the humerus on either side of the deltoid insertion

Distal attachment

Anterior aspect of coronoid process and ulnar tuberosity

Other muscles involved in elbow flexion

- Biceps brachii
- Brachioradialis
- Pronator teres

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

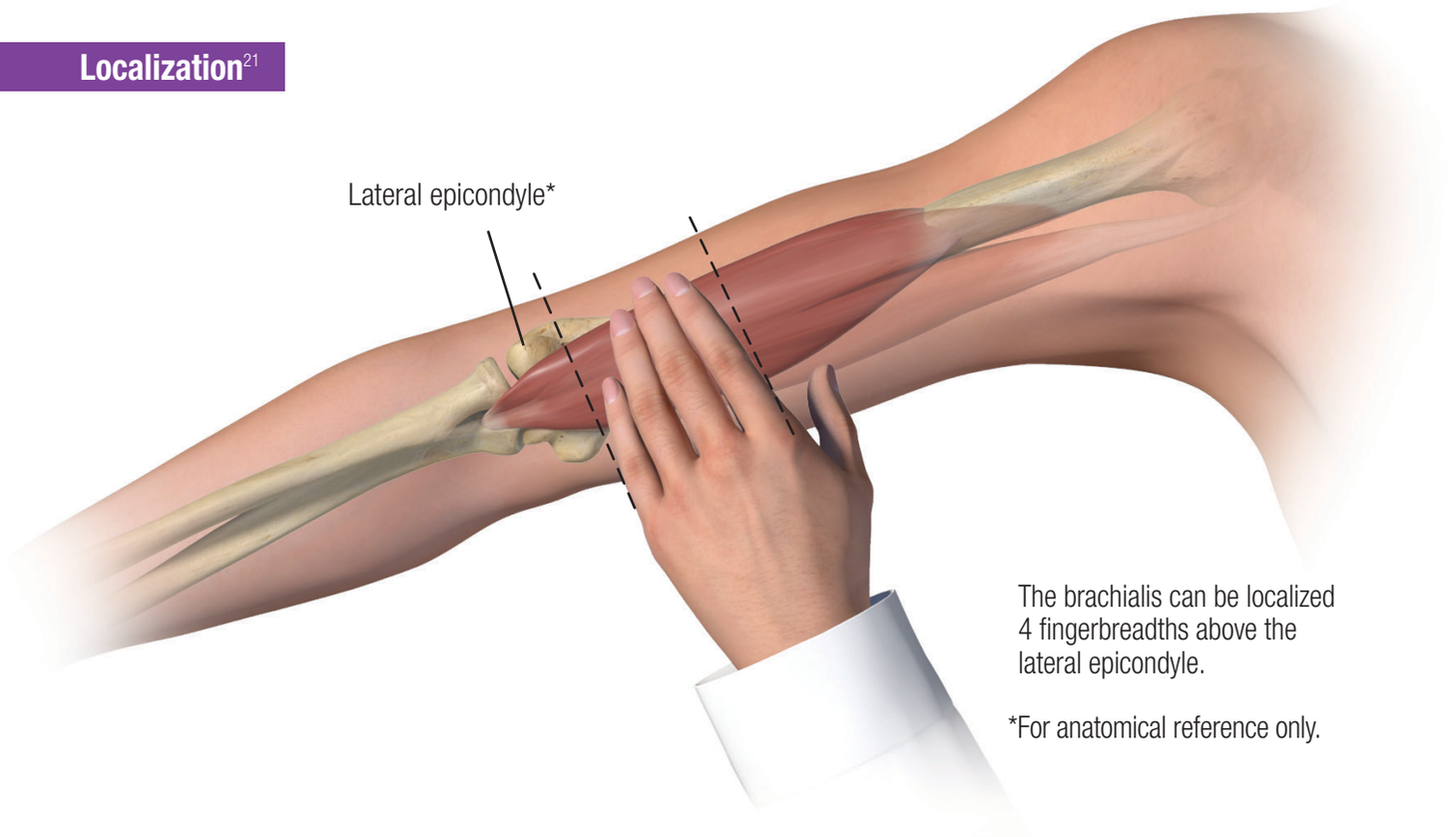
Human Albumin and Transmission of Viral Diseases

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).

Please see additional Important Safety Information throughout.

Brachialis (continued)

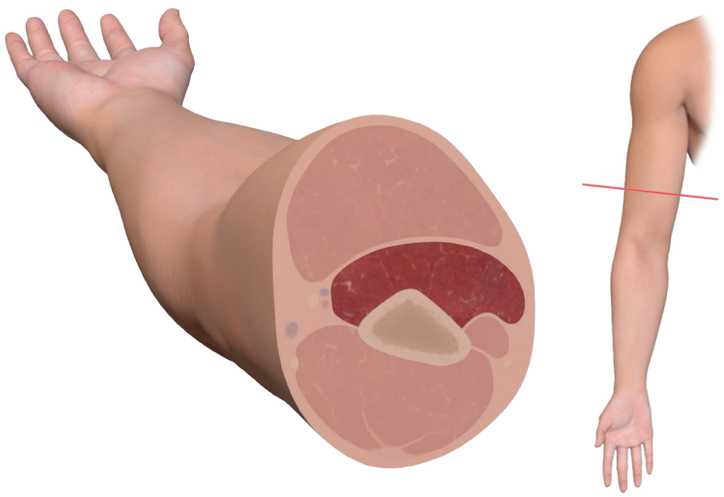
Localization[21]



The brachialis can be localized 4 fingerbreadths above the lateral epicondyle.

*For anatomical reference only.

Cross-sectional anatomy: upper arm



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.

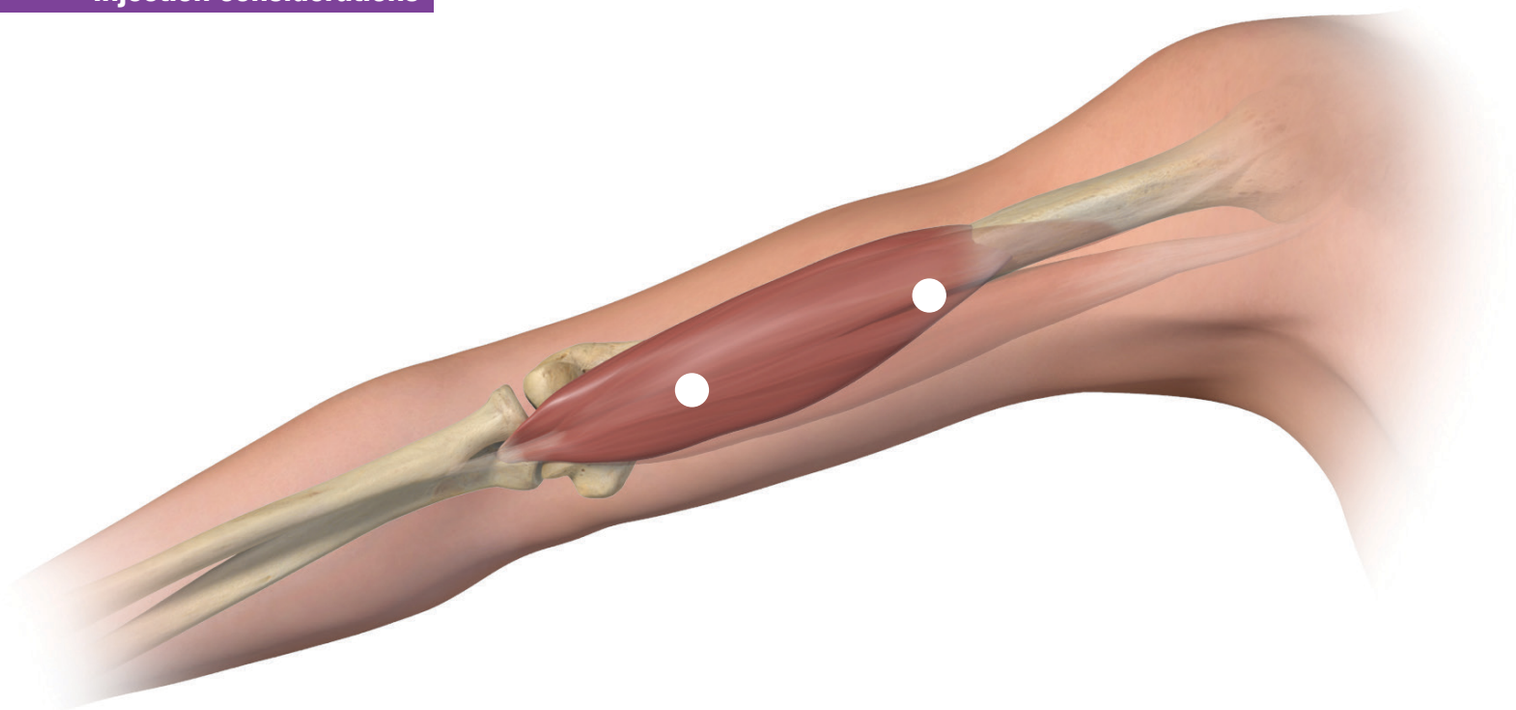
BOTOX® onabotulinumtoxinA injection

Brachialis (continued)

Ultrasound

EMG/E-Stim

Injection considerations



Dots represent injection sites.

- Moving the bulk of the biceps medially may facilitate access to this muscle
- If possible, actively flex the elbow with the forearm fully pronated to help localize
  - Use minimal resistance for this maneuver to avoid activating the biceps
- Ultrasound is recommended when injecting this muscle
  - Helps with targeting the midbelly (which is more distal) and avoiding the neurovascular bundle
  - Helps to visually differentiate this muscle from the biceps
- It may be helpful to consider the 3 approved elbow flexors (biceps brachii, brachialis, brachioradialis) collectively when determining which approved BOTOX® dose to use
- If the needle is inserted too medially, it may end up in the biceps

BOTOX®
onabotulinumtoxinA injection

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BOTOXDigitalTools.com

Notes

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Adult Lower Limb Spasticity
The most frequently reported adverse reactions following injection of BOTOX for lower limb spasticity include arthralgia, back pain, myalgia, upper respiratory tract infection, and injection-site pain.

Please see additional Important Safety Information throughout.

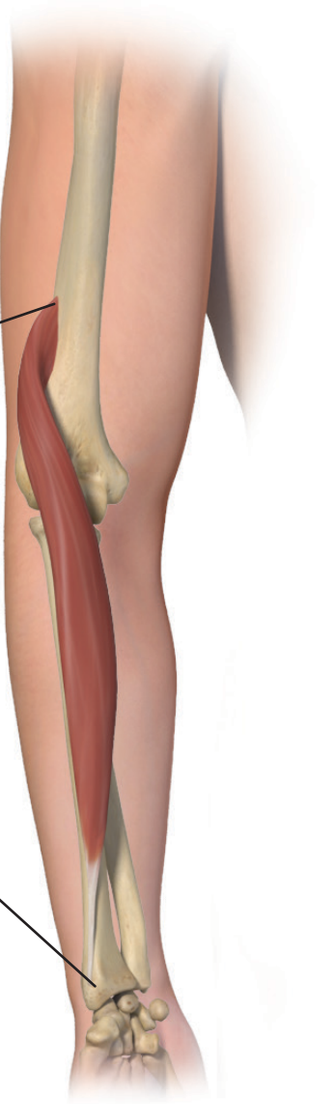
BOTOX® onabotulinumtoxinA injection

Brachioradialis

▶ BOTOX® dose: 45 Units to 75 Units divided in 1-2 sites

Muscle action[14]

Flexes the elbow



Proximal attachment

Lateral supracondylar ridge of the humerus

Distal attachment

Lateral aspect of the radius, just proximal to its styloid process

Other muscles involved in elbow flexion

- Biceps brachii
- Brachialis
- Pronator teres

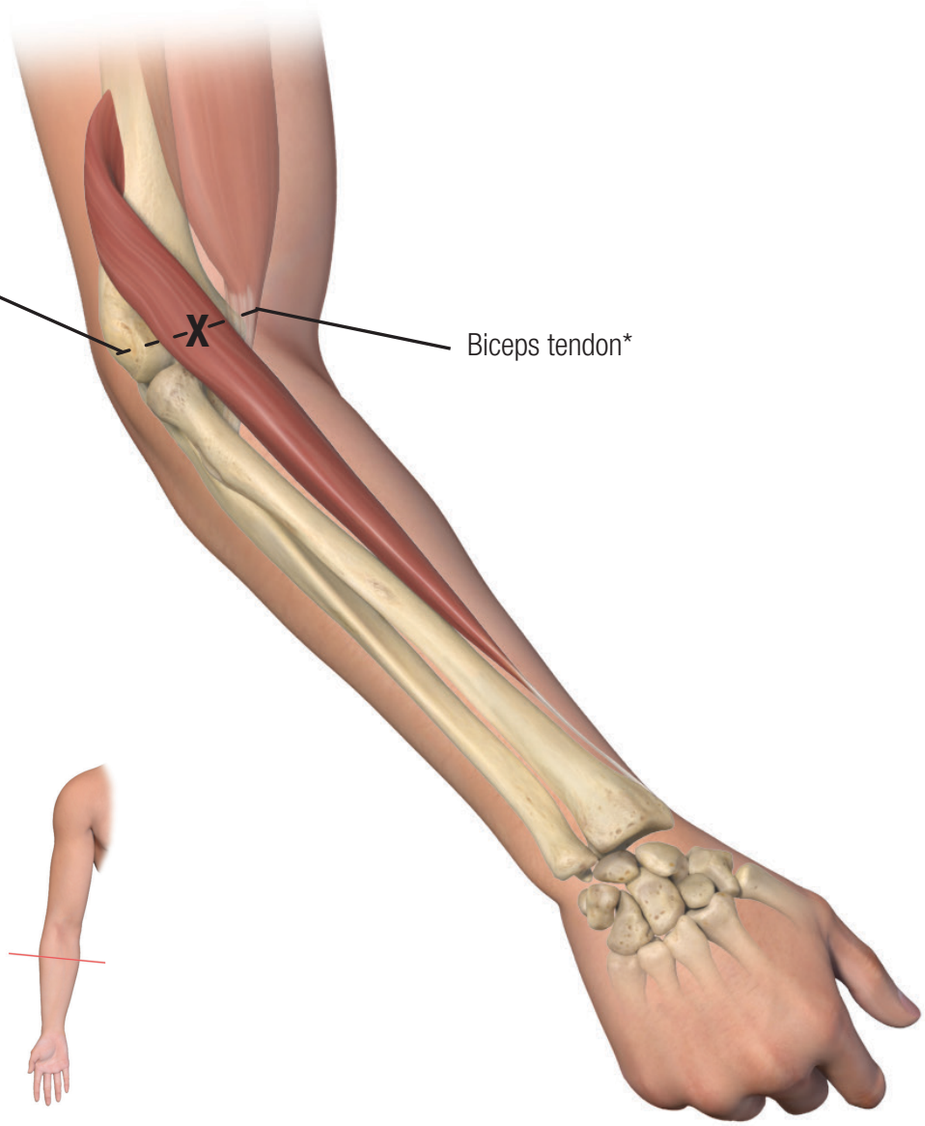
IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Postmarketing Experience
Adverse reactions that have been identified during postapproval use of BOTOX are discussed in greater detail in *Postmarketing Experience* (Section 6.3 of the Prescribing Information).

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Brachioradialis (continued)

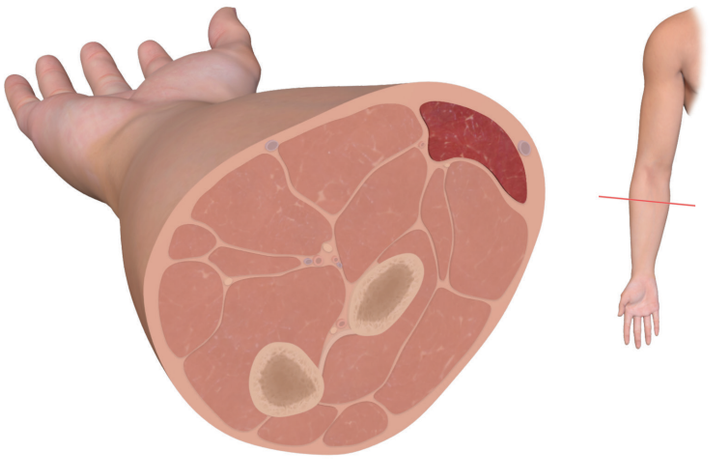
Localization[20]



The brachioradialis can be localized midway between the biceps tendon and lateral epicondyle along flexor crease.

*For anatomical reference only.

Cross-sectional anatomy: upper forearm



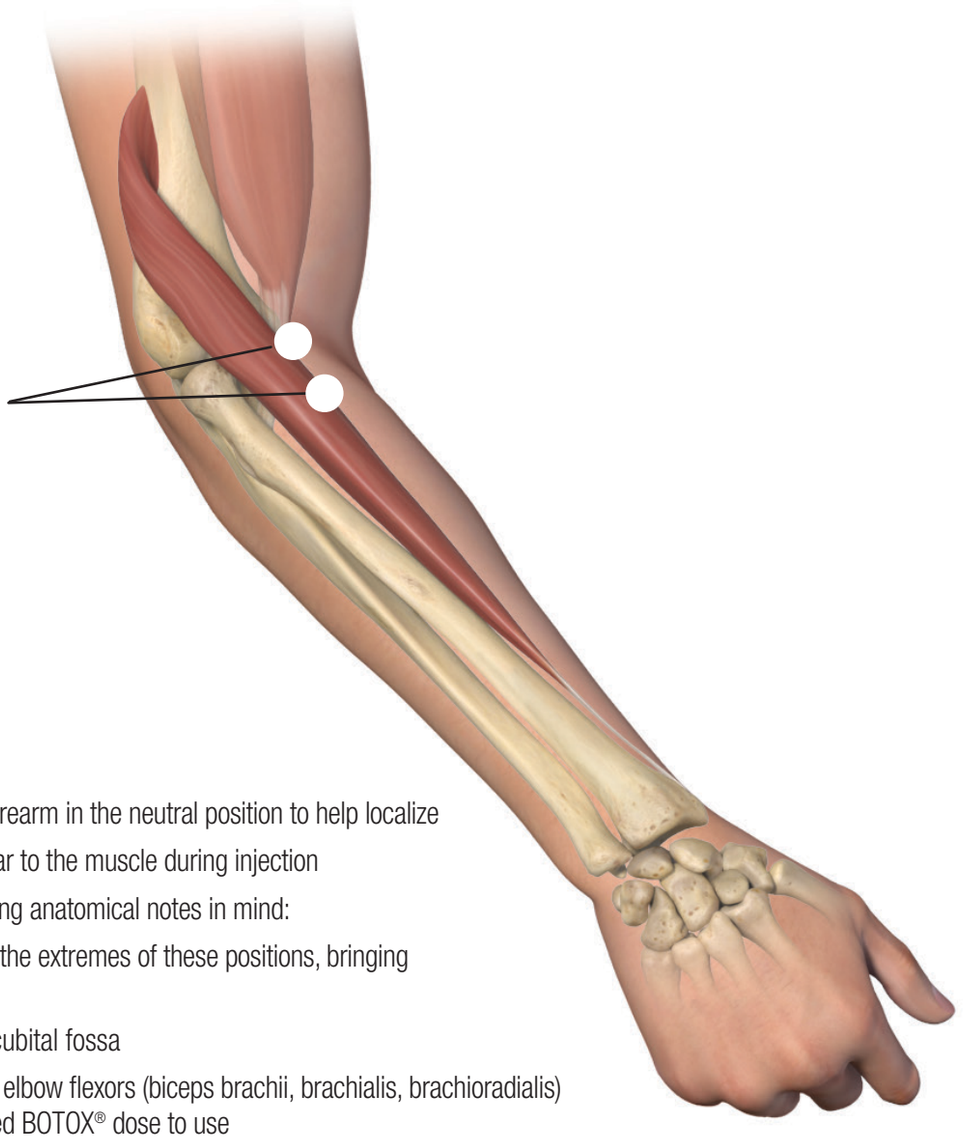
IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Postmarketing Experience (continued)
There have been spontaneous reports of death, sometimes associated with dysphagia, pneumonia, and/or other significant debility or anaphylaxis, after treatment with botulinum toxin. There have 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.

Brachioradialis (continued)

Ultrasound EMG/E-Stim

Injection considerations



Dots represent injection sites.

- If possible, actively flex the elbow with the forearm in the neutral position to help localize
- Consider positioning the needle perpendicular to the muscle during injection
- When targeting this muscle, keep the following anatomical notes in mind:
  - It can act as a supinator or pronator from the extremes of these positions, bringing the forearm into the neutral position
  - It forms the lateral boundary of the antecubital fossa
- It may be helpful to consider the 3 approved elbow flexors (biceps brachii, brachialis, brachioradialis) collectively when determining which approved BOTOX® dose to use
- If the needle is inserted too laterally, it may end up in the wrong muscle

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

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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.

WARNINGS AND PRECAUTIONS

Spread of Toxin Effect

See *Boxed Warning*.

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.

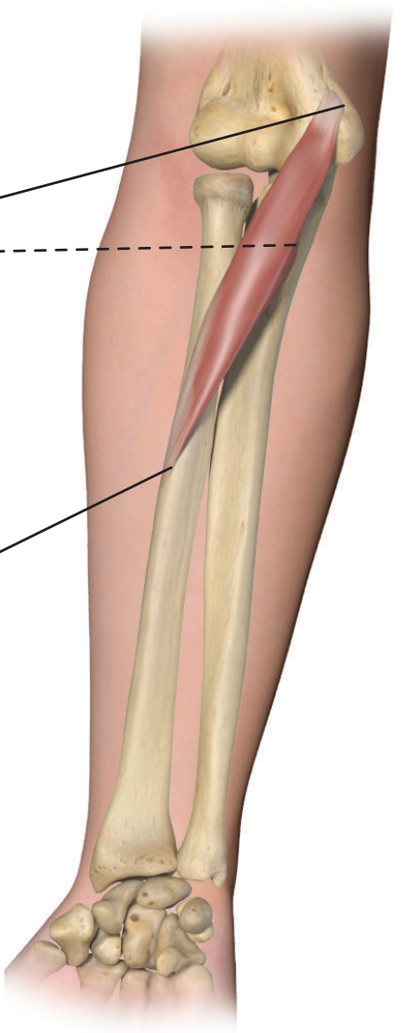
BOTOX®
onabotulinumtoxinA injection

Pronator teres

▶ BOTOX® dose: 15 Units to 25 Units in 1 site

Muscle action[14]

Pronates the forearm and aids with elbow flexion



Proximal attachments

Humeral head arises just proximal to the medial epicondyle of the humerus

Ulnar head arises from the medial side of the coronoid process of the ulna

Distal attachment

Lateral surface of the radial shaft

Other muscles involved in forearm pronation and/or elbow flexion

- Pronator quadratus (pronation only)
- Biceps brachii (flexion only)
- Brachialis (flexion only)
- Brachioradialis (flexion only)

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

Serious Adverse Reactions With Unapproved Use

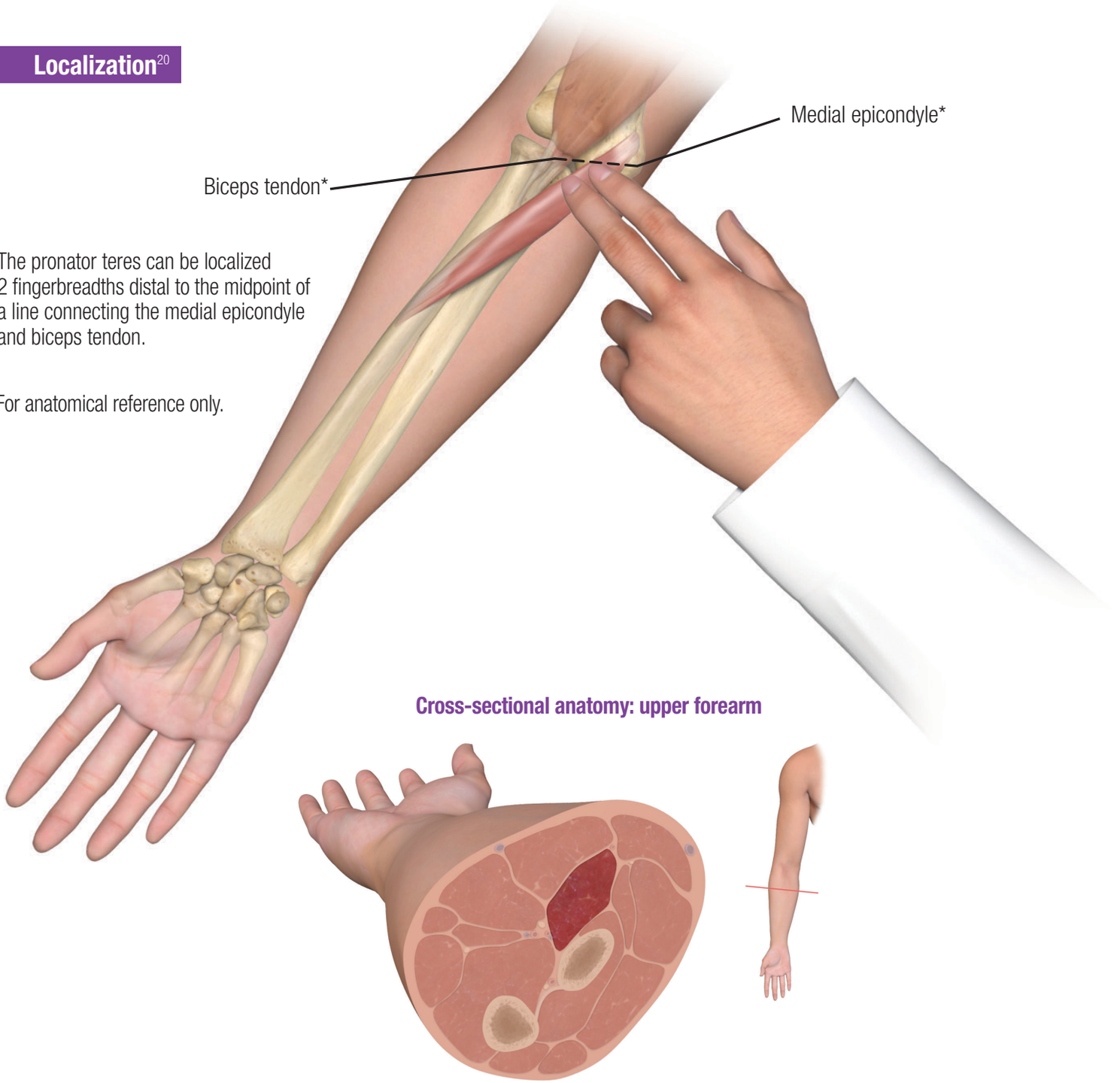
Serious adverse reactions, including excessive weakness, dysphagia, and aspiration pneumonia, with some adverse reactions associated with fatal outcomes, have been reported in patients who received BOTOX injections for unapproved uses. In these cases, the adverse reactions were not necessarily related 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

Pronator teres (continued)

Localization[20]



The pronator teres can be localized 2 fingerbreadths distal to the midpoint of a line connecting the medial epicondyle and biceps tendon.

*For anatomical reference only.

Cross-sectional anatomy: upper forearm

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.

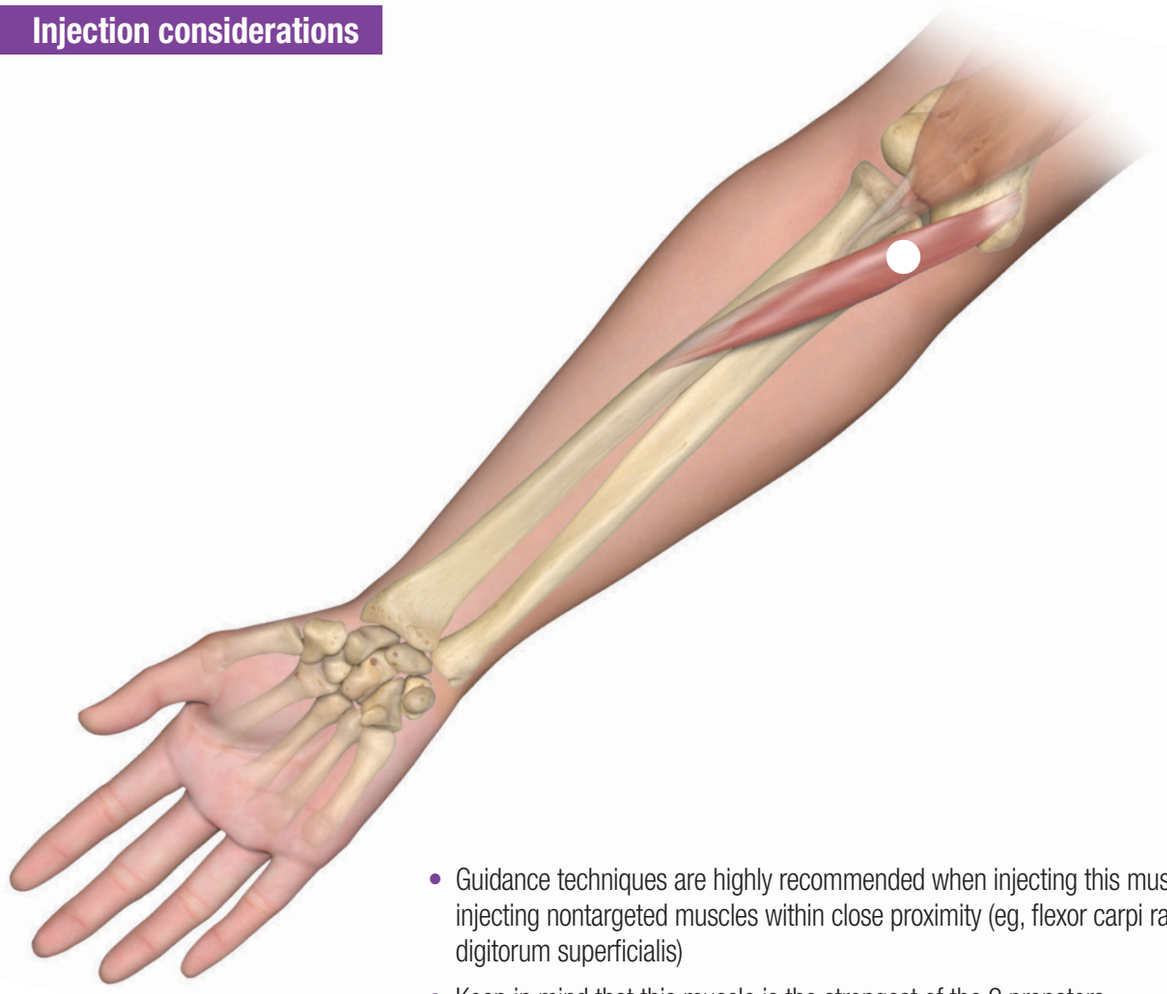
BOTOX®
onabotulinumtoxinA injection

Pronator teres (continued)

Ultrasound

EMG/E-Stim

Injection considerations



Dot represents injection site.

- Guidance techniques are highly recommended when injecting this muscle to avoid inadvertently injecting nontargeted muscles within close proximity (eg, flexor carpi radialis, flexor digitorum superficialis)
- Keep in mind that this muscle is the strongest of the 2 pronators
- In patients where both the flexor carpi radialis and pronator teres are being targeted for BOTOX®, consider injecting these muscles together, starting with the pronator teres, which is superficial to the flexor carpi radialis in the proximal portion of the forearm

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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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.

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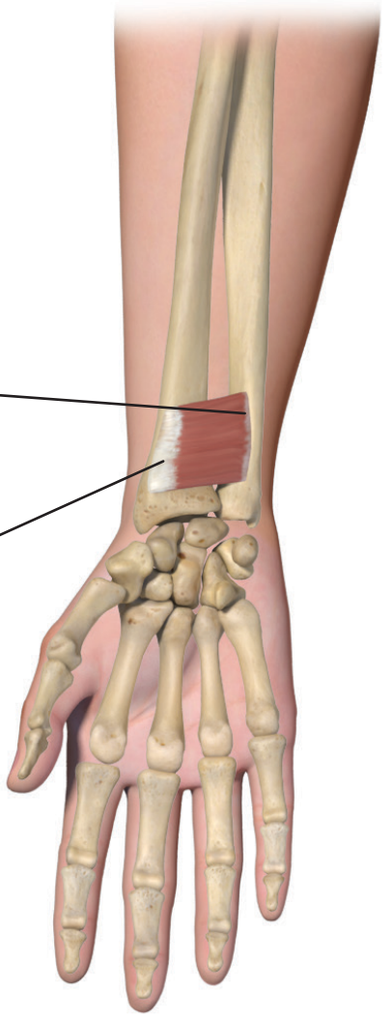
Pronator quadratus

▶ BOTOX® dose: 10 Units to 50 Units in 1 site

Muscle action[14]

Pronates the forearm



Proximal attachment

Distal quarter of the anterior surface of the ulna

Distal attachment

Distal quarter of the anterior surface of the radius

Other muscle involved in forearm pronation

- Pronator teres

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*).

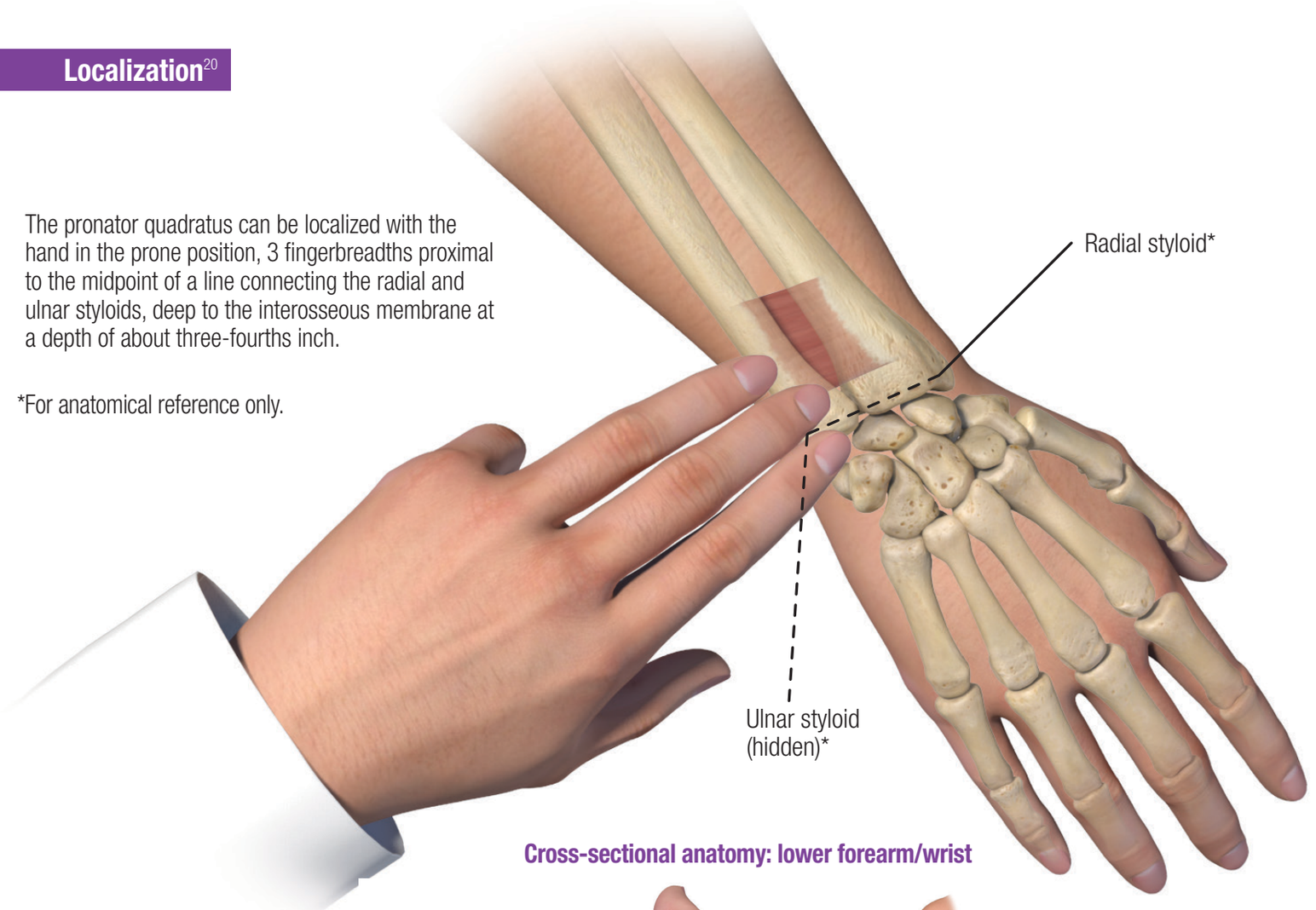
Please see additional Important Safety Information throughout.

Pronator quadratus (continued)

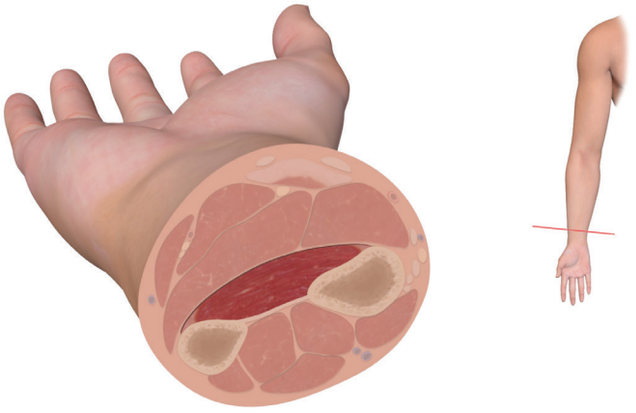
Localization[20]

The pronator quadratus can be localized with the hand in the prone position, 3 fingerbreadths proximal to the midpoint of a line connecting the radial and ulnar styloids, deep to the interosseous membrane at a depth of about three-fourths inch.

*For anatomical reference only.



Cross-sectional anatomy: lower forearm/wrist

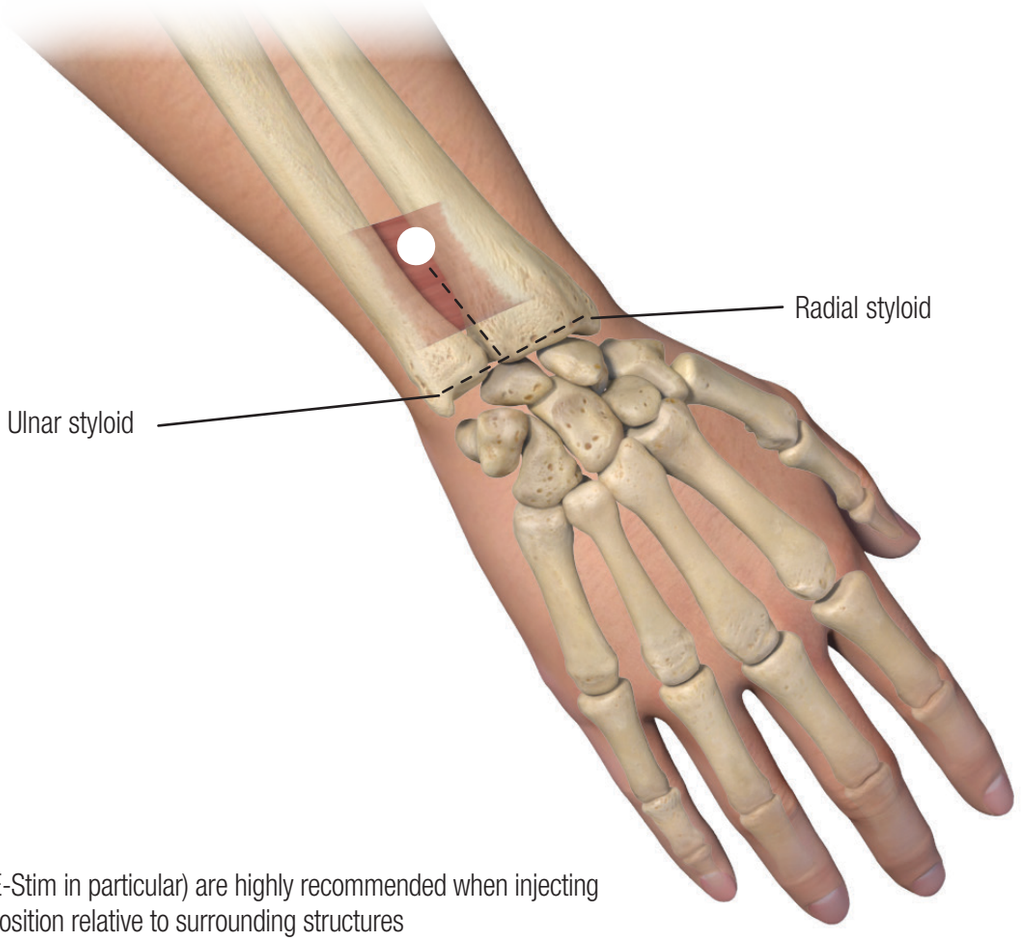


Pronator quadratus (continued)

Ultrasound

EMG/E-Stim

Injection considerations



Dot represents injection site.

- Guidance techniques (E-Stim in particular) are highly recommended when injecting this muscle due to its position relative to surrounding structures
- This muscle is the weaker of the 2 pronators and should be targeted when deemed necessary by the physician
  - Localization is critical to avoid inadvertently injecting the wrong muscles
- Consider a dorsal approach to help avoid neurovasculature
- Note that the deep muscle fibers of this muscle act as a binder between the radius and the ulna

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

Bronchitis and Upper Respiratory Tract Infections in Patients Treated for Spasticity

Bronchitis was reported more frequently as an adverse reaction in adult patients treated for upper limb spasticity with BOTOX (3% at 251 Units to 360 Units total dose) compared to placebo (1%).

Please see additional Important Safety Information throughout.

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IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Bronchitis and Upper Respiratory Tract Infections in Patients Treated for Spasticity (continued)
In adult patients with reduced lung function treated for upper limb spasticity, upper respiratory tract infections were also reported more frequently as adverse reactions in patients treated with BOTOX (11% at 360 Units total dose; 8% at 240 Units total dose) compared to placebo (6%). In adult patients treated for lower limb spasticity, upper respiratory tract infections were reported more frequently as an adverse reaction in patients treated with BOTOX (2% at 300 Units to 400 Units total dose) compared to placebo (1%).

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Flexor carpi radialis

▶ BOTOX® dose: 12.5 Units to 50 Units (1 site)

Muscle action[14]

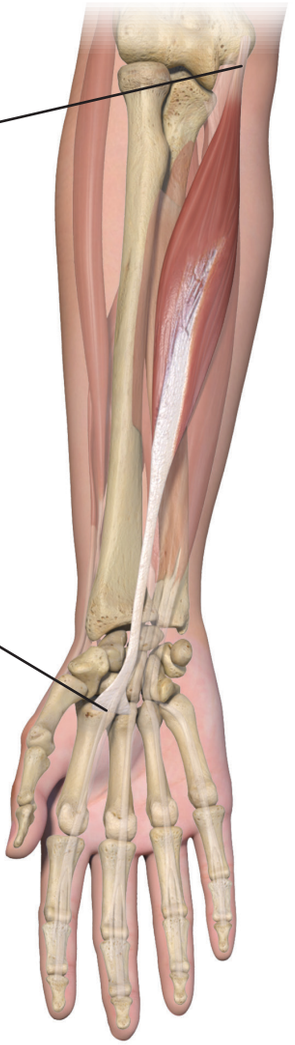
Flexes the wrist and abducts (radially deviates) the hand

Proximal attachment

Medial epicondyle of the humerus (via the common flexor tendon)

Distal attachment

Palmar surface of the base of the second metacarpal



Other muscles involved in wrist flexion/abduction

- Flexor carpi ulnaris (flexion only)
- Flexor digitorum superficialis (flexion only)
- Flexor digitorum profundus (flexion only)
- Flexor pollicis longus (flexion only)
- Palmaris longus (flexion only)*
- Extensor carpi radialis longus (abduction only)*
- Abductor pollicis longus (abduction only)*
- Extensor pollicis longus (abduction only)[20,]*

*For anatomical reference only.

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.

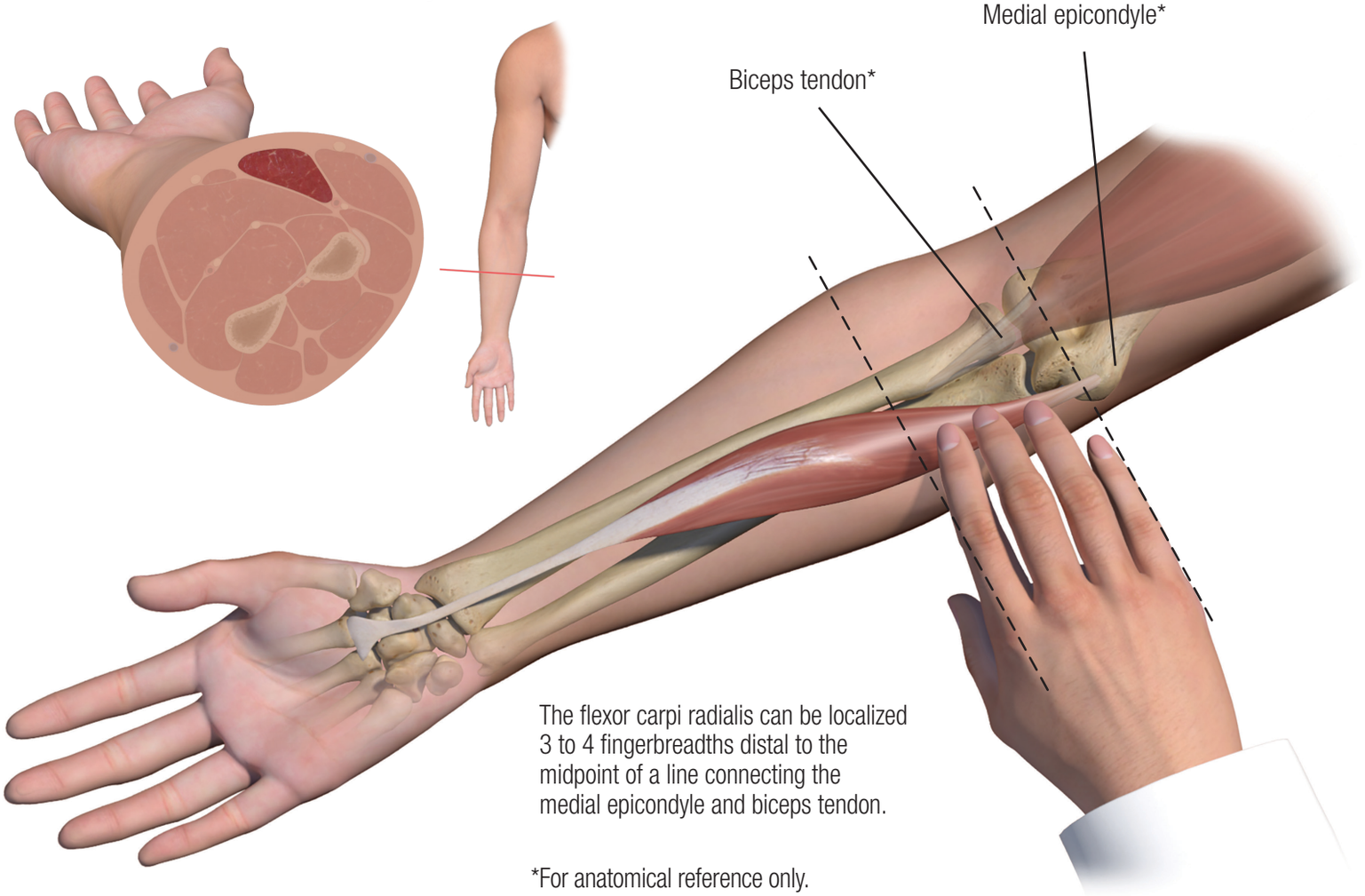
Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Flexor carpi radialis (continued)

Localization[20]

Cross-sectional anatomy: middle forearm



The flexor carpi radialis can be localized 3 to 4 fingerbreadths distal to the midpoint of a line connecting the medial epicondyle and biceps tendon.

*For anatomical reference only.

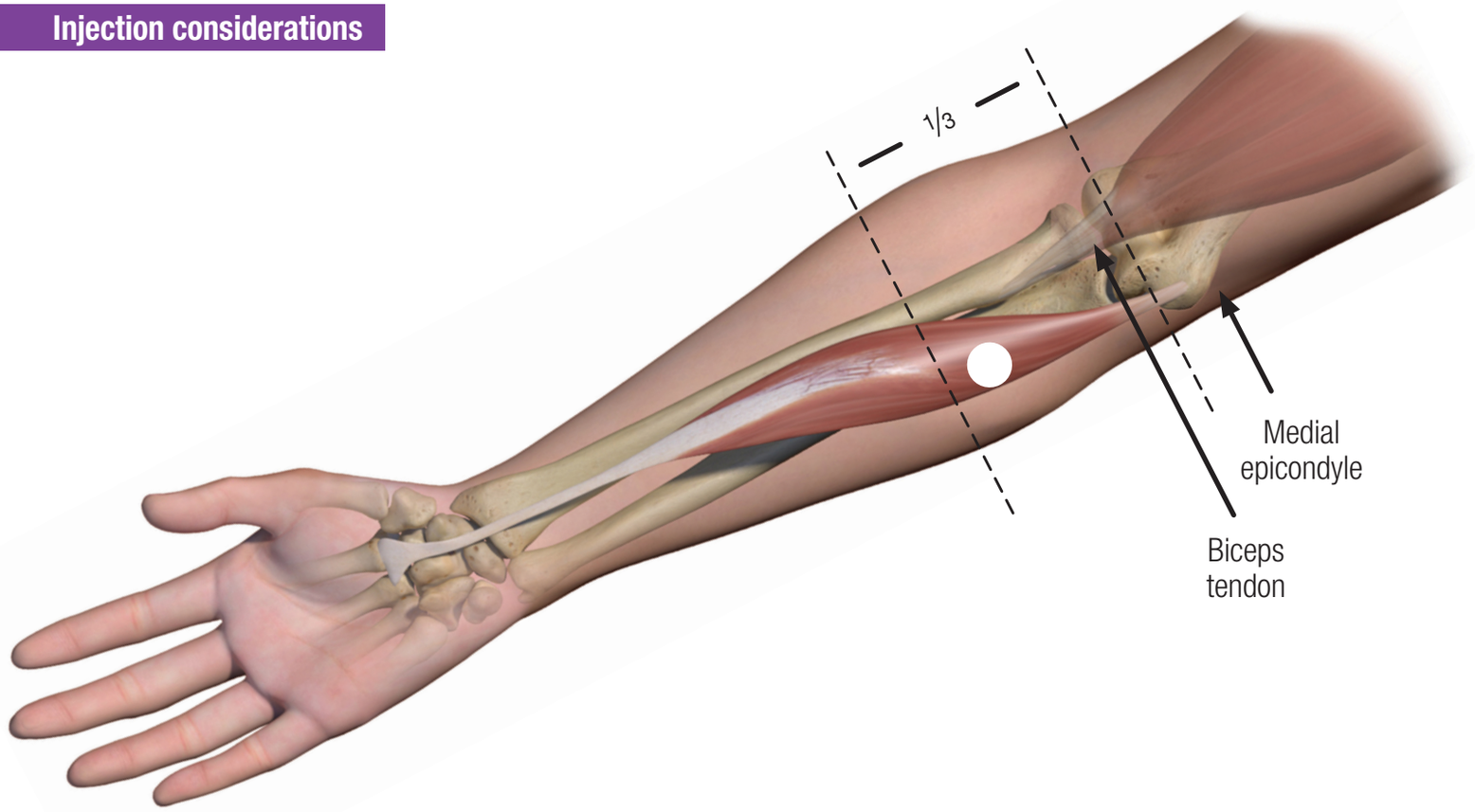
IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS
Adverse reactions to BOTOX for injection are discussed in greater detail in the following sections: *Boxed Warning*, *Contraindications*, and *Warnings and Precautions*.

Please see additional Important Safety Information throughout.

Flexor carpi radialis (continued)

Ultrasound EMG/E-Stim

Injection considerations



Dot represents injection site.

- If possible, place the forearm in a neutral position, put 1 finger on the bicep tendon and 1 finger on the medial epicondyle, bisect the line, and palpate the muscle with passive flexion
- Consider injecting in the proximal 1/3 of the forearm, in the largest part of the muscle
  - If you are in the mid forearm, you may be in the wrong muscle
- Avoid going too deep to avoid inadvertent injection of neighboring muscles

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Adult Upper Limb Spasticity
The most frequently reported adverse reactions following injection of BOTOX for upper limb spasticity include pain in extremity, muscular weakness, fatigue, nausea, and bronchitis.

Please see additional Important Safety Information throughout.

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IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Adult Lower Limb Spasticity
The most frequently reported adverse reactions following injection of BOTOX for lower limb spasticity include arthralgia, back pain, myalgia, upper respiratory tract infection, and injection-site pain.

Please see additional Important Safety Information throughout.

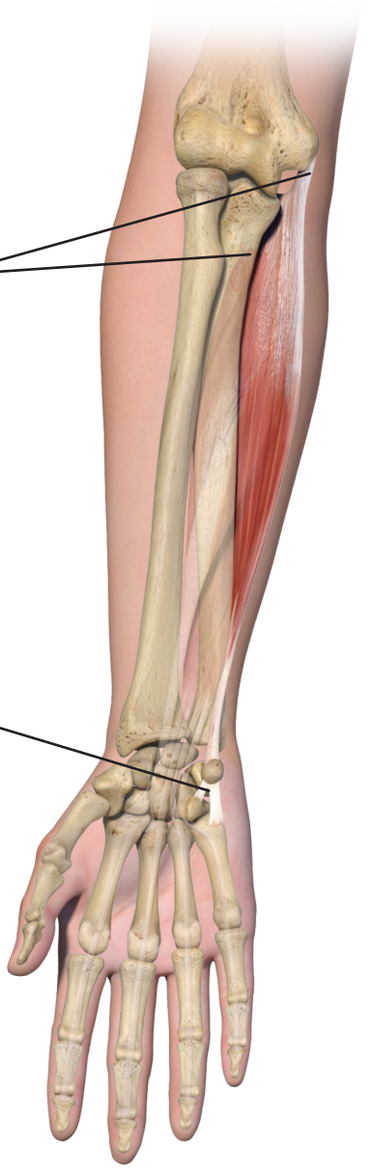
BOTOX® onabotulinumtoxinA injection

Flexor carpi ulnaris

▶ BOTOX® dose: 12.5 Units to 50 Units (1 site)

Muscle action[14]

Flexes the wrist and adducts (ulnarly deviates) the hand



Proximal attachments

Humeral head arises from the medial epicondyle (via the common flexor tendon). Ulnar head arises from the olecranon and proximal two-thirds of the ulna

Distal attachments

To the pisiform and further to the hamate and fifth metacarpal

Other muscles involved in wrist flexion/adduction

- Flexor carpi radialis (flexion only)
- Flexor digitorum profundus (flexion only)
- Flexor digitorum superficialis (flexion only)
- Flexor pollicis longus (flexion only)
- Palmaris longus (flexion only)*
- Extensor carpi ulnaris (adduction only)*

*For anatomical reference only.

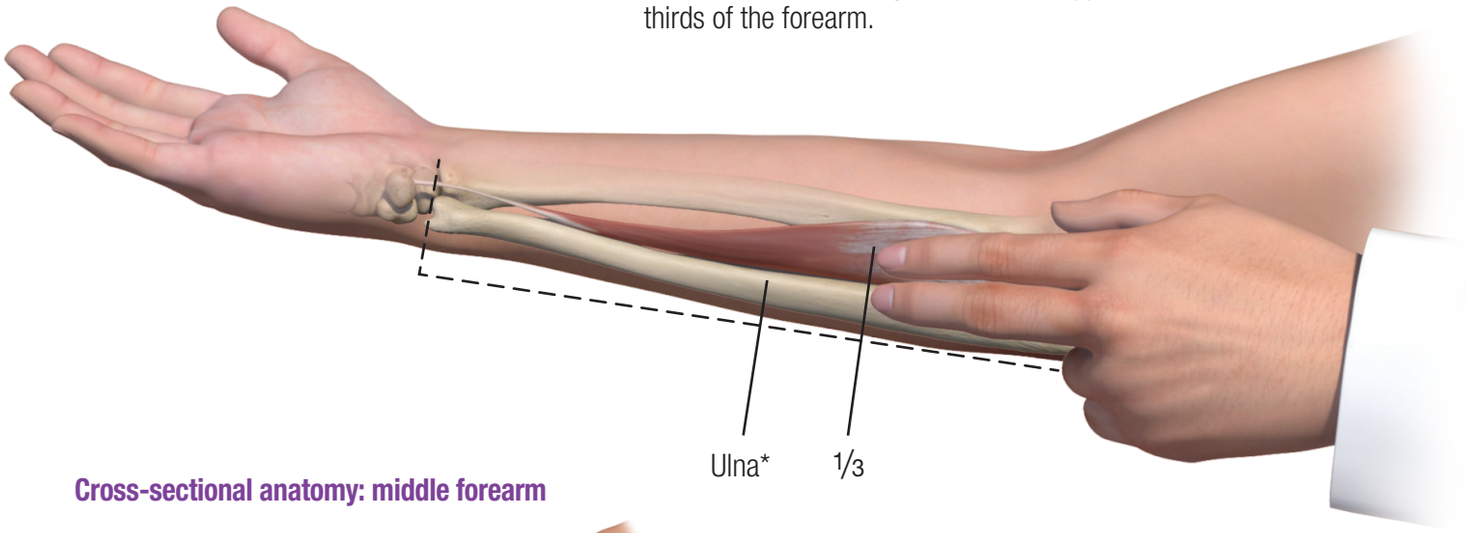
IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Postmarketing Experience
Adverse reactions that have been identified during postapproval use of BOTOX are discussed in greater detail in *Postmarketing Experience* (Section 6.3 of the Prescribing Information).

Please see additional Important Safety Information throughout.

Flexor carpi ulnaris (continued)

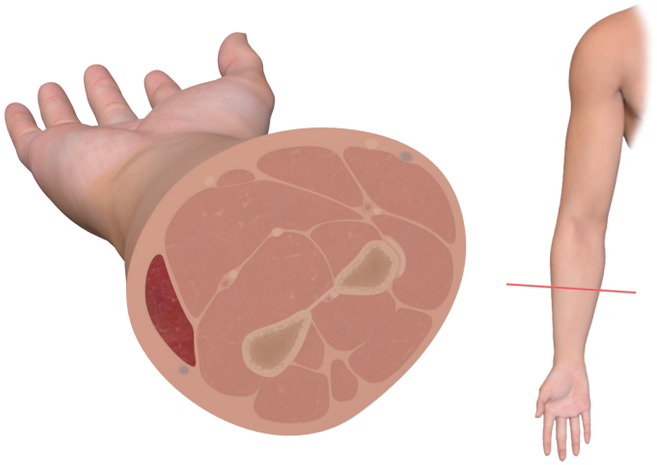
Localization[20]

The flexor carpi ulnaris can be localized 2 fingerbreadths volar to the ulna at the junction of the upper and middle thirds of the forearm.



*For anatomical reference only.

Cross-sectional anatomy: middle forearm

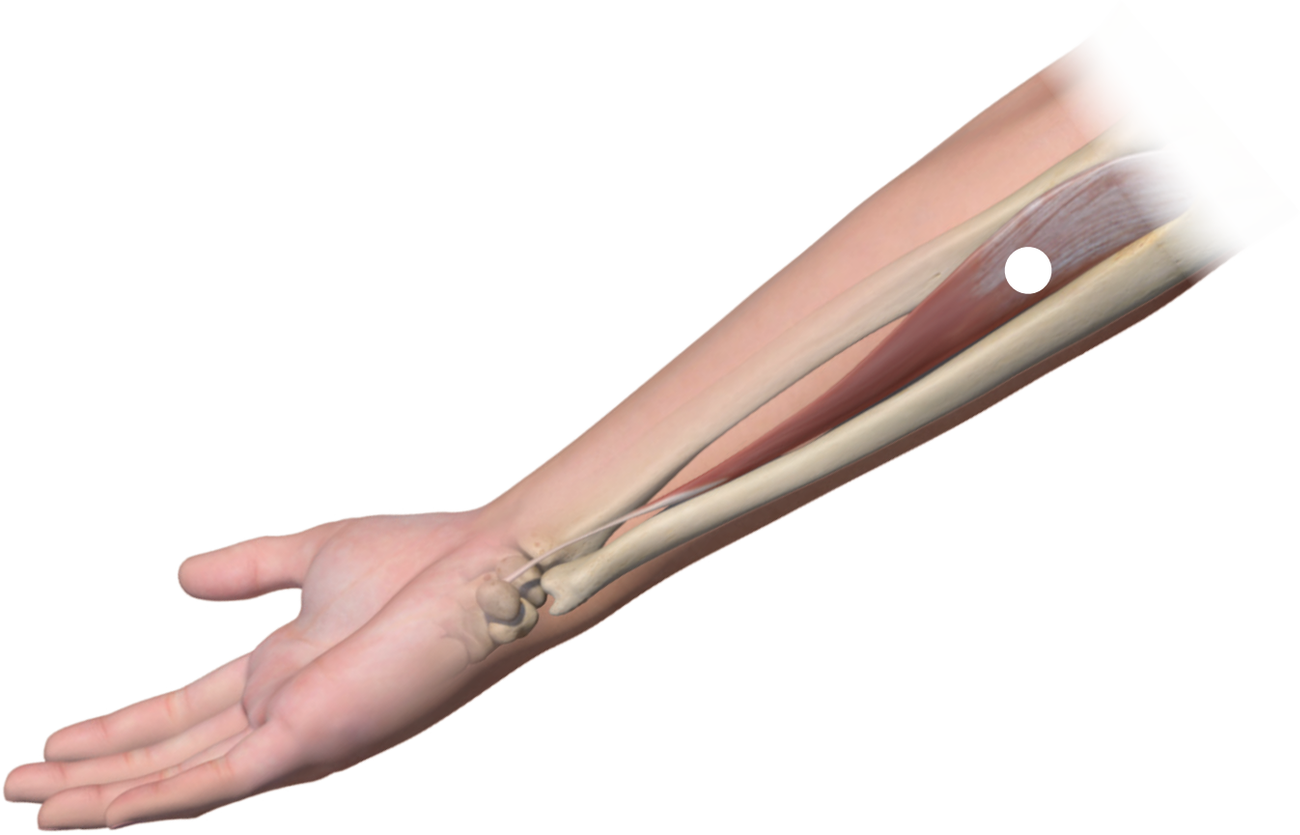


Flexor carpi ulnaris (continued)

Ultrasound

EMG/E-Stim

Injection considerations



Dot represents injection site.

- If possible, position the limb in a comfortable position and localize using 2 fingerbreadths volar to the ulna
- Consider targeting the injection site in the ulnar portion of the volar forearm
- This muscle is very thin and superficial, so be aware of the surrounding nerves, arteries, and veins that are in the trajectory of the needle path

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.

Please see additional Important Safety Information throughout.

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IMPORTANT SAFETY INFORMATION (continued)
DRUG INTERACTIONS (continued)
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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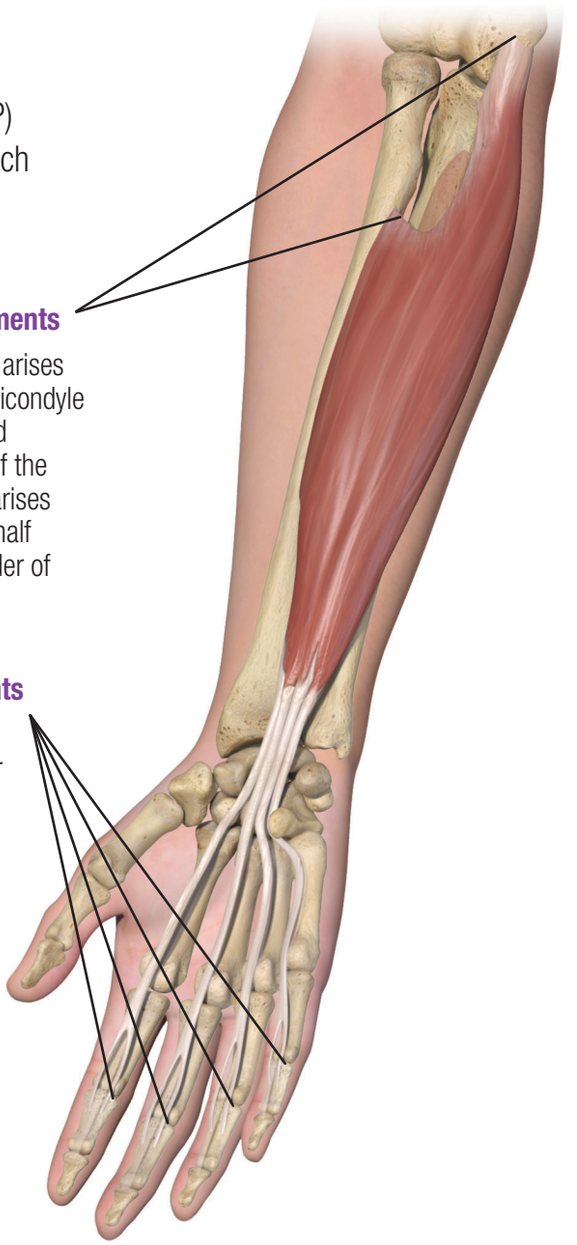
Flexor digitorum superficialis (sublimis)

▶ BOTOX® dose: 30 Units to 50 Units (1 site)

Muscle action[14]

Primarily finger flexion of proximal interphalangeal (PIP) joints, but can also flex any or all of the joints over which it passes including metacarpophalangeal (MCP) joints



Proximal attachments

Humeroulnar head arises from the medial epicondyle of the humerus and coronoid process of the ulna. Radial head arises from the proximal half of the anterior border of the radius

Distal attachments

Medial and lateral sides of the palmar surface of the middle phalanges

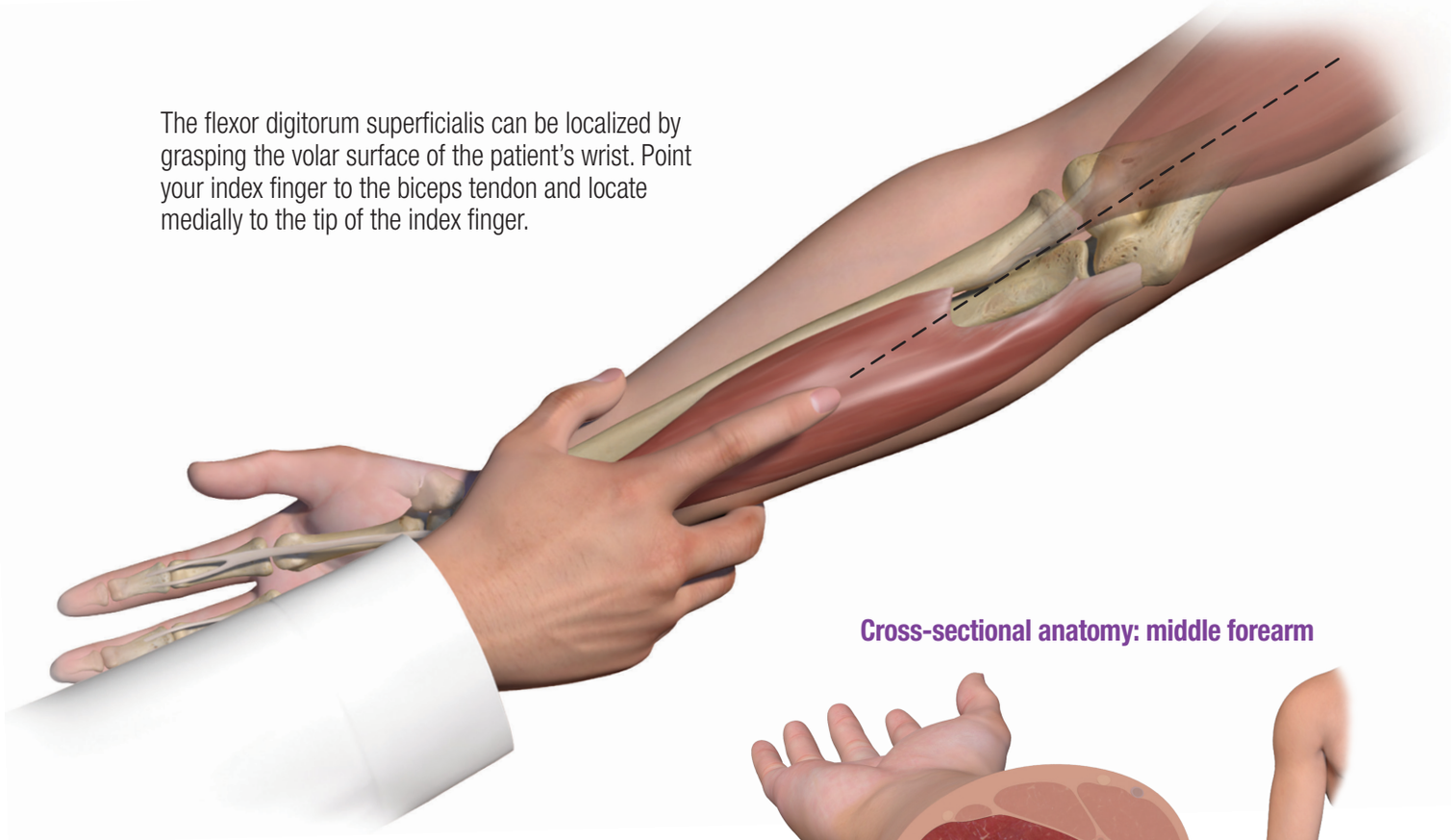
Other muscles involved in finger flexion

- Flexor digitorum profundus
- Lumbricals (MCP joints)
- Interossei (MCP joints)

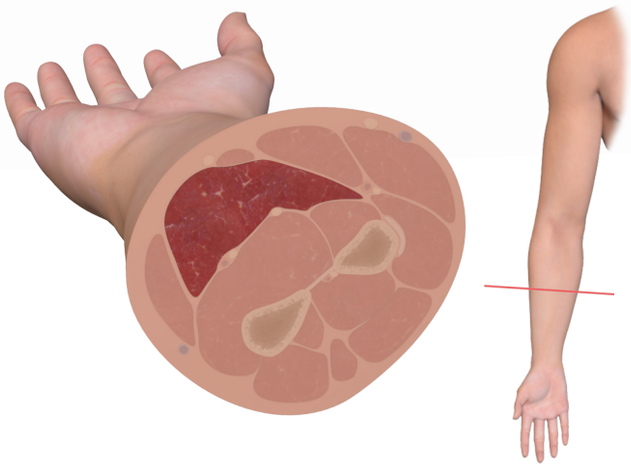
Flexor digitorum superficialis (sublimis) (continued)

Localization[20]

The flexor digitorum superficialis can be localized by grasping the volar surface of the patient's wrist. Point your index finger to the biceps tendon and locate medially to the tip of the index finger.



Cross-sectional anatomy: middle forearm

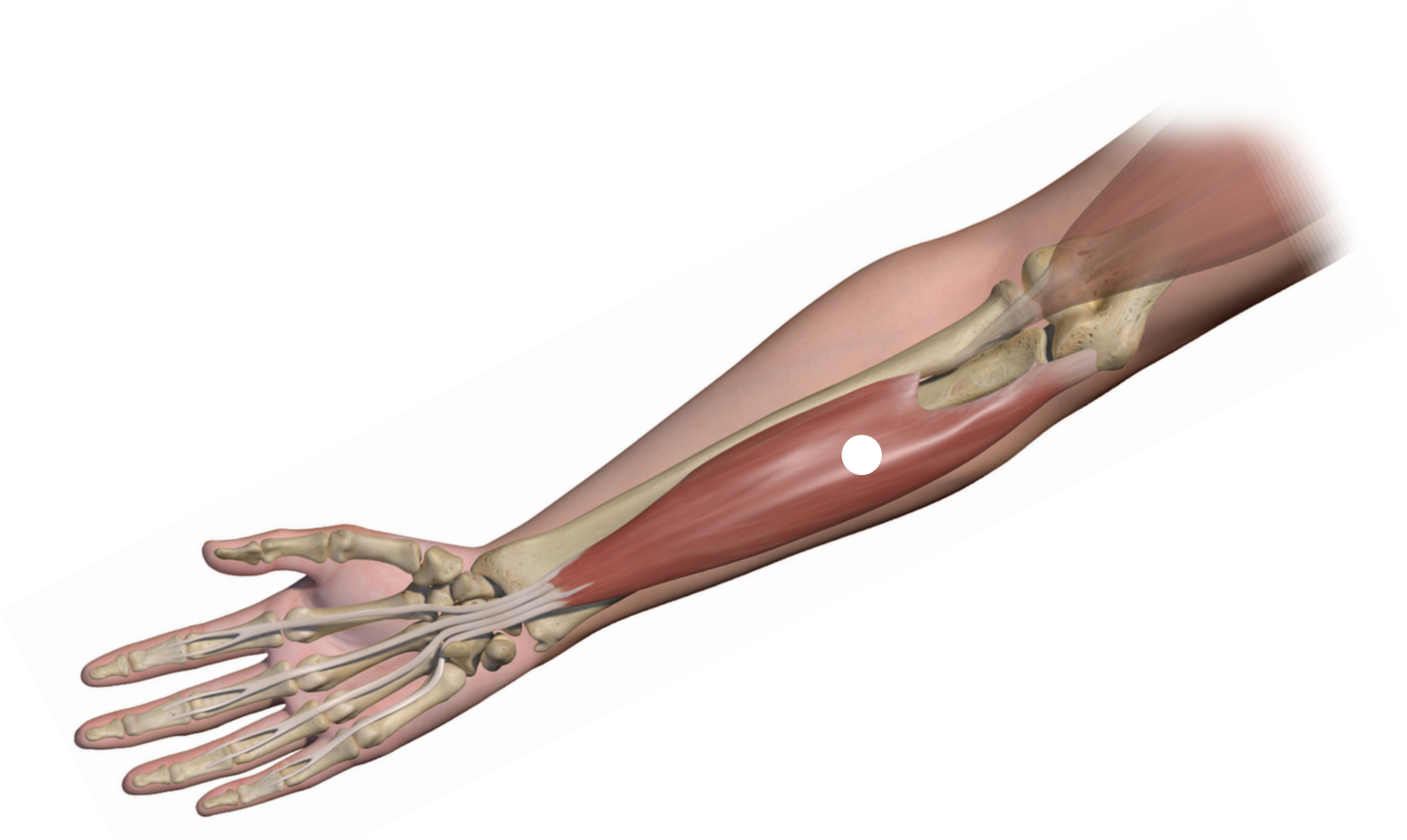


BOTOX® onabotulinumtoxinA injection

Flexor digitorum superficialis (sublimis) (continued)

Ultrasound EMG/E-Stim

Injection considerations



Dot represents injection site.

- Target this muscle when the PIP joints are spastic
- The finger flexors are located in the middle third to half of the forearm. Localization of this muscle may be difficult
- Passively extend the PIP joints to help localize the muscle. The use of E-Stim is highly recommended
- Once the muscle has been anatomically localized, use EMG and/or E-Stim guidance to further identify the muscle
- If the fingers can be stretched out, it makes identifying the superficialis and profundus with E-Stim easier

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.

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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.

Please see additional Important Safety Information throughout.

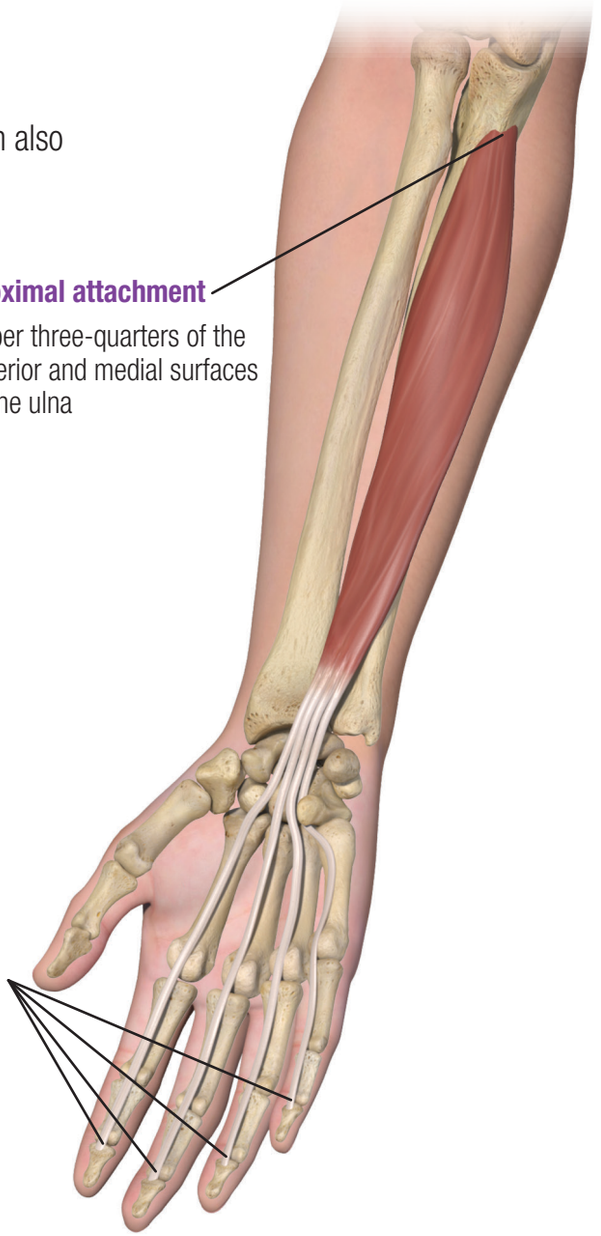
BOTOX® onabotulinumtoxinA injection

Flexor digitorum profundus

▶ BOTOX® dose: 30 Units to 50 Units (1 site)

Muscle action[14]

Primarily finger flexion (only muscle capable of flexing the distal interphalangeal joints), but can also flex any or all of the joints over which it passes



Other muscles involved in finger flexion

- Flexor digitorum superficialis (sublimis)
- Lumbricals (MCP joints)
- Interossei (MCP joints)

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Serious Adverse Reactions With Unapproved Use (continued)
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.

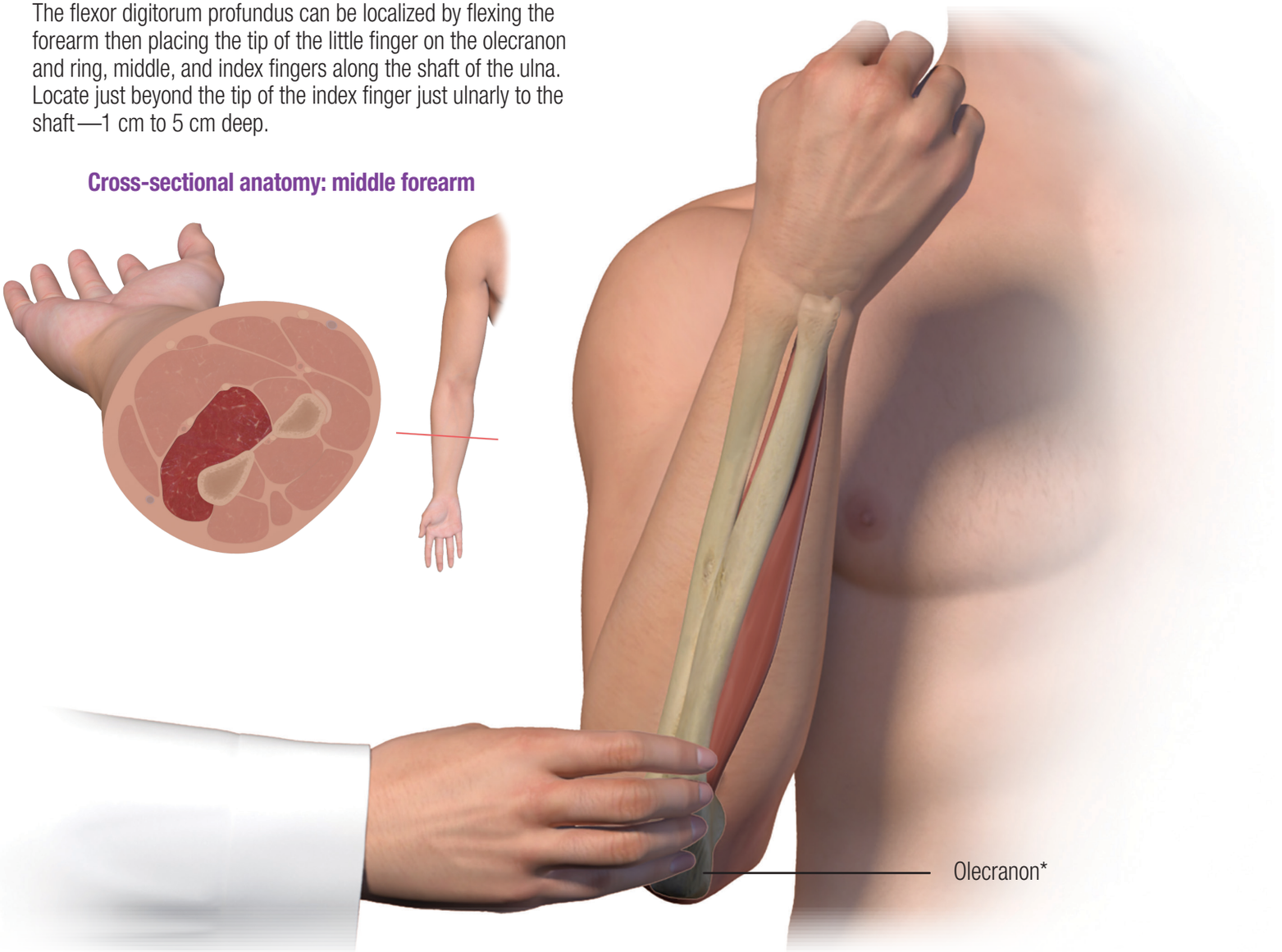
BOTOX®
onabotulinumtoxinA injection

Flexor digitorum profundus (continued)

Localization[20]

The flexor digitorum profundus can be localized by flexing the forearm then placing the tip of the little finger on the olecranon and ring, middle, and index fingers along the shaft of the ulna. Locate just beyond the tip of the index finger just ulnarly to the shaft—1 cm to 5 cm deep.

Cross-sectional anatomy: middle forearm



*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.

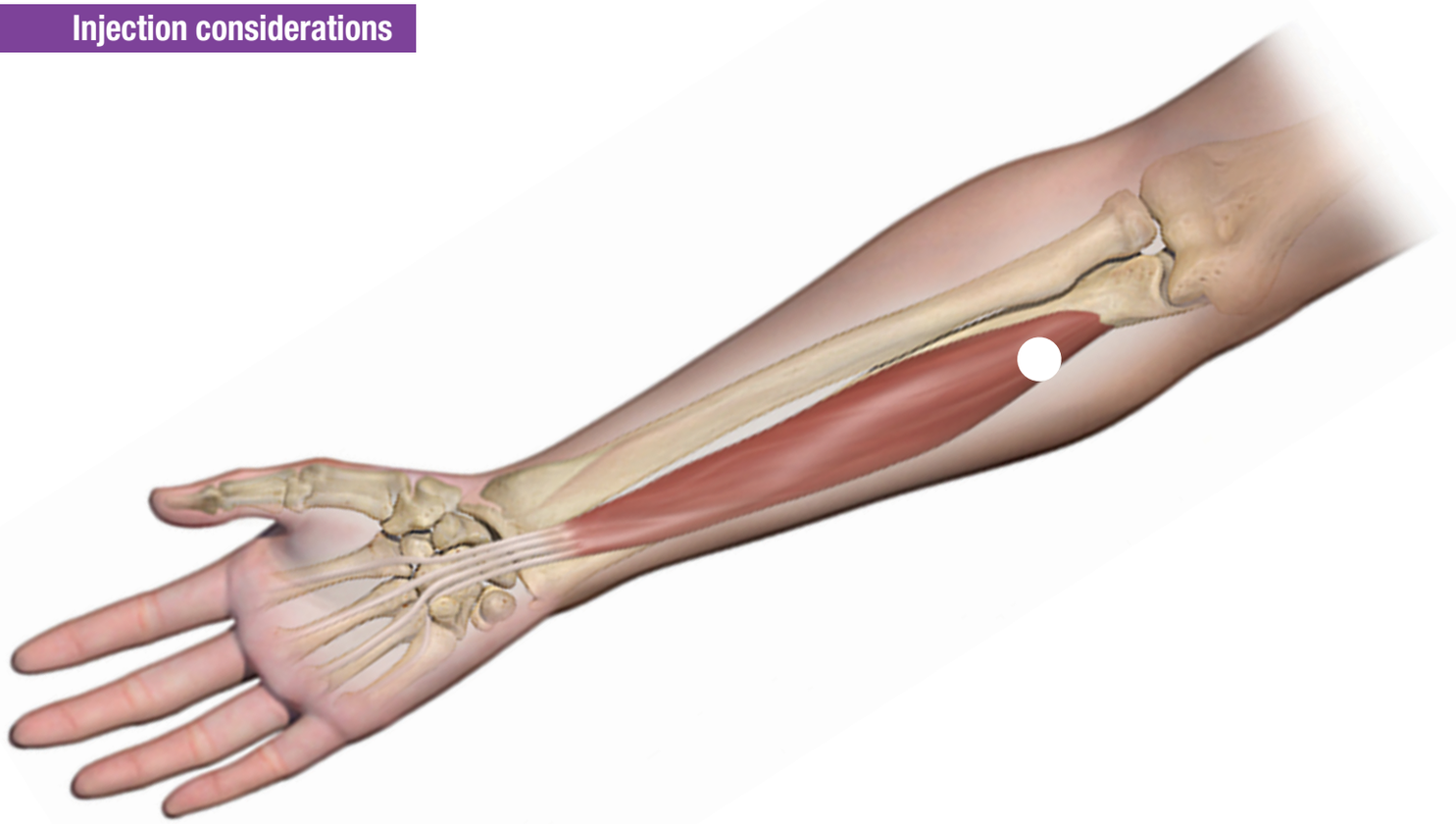
BOTOX® onabotulinumtoxinA injection

Flexor digitorum profundus (continued)

Ultrasound

EMG/E-Stim

Injection considerations



Dot represents injection site.

- If possible, position the elbow bent and forearm vertical
- Consider injecting proximal toward the elbow, at the largest part of the muscle. Note that the muscle is deeper in the anatomy of the arm
- If there is more spasticity in fingers 2 and 3, advance your needle more laterally
- The finger flexors are located in the middle half of the forearm. Target this muscle when the distal interphalangeal joints are closed
- Be aware of the surrounding nerves, arteries, and veins that are in the trajectory of the needle path

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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

Flexor pollicis longus

▶ BOTOX® dose: 20 Units (1 site)

Muscle action[14, 15]

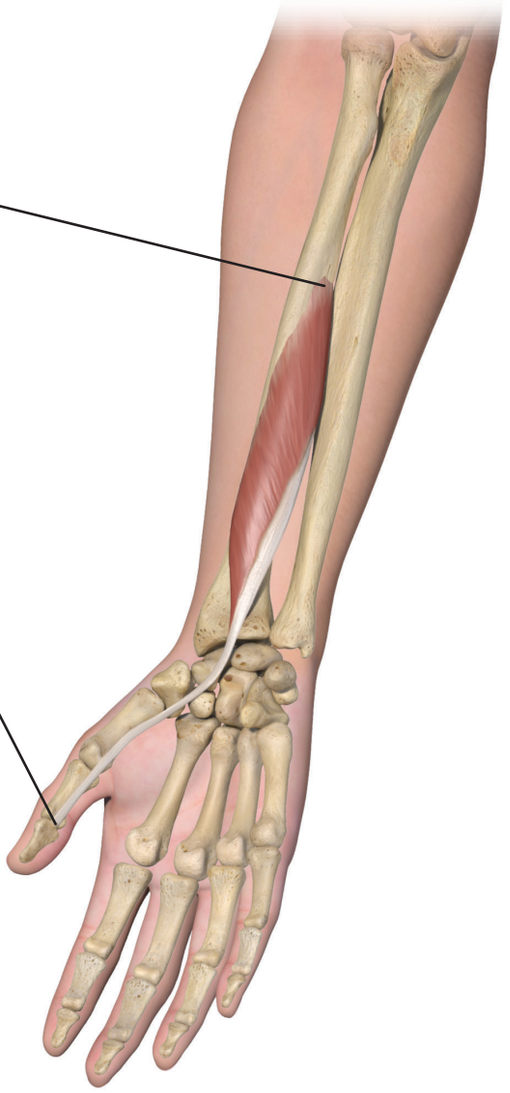
Flexes thumb, but can also be involved in wrist flexion

Proximal attachment

Anterior surface of the radius (adjacent to the interosseous membrane)

Distal attachment

Palmar surface of the base of the distal phalanx of the thumb



Other muscles involved in thumb flexion or wrist flexion

- Flexor pollicis brevis (thumb flexion)
- Flexor carpi ulnaris (wrist flexion)
- Opponens pollicis (thumb flexion)
- Flexor carpi radialis (wrist flexion)

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

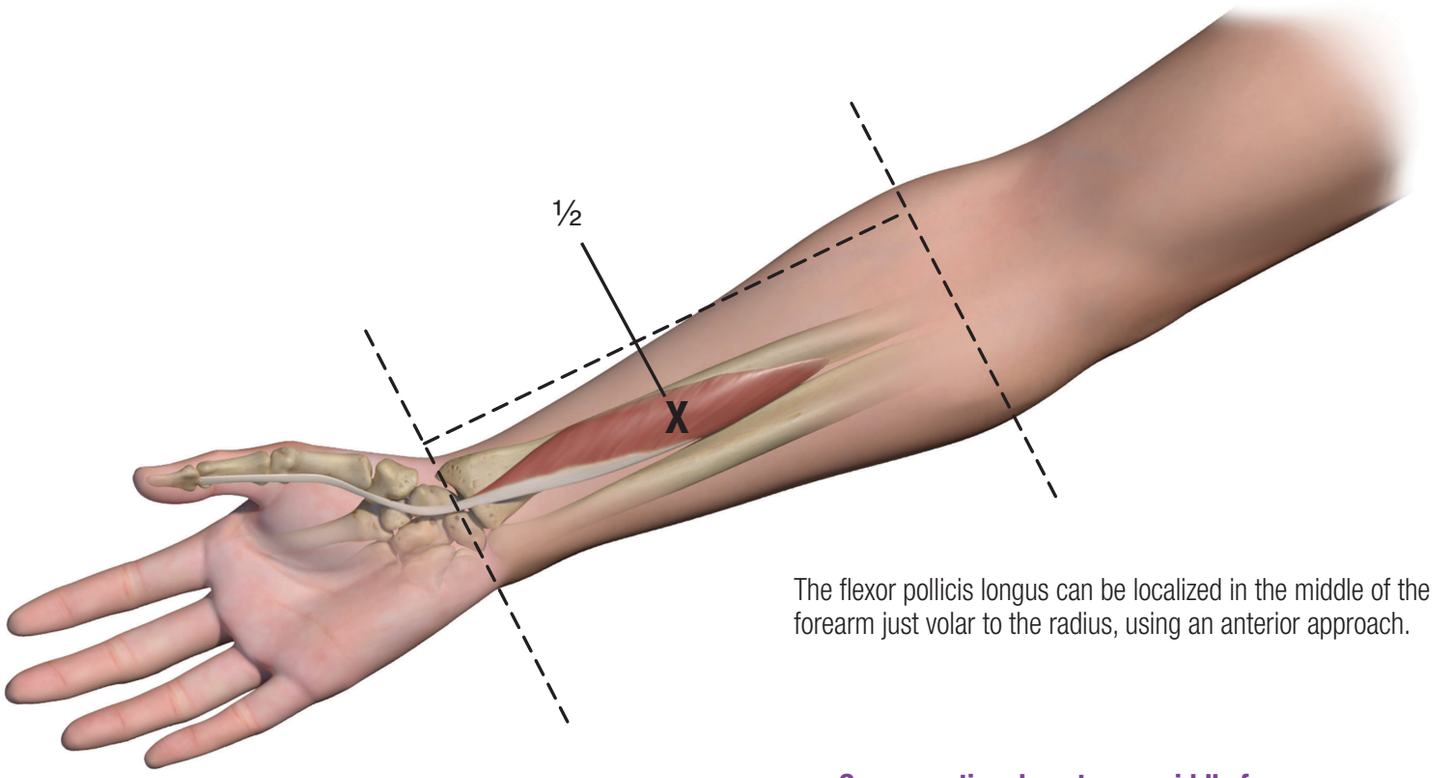
Pulmonary Effects of BOTOX in Patients With Compromised Respiratory Status Treated for Spasticity

Patients with compromised respiratory status treated with BOTOX for spasticity should be monitored closely.

Please see additional Important Safety Information throughout.

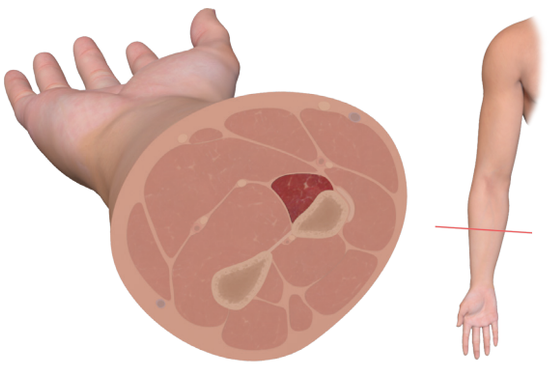
Flexor pollicis longus (continued)

Localization[20]



The flexor pollicis longus can be localized in the middle of the forearm just volar to the radius, using an anterior approach.

Cross-sectional anatomy: middle forearm



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

Bronchitis and Upper Respiratory Tract Infections in Patients Treated for Spasticity

Bronchitis was reported more frequently as an adverse reaction in adult patients treated for upper limb spasticity with BOTOX (3% at 251 Units to 360 Units total dose) compared to placebo (1%). In adult patients with reduced lung function treated for upper limb spasticity, upper respiratory tract infections were also reported more frequently as adverse reactions in patients treated with BOTOX (11% at 360 Units total dose; 8% at 240 Units total dose) compared to placebo (6%). In adult patients treated for lower limb spasticity, upper respiratory tract infections were reported more frequently as an adverse reaction in patients treated with BOTOX (2% at 300 Units to 400 Units total dose) compared to placebo (1%).

Please see additional Important Safety Information throughout.

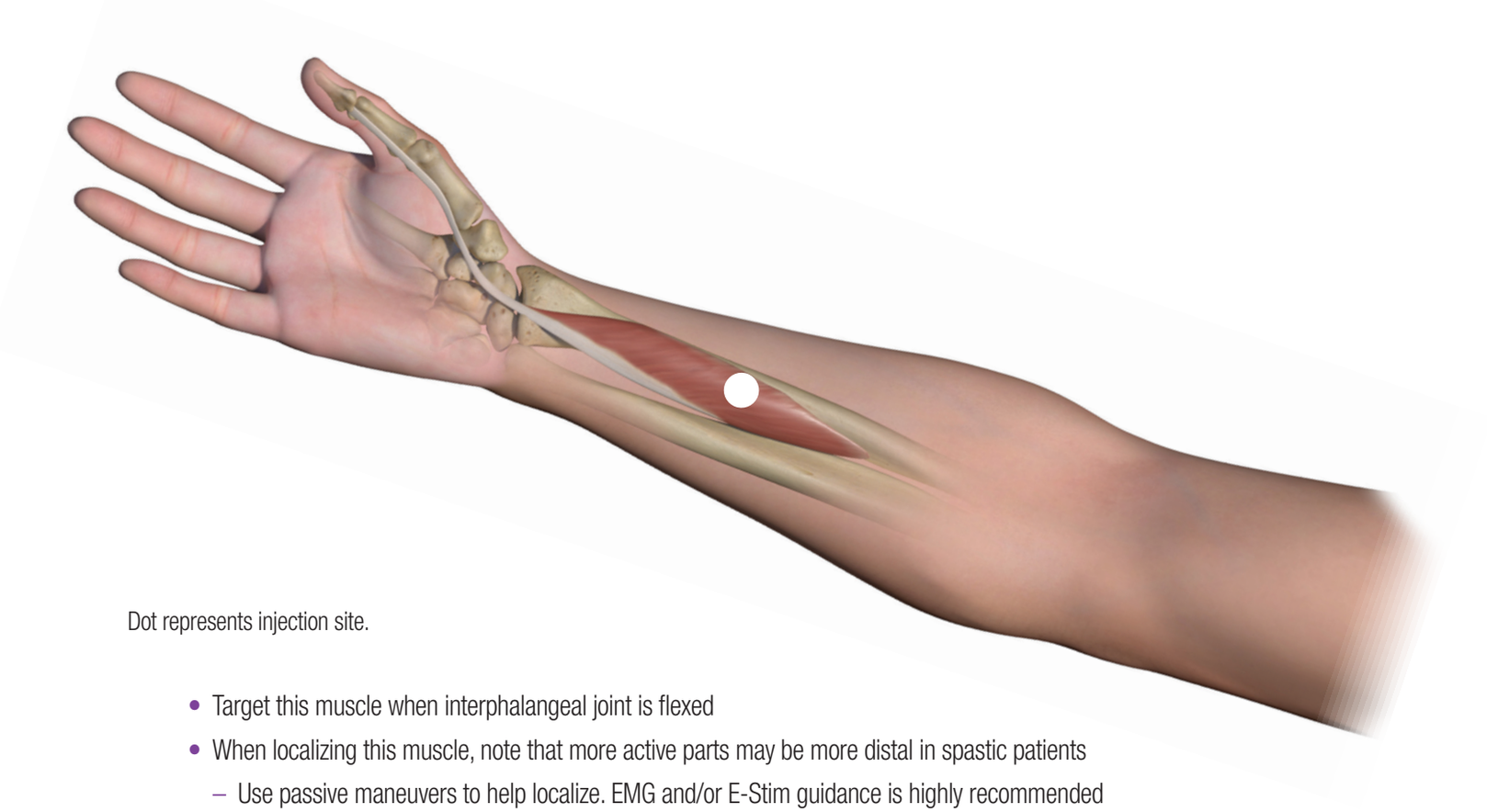
BOTOX® onabotulinumtoxinA injection

Flexor pollicis longus (continued)

Ultrasound

EMG/E-Stim

Injection considerations



Dot represents injection site.

- Target this muscle when interphalangeal joint is flexed
- When localizing this muscle, note that more active parts may be more distal in spastic patients
  - Use passive maneuvers to help localize. EMG and/or E-Stim guidance is highly recommended
  - Stabilize the joints prior to injection
- It may be helpful to palpate the radius and then slide to the ulnar side of the radius. Consider inserting the needle volar and lateral to the midline about two-thirds the distance of the forearm from the medial epicondyle

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Notes

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.

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Flexor pollicis brevis

▶ BOTOX® dose: 5 Units to 25 Units in 1 site

Muscle action[14]

Flexes the thumb (MCP joint)

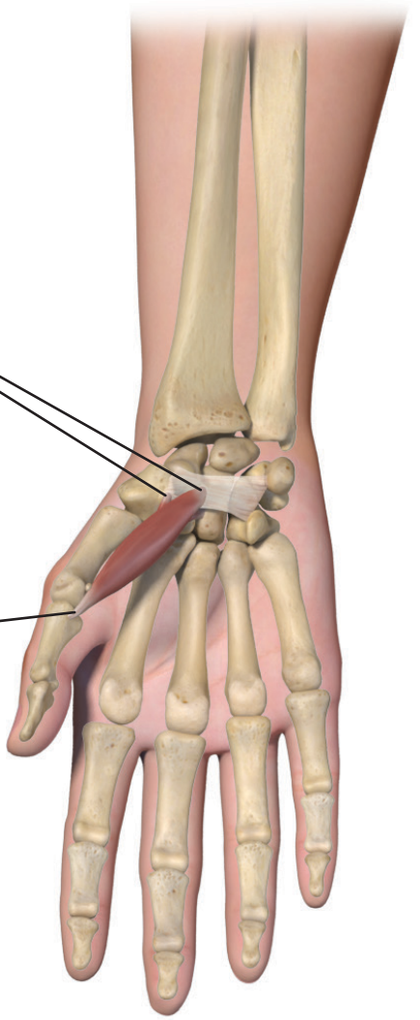
Proximal attachments

Superficial head arises from the flexor retinaculum and the tubercle of the trapezium

Deep head arises from the trapezoid and capitate bones

Distal attachment

Base of the proximal phalanx of the thumb



Other muscles involved in thumb flexion

- Flexor pollicis longus
- Opponens pollicis

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Adult Upper Limb Spasticity
The most frequently reported adverse reactions following injection of BOTOX for upper limb spasticity include pain in extremity, muscular weakness, fatigue, nausea, and bronchitis.

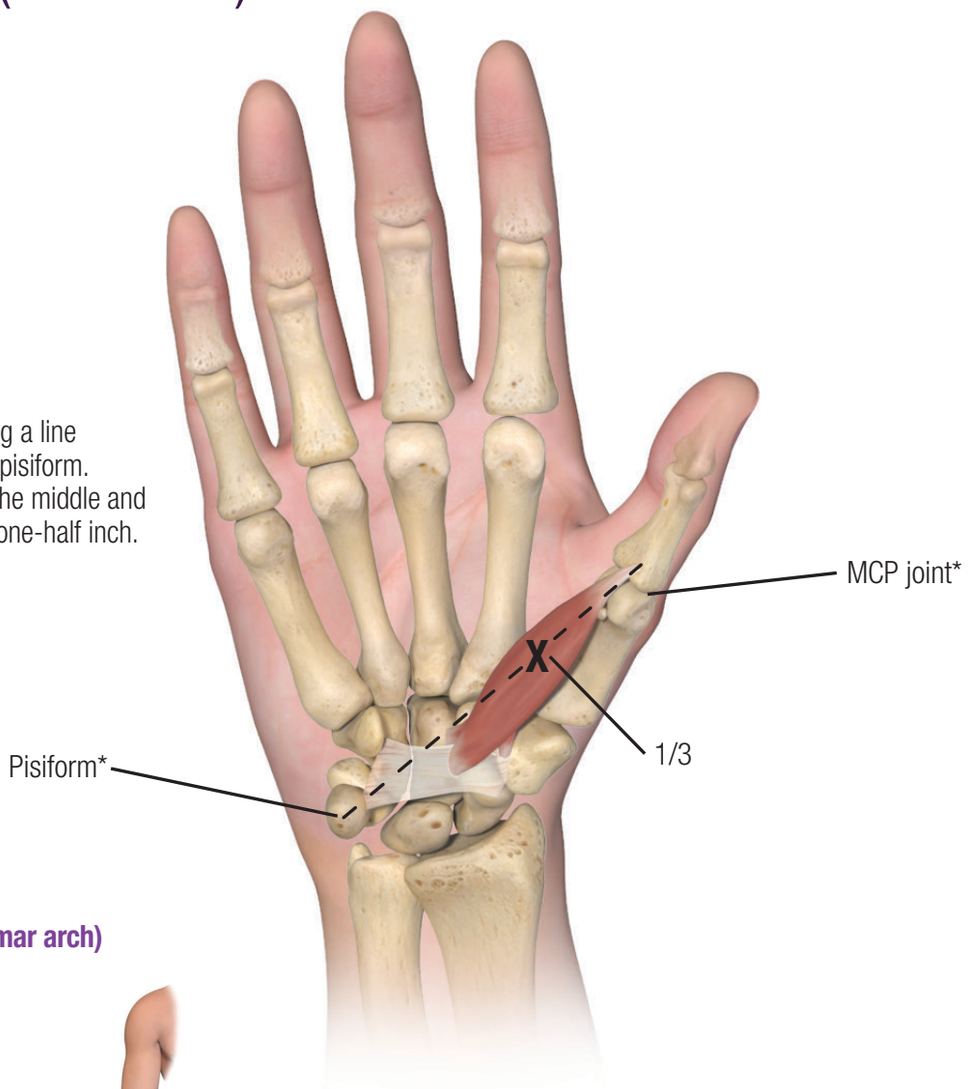
Please see additional Important Safety Information throughout.

Flexor pollicis brevis (continued)

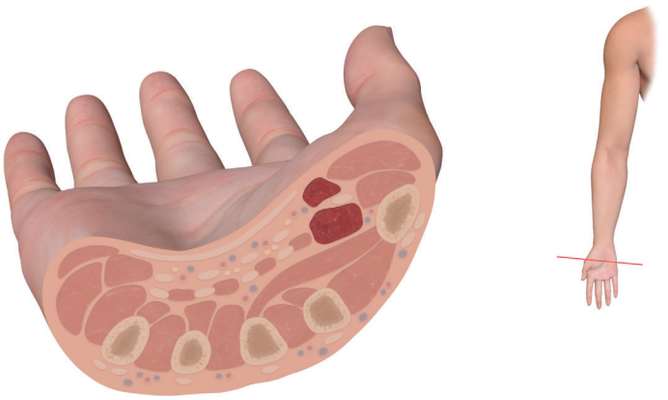
Localization[20]

The flexor pollicis brevis can be localized by drawing a line between the ulnar aspect of the MCP joint and the pisiform. The muscle can be found at the junction between the middle and radial thirds of this line at a depth of one-fourth to one-half inch.

*For anatomical reference only.



Cross-sectional anatomy: hand (palmar arch)



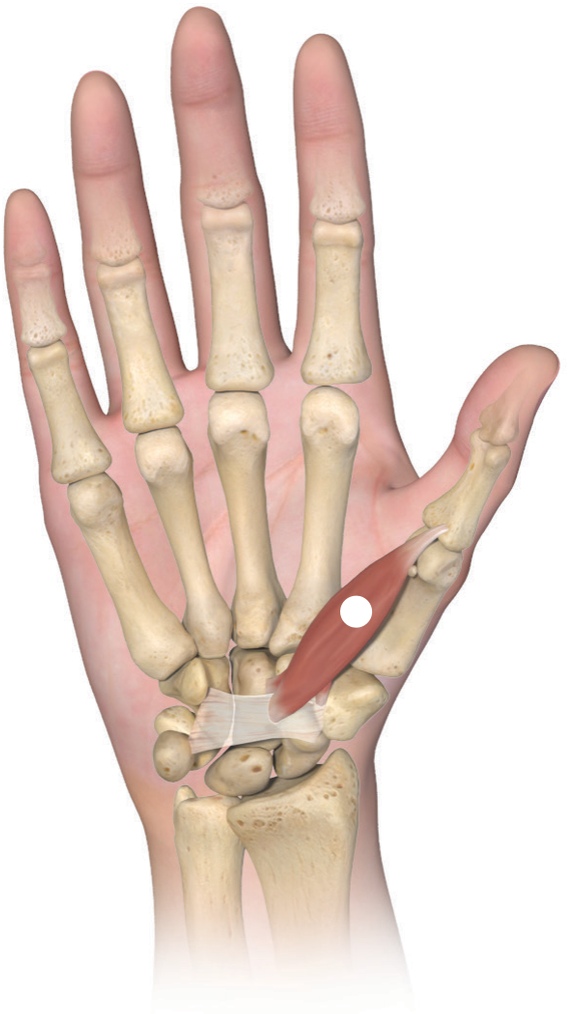
IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Adult Lower Limb Spasticity
The most frequently reported adverse reactions following injection of BOTOX for lower limb spasticity include arthralgia, back pain, myalgia, upper respiratory tract infection, and injection-site pain.

Please see additional Important Safety Information throughout.

Flexor pollicis brevis (continued)

Injection considerations

30-Gauge Needle



Dot represents injection site.

- Advise the patient that this may be a painful injection
  - Consider using a 30-gauge needle
  - Consider utilizing a distractive strategy during injection (eg, pinching the patient's forearm)
  - To help make this a quick injection, consider relying on palpation/anatomical landmarks only when localizing this muscle
- If the needle is inserted too deeply, it may be in the opponens pollicis
- When localizing this muscle, note that 2 sesamoid bones are easily palpable in the tendon at the MCP joint

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

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Notes

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.

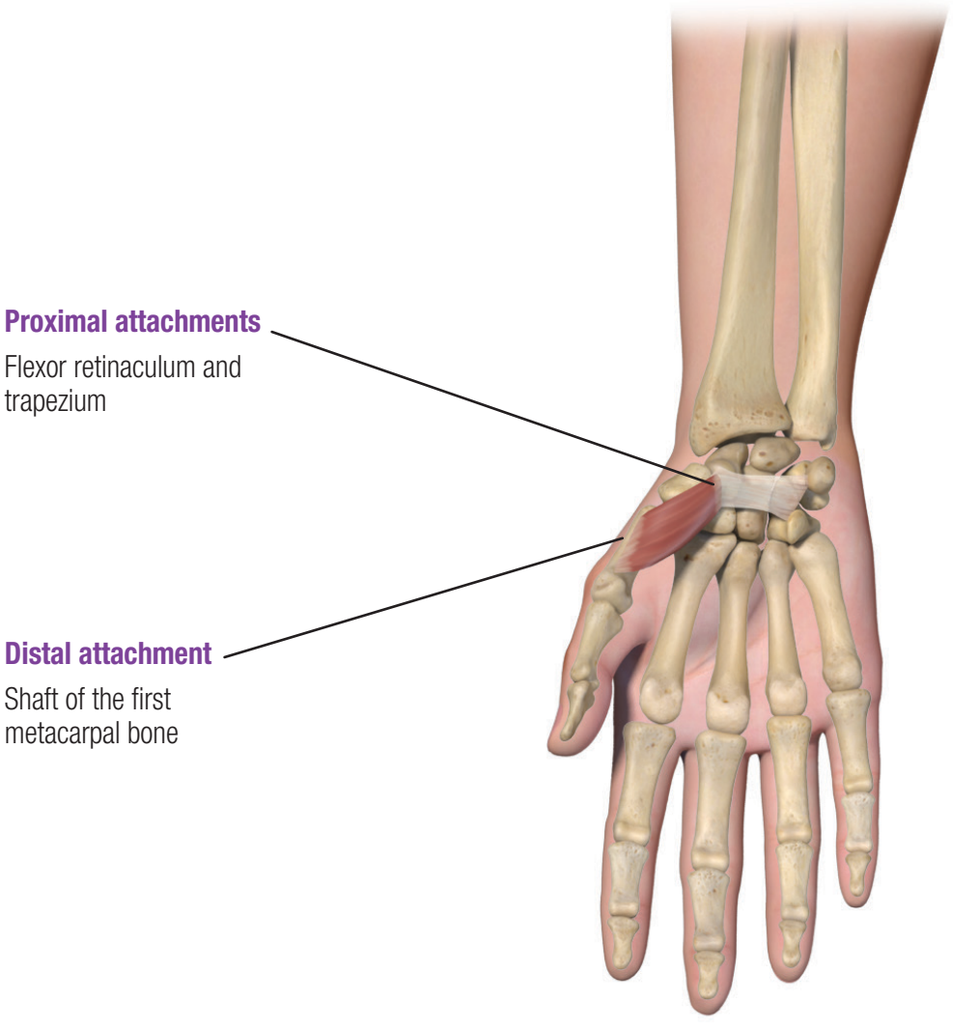
BOTOX® onabotulinumtoxinA injection

Opponens pollicis

▶ BOTOX® dose: 5 Units to 25 Units in 1 site

Muscle action[14]

Flexes the metacarpal bone of the thumb



IMPORTANT SAFETY INFORMATION (continued)

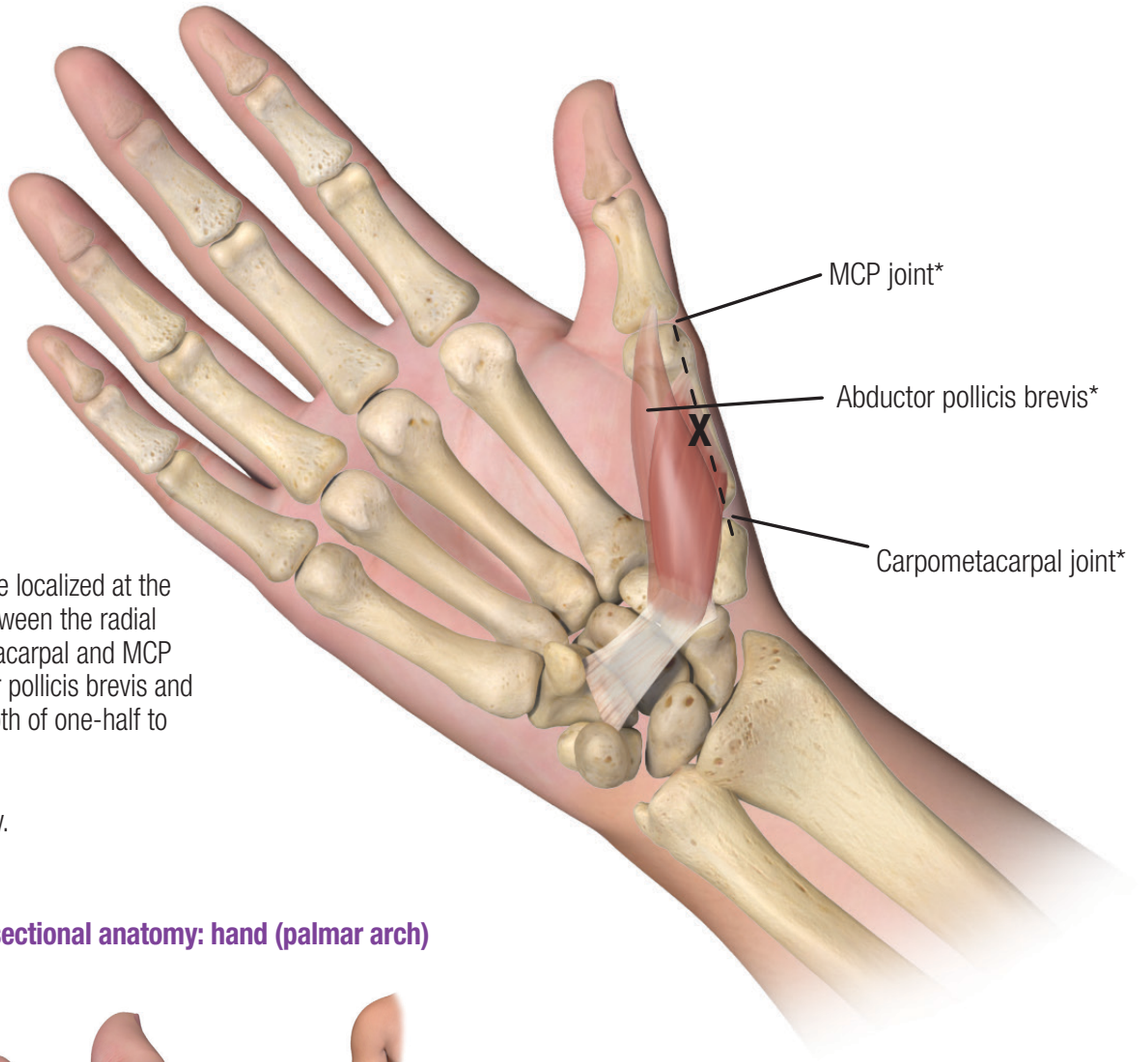
DRUG INTERACTIONS

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

Opponens pollicis (continued)

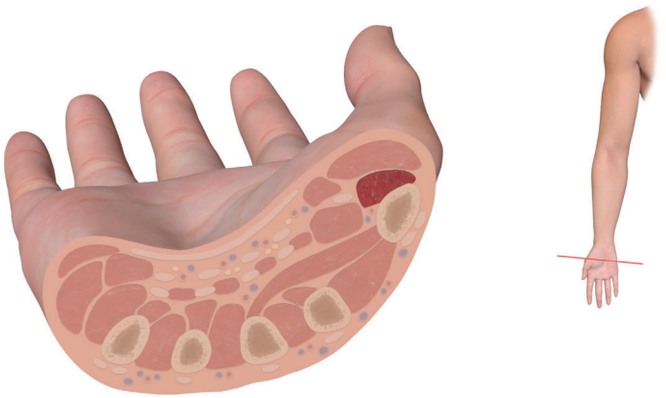
Localization[20]



The opponens pollicis can be localized at the midpoint of a line drawn between the radial aspect of the first carpometacarpal and MCP joints, between the abductor pollicis brevis and the first metacarpal at a depth of one-half to three-fourths inch.

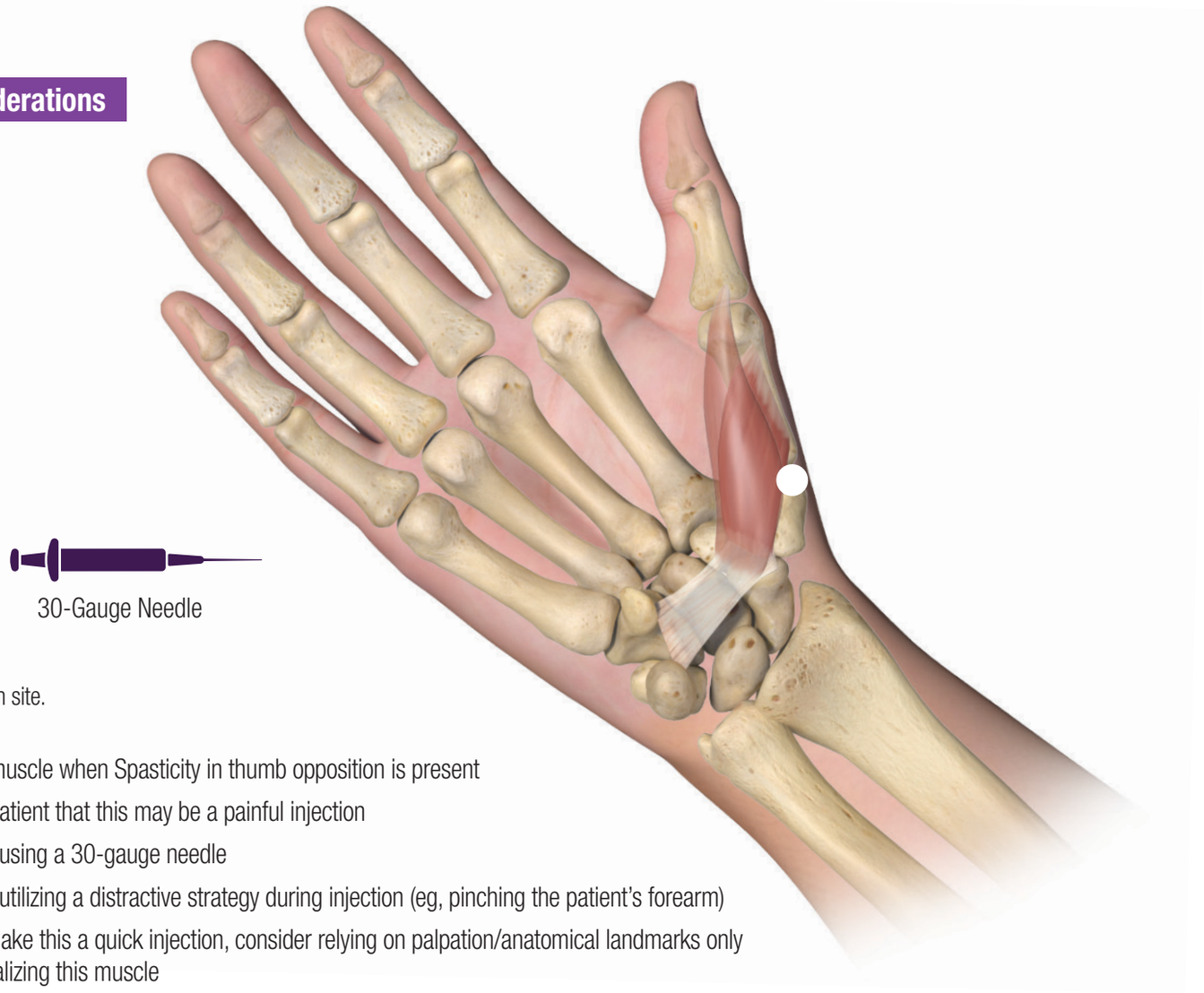
*For anatomical reference only.

Cross-sectional anatomy: hand (palmar arch)



Opponens pollicis (continued)

Injection considerations



30-Gauge Needle

Dot represents injection site.

- Target this muscle when Spasticity in thumb opposition is present
- Advise the patient that this may be a painful injection
  - Consider using a 30-gauge needle
  - Consider utilizing a distractive strategy during injection (eg, pinching the patient's forearm)
  - To help make this a quick injection, consider relying on palpation/anatomical landmarks only when localizing this muscle
- Consider placing the needle just inferior to the edge of the 1st metacarpal bone
  - If the needle is inserted too deeply, it may be in the adductor pollicis; if inserted too medially, it may be in the wrong muscle

BOTOX® onabotulinumtoxinA injection

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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®
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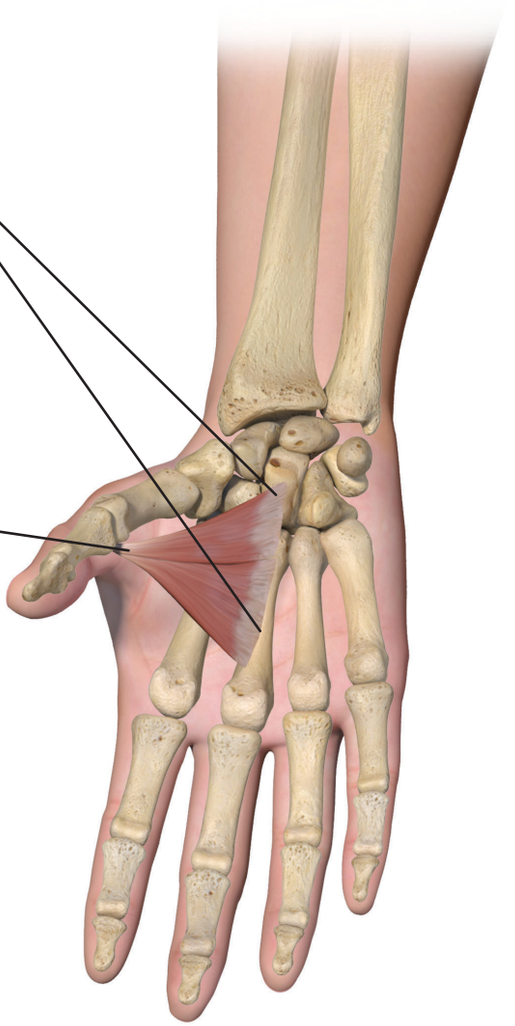
Adductor pollicis

▶ BOTOX® dose: 20 Units (1 site)

Muscle action[14]

Adducts the thumb



Proximal attachments

Oblique head is attached to the capitate bone and the bases of the second and third metacarpal bones. The transverse head is attached to the distal two-thirds of the palmar surface of the third metacarpal

Distal attachment

Base of the proximal phalanx of the thumb

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.

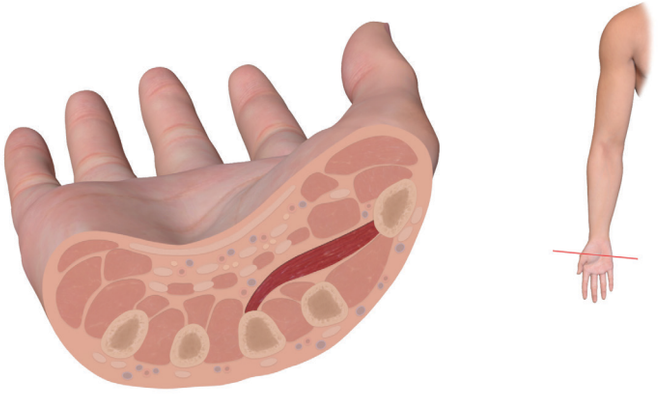
Please see additional Important Safety Information throughout.

Adductor pollicis (continued)

Localization[20]

The adductor pollicis is localized at the free edge of the first webspace, in between the proximal end of the first metacarpal and the middle of the third metacarpal bones.

Cross-sectional anatomy: hand (palmar arch)



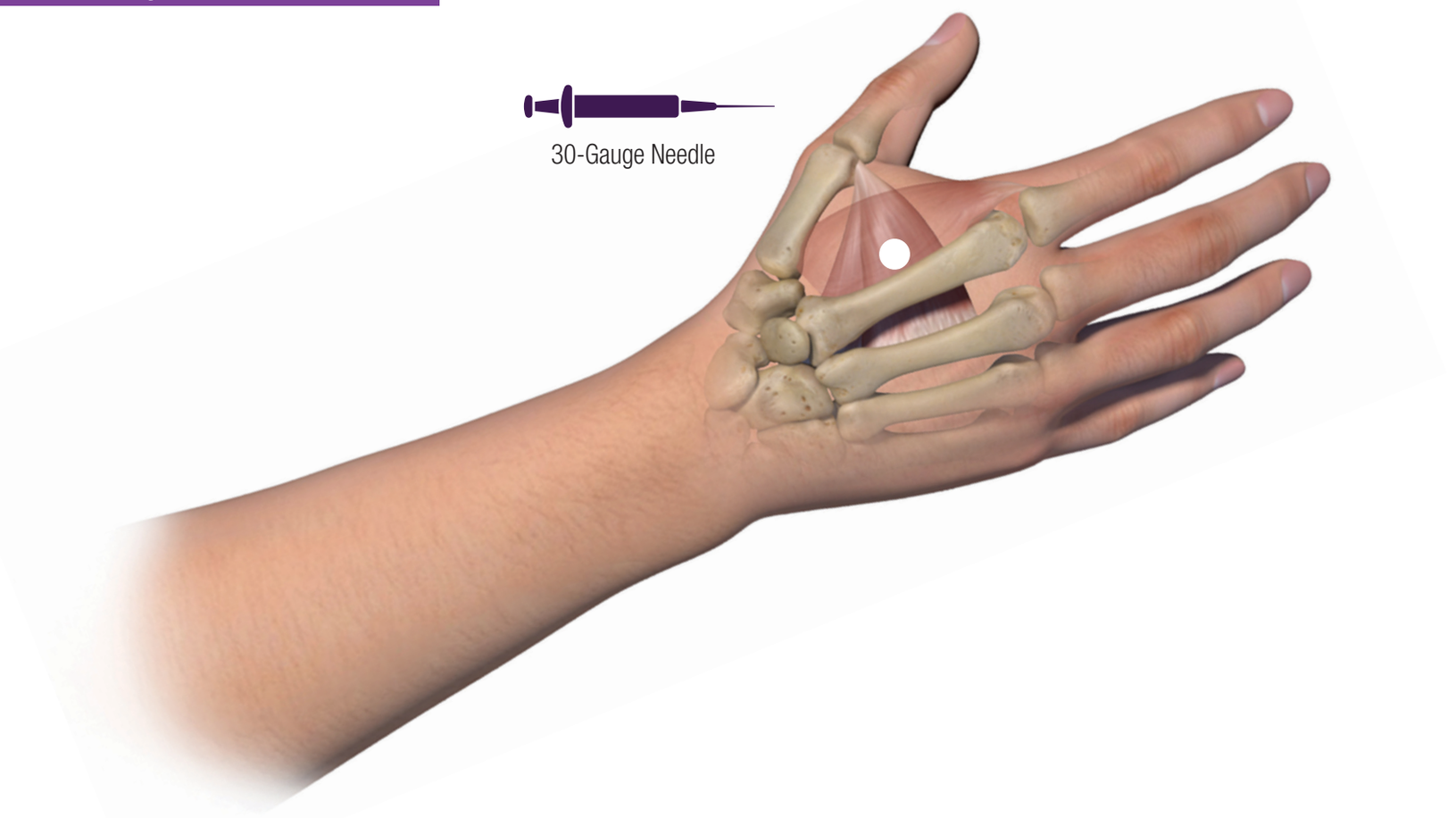
IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Serious Adverse Reactions With Unapproved Use (continued)
In these cases, the adverse reactions were not necessarily related to distant spread of toxin, but may have resulted from the administration of BOTOX to the site of 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

Adductor pollicis (continued)

Injection considerations



Dot represents injection site.

- This muscle is most often injected when trying to position the thumb for a wrist/hand orthosis
- Consider inserting the needle from the backside of the hand and injecting quickly to minimize pain
- It is often a painful injection site, so consider the use of a 30-gauge needle

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.

Please see additional Important Safety Information throughout.

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Notes

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Hypersensitivity Reactions (continued)
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®
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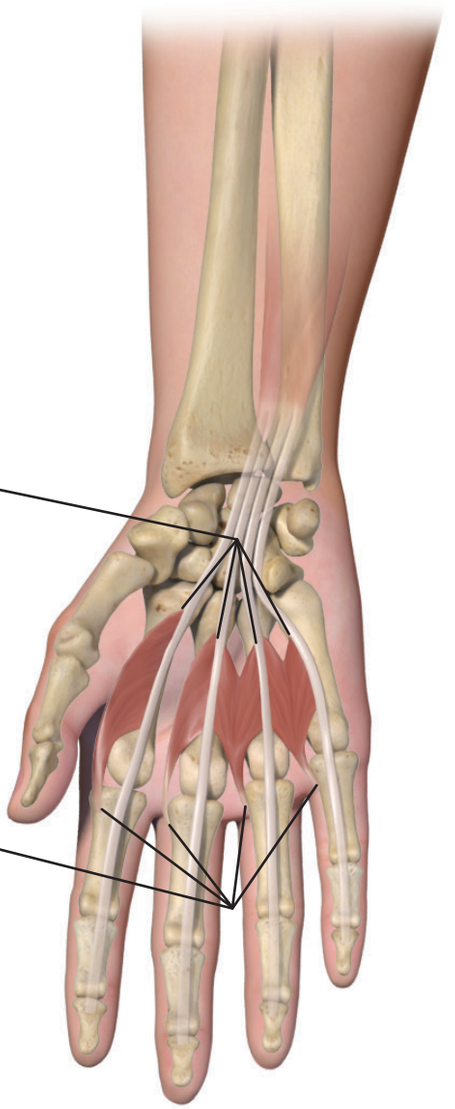
Lumbricals

▶ BOTOX® dose: 5 Units to 10 Units in 1 site per muscle

Muscle action[14]

Flex the MCP joints and extend the interphalangeal (IP) joints of digits 2 through 5



Proximal attachments

Tendons of the flexor digitorum profundus

Distal attachments

Lateral margins of the dorsal digital expansion of the extensor digitorum*

*For anatomical reference only.

Other muscles involved in MCP flexion or IP extension

- Flexor digitorum superficialis (sublimis) (MCP flexion)
- Flexor digitorum profundus (MCP flexion)
- Interossei (IP extension)

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.

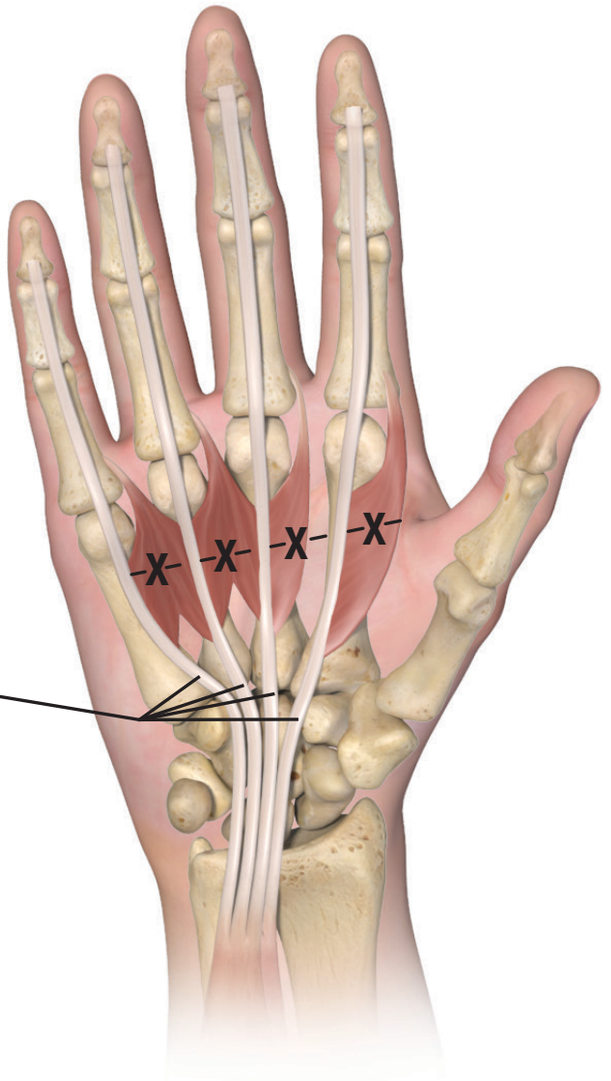
Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

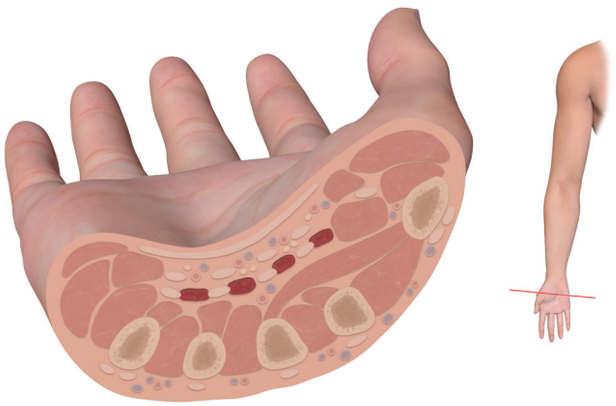
Lumbricals (continued)

Localization[20]

The lumbricals can be localized just proximal to the MCP joints and radial to the flexor tendon.



Cross-sectional anatomy: hand (palmar arch)

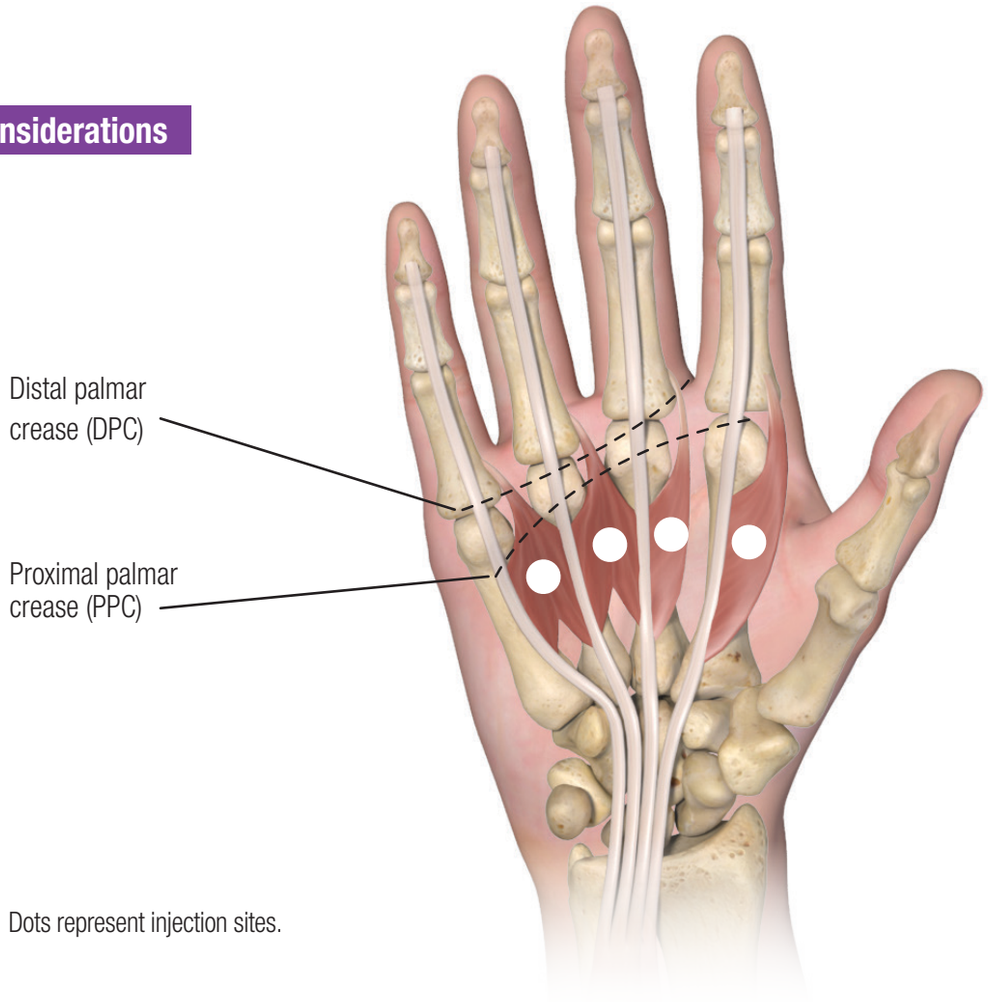


*For anatomical reference only.

Lumbricals (continued)

Ultrasound EMG/E-Stim

Injection considerations



Dots represent injection sites.

- When injecting both the lumbricals and/or interossei, consider limiting the combined total dose to 50 Units per hand
- Carefully consider the functional anatomy of these muscles and only target if deemed clinically necessary (eg, when the MCP joints are spastic). Physicians should consider their level of comfort and expertise with injecting this muscle group before proceeding
- Guidance techniques are highly recommended for these muscles to avoid inadvertent injection of nontargeted muscles, such as the interossei
- Consider the following when determining how to approach injection:
  - Dorsal approach is typically less painful, but localization is more challenging
  - Palmar approach is typically more painful, but localization is more straightforward
  - A 30-gauge needle and/or cold spray may help minimize injection pain
- When localizing for injection, note that the MCP joints have a direct relationship with both the PPC and DPC
  - The DPC lies over the 3rd, 4th, and 5th MCP joints
  - The PPC lies over the 2nd MCP joint

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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®
onabotulinumtoxinA injection

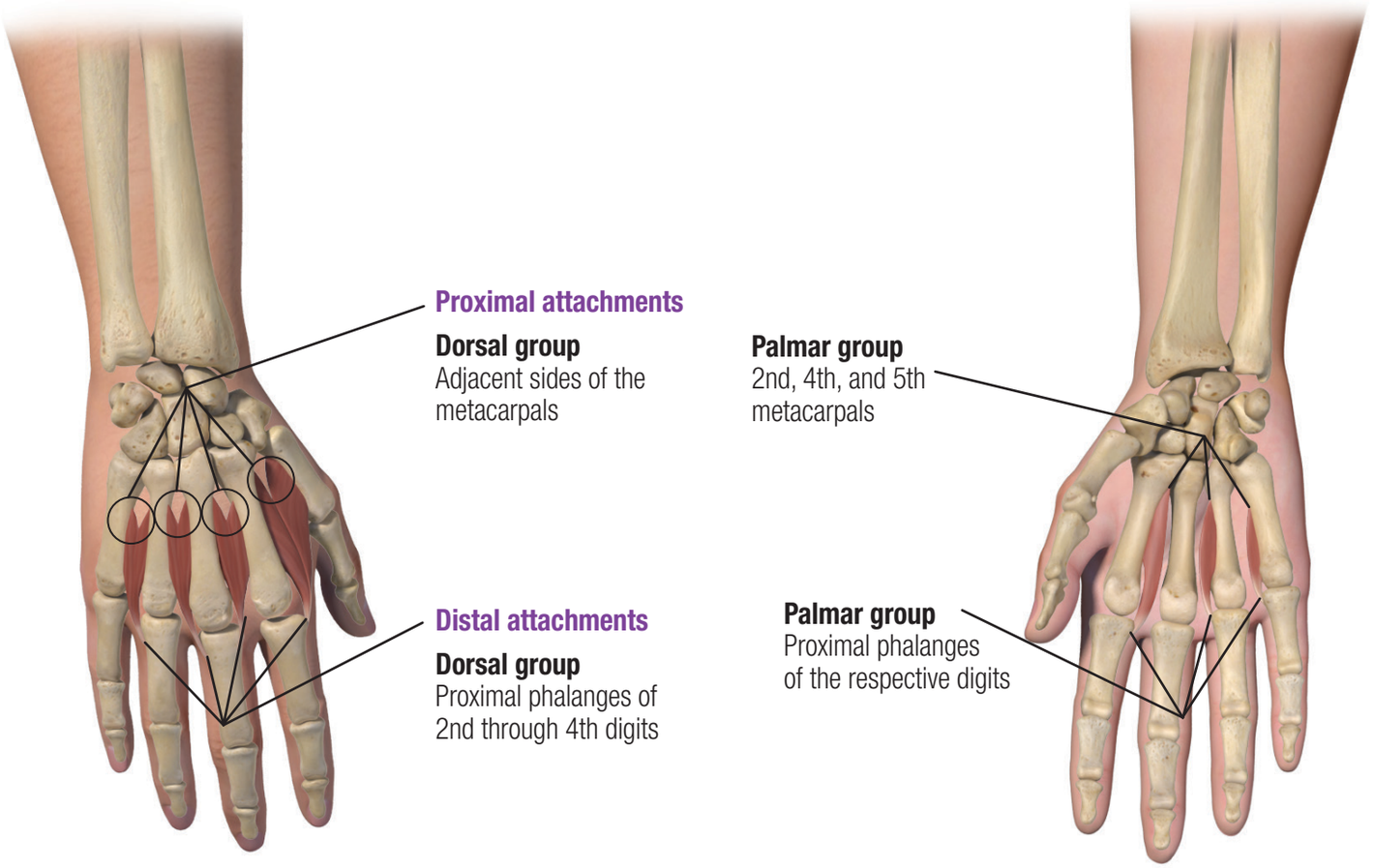
Interossei

▶ BOTOX® dose: 5 Units to 10 Units in 1 site per muscle

Muscle action[14]

Dorsal group: Abducts the 2nd, 3rd, and 4th digits away from a longitudinal axis that passes through the midline of the hand (3rd metacarpal). Also contributes to MCP flexion

Palmar group: Adducts the 2nd, 4th, and 5th digits toward the longitudinal axis that passes through the midline of the hand (3rd metacarpal). Also contributes strongly to MCP flexion and weak IP extension



Other muscles involved in MCP flexion or IP extension

- Flexor digitorum superficialis (sublimis) (MCP flexion)
- Lumbricals (IP extension)
- Flexor digitorum profundus (MCP flexion)

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Pulmonary Effects of BOTOX in Patients With Compromised Respiratory Status Treated for Spasticity
Patients with compromised respiratory status treated with BOTOX for spasticity should be monitored closely.

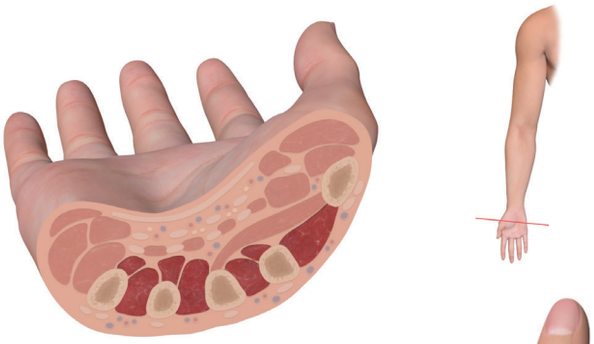
Please see additional Important Safety Information throughout.

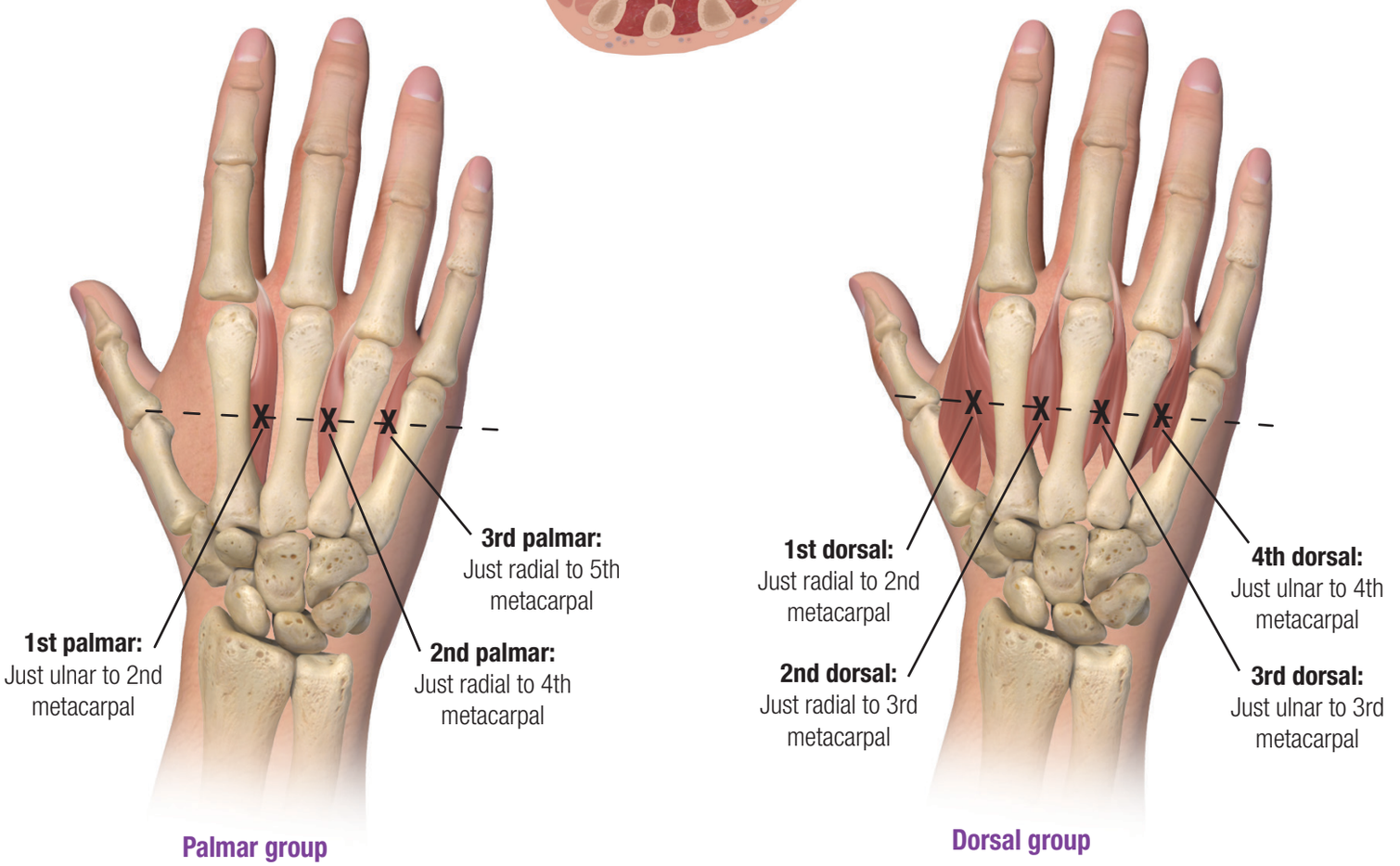
Interossei (continued)

Localization[20]

The common landmark for both dorsal and palmar interossei is a transmetacarpal line perpendicular to the long axis of the hand at the level of the first MCP joint. Individual muscles can be localized as detailed (see Xs in diagram and notes below).

Cross-sectional anatomy: hand (palmar arch)





Palmar group **Dorsal group**

Note: This group is at a depth of about one-fourth inch.

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

Bronchitis and Upper Respiratory Tract Infections in Patients Treated for Spasticity

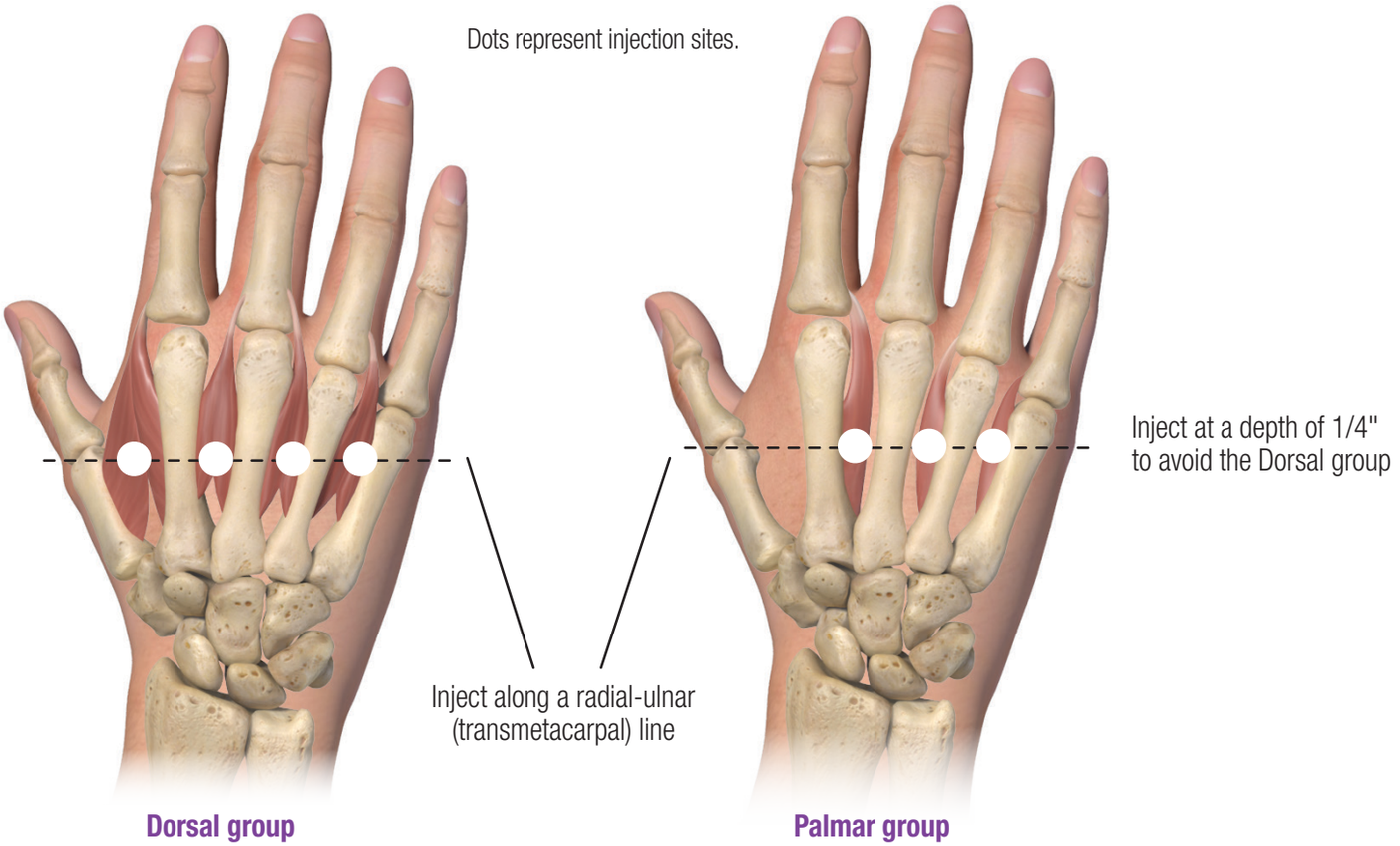
Bronchitis was reported more frequently as an adverse reaction in adult patients treated for upper limb spasticity with BOTOX (3% at 251 Units to 360 Units total dose) compared to placebo (1%). In adult patients with reduced lung function treated for upper limb spasticity, upper respiratory tract infections were also reported more frequently as adverse reactions in patients treated with BOTOX (11% at 360 Units total dose; 8% at 240 Units total dose) compared to placebo (6%).

Please see additional Important Safety Information throughout.

Interossei (continued)

Ultrasound EMG/E-Stim

Injection considerations



- When injecting both the lumbricals and/or interossei, consider limiting the combined total dose to 50 Units per hand
- Carefully consider the functional anatomy of these muscles and only target if deemed clinically necessary. Physicians should consider their level of comfort and expertise with injecting these muscles before proceeding
- Guidance techniques are highly recommended for these muscles to avoid inadvertent injection of nontargeted muscles, such as the lumbricals
- Consider the following when determining how to approach these muscles:
  - Dorsal approach is typically less painful, but localization is more challenging
  - Palmar approach is typically more painful, but localization is more straightforward
  - A 30-gauge needle and/or cold spray may help minimize injection pain
- **For the Dorsal group:** Consider orienting the needle along the radial-ulnar line to more effectively target these muscles within the interosseous space
- **For the Palmar group:** If the needle is inserted too superficially, it may be in the Dorsal group; if inserted too deeply, it may be in the adductor pollicis

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Bronchitis and Upper Respiratory Tract Infections in Patients Treated for Spasticity (continued)
In adult patients treated for lower limb spasticity, upper respiratory tract infections were reported more frequently as an adverse reaction in patients treated with BOTOX (2% at 300 Units to 400 Units total dose) compared to placebo (1%).

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

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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®
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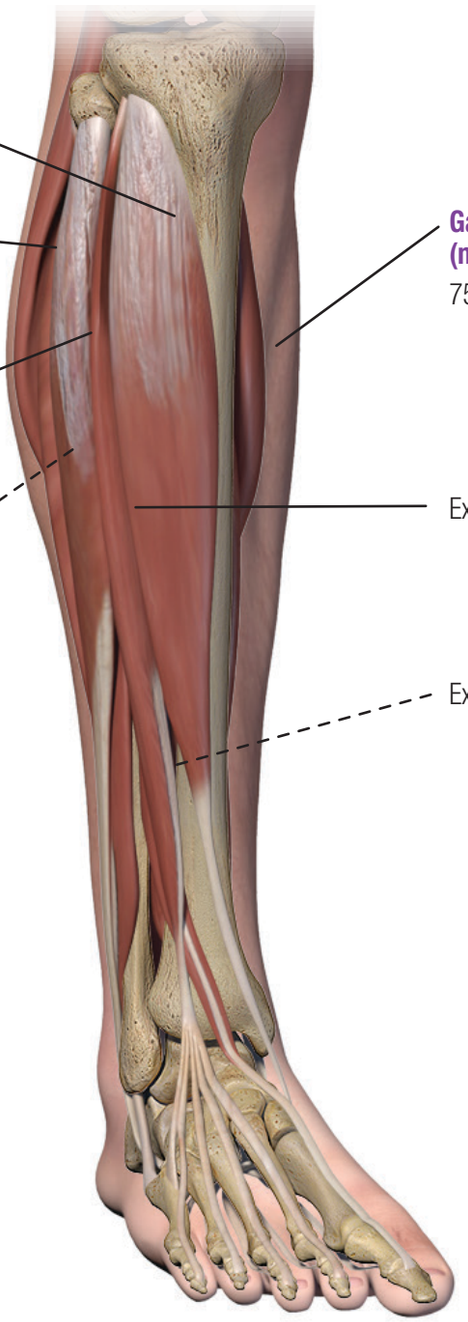
Main muscles involved in Adult Lower Limb Spasticity

Muscles listed in purple are those approved for BOTOX® injection[4]

Anterior view



Tibialis anterior*

Gastrocnemius (lateral head)
75 Units divided in 3 sites

Fibularis longus*

Soleus (hidden)
75 Units divided in 3 sites

Gastrocnemius (medial head)
75 Units divided in 3 sites

Extensor digitorum longus*

Extensor hallucis longus (hidden)*

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

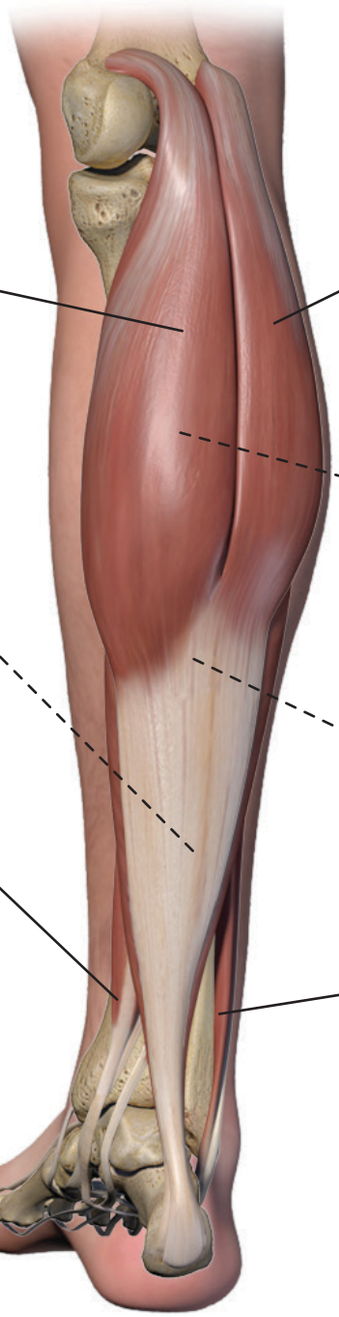
Please see additional Important Safety Information throughout.

Approved Muscles Involved in Common Postures

Ankle flexors
Gastrocnemius
Soleus
Tibialis posterior

Toe Flexors
Flexor digitorum longus
Flexor hallucis longus

Posterior view



Gastrocnemius (medial head)
75 Units divided in 3 sites

Gastrocnemius (lateral head)
75 Units divided in 3 sites

Flexor hallucis longus (hidden)
50 Units divided in 2 sites

Tibialis posterior (hidden)
75 Units divided in 3 sites

Flexor digitorum longus
50 Units divided in 2 sites

Soleus (hidden)
75 Units divided in 3 sites

Fibularis longus*

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

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Adult Upper Limb Spasticity
The most frequently reported adverse reactions following injection of BOTOX for upper limb spasticity include pain in extremity, muscular weakness, fatigue, nausea, and bronchitis.

Please see additional Important Safety Information throughout.

Gastrocnemius

▶ BOTOX® dose: 75 Units divided in 3 sites (medial head) and 75 Units divided in 3 sites (lateral head)

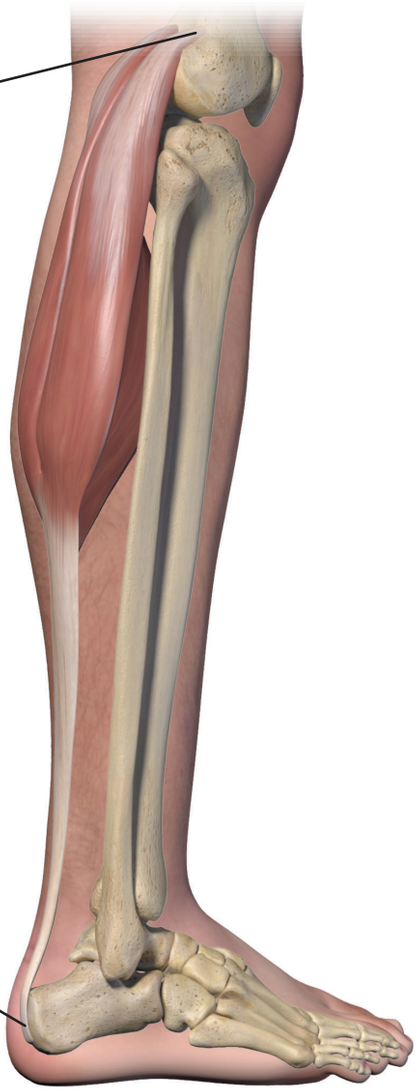
Muscle action[14]

Involved in plantarflexion and flexing the knee

Proximal attachments

Lateral head: Lateral surface of the lateral condyle and to the lower part of the corresponding supracondylar line

Medial head: Popliteal surface of the femur just above the medial condyle



Distal attachment

Posterior surface of calcaneus by calcaneal tendon

Other muscles involved in plantarflexion

- Soleus
- Tibialis posterior
- Flexor digitorum longus
- Flexor hallucis longus
- Fibularis longus*

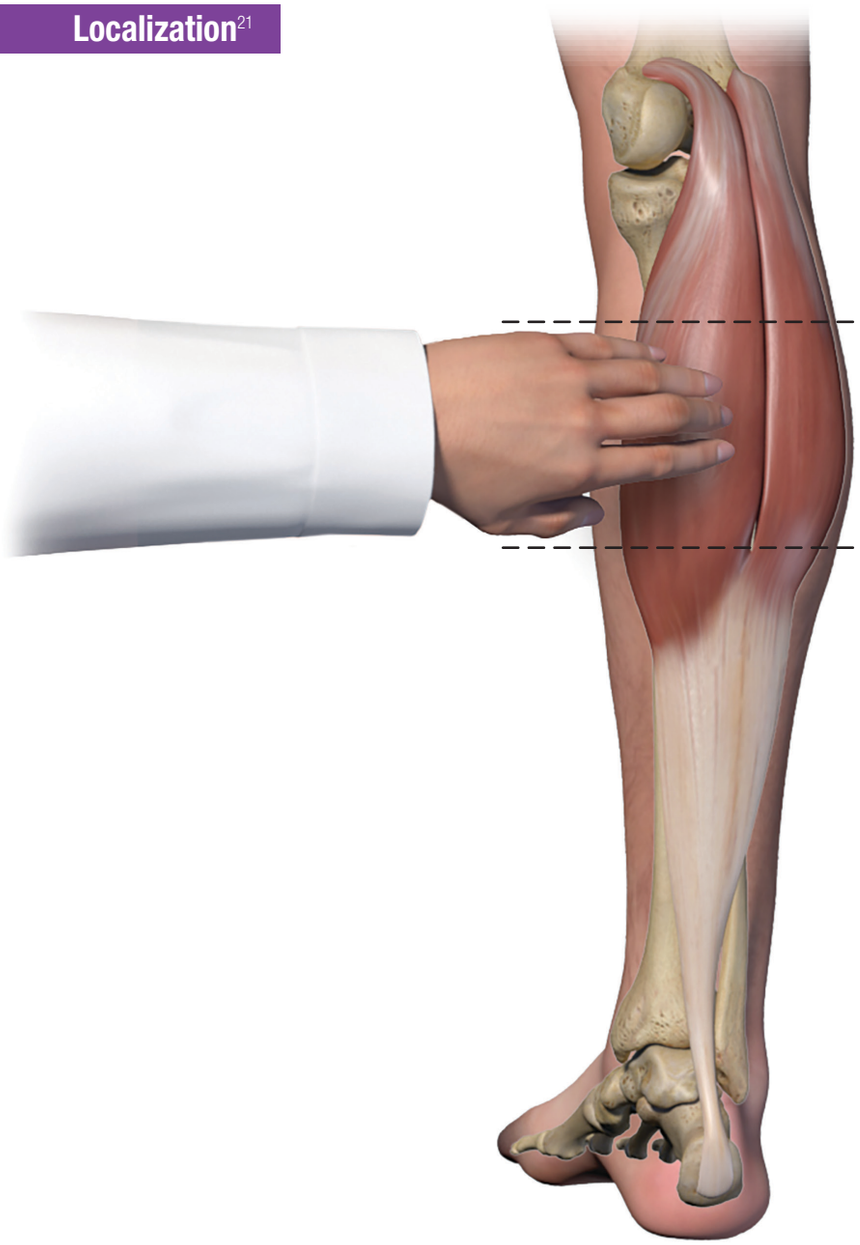
*For anatomical reference only.

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Adult Lower Limb Spasticity
The most frequently reported adverse reactions following injection of BOTOX for lower limb spasticity include arthralgia, back pain, myalgia, upper respiratory tract infection, and injection-site pain.

Please see additional Important Safety Information throughout.

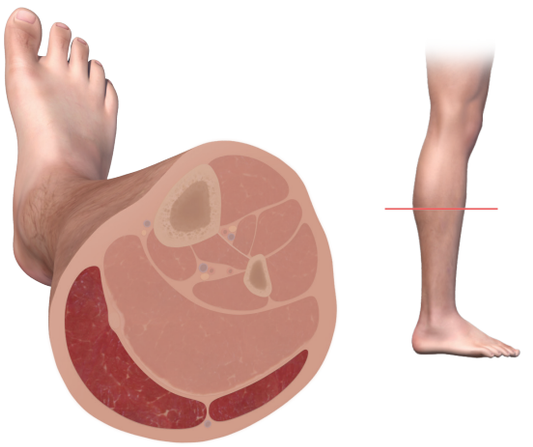
Gastrocnemius (continued)

Localization[21]



Midbelly is located three-quarters the distance from heel to popliteal crease.

Cross-sectional anatomy: midcalf



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.

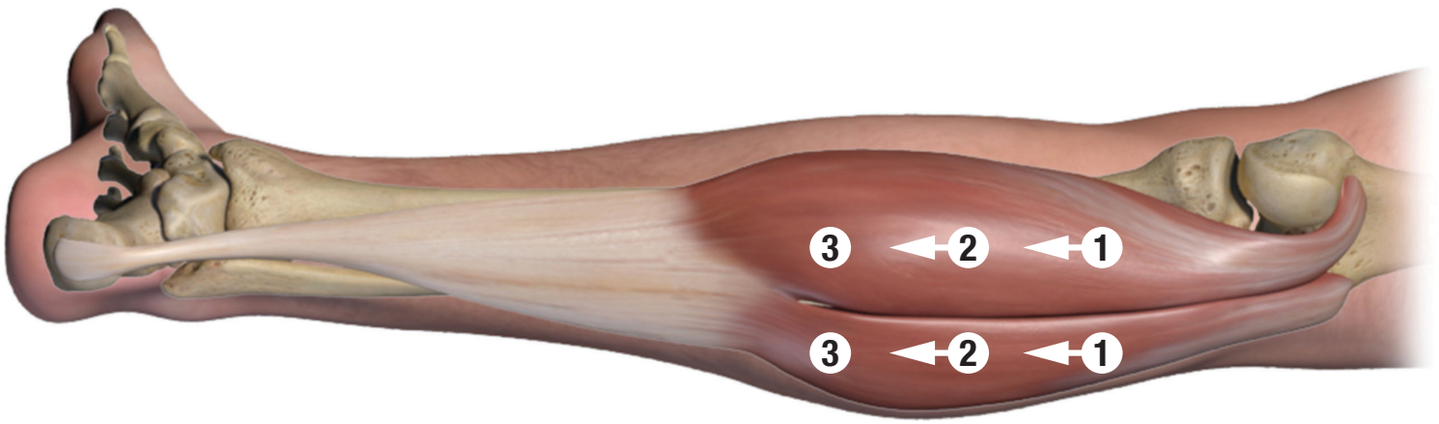
BOTOX® onabotulinumtoxinA injection

Gastrocnemius (continued)

Ultrasound

EMG/E-Stim

Injection considerations



Dots represent injection sites.

- Gastrocnemius and soleus muscles make up the triceps surae and should be thought of as a complex
- The gastrocnemius crosses both the knee and ankle
- Position patient prone when possible
- Consider following a straight line from proximal to distal in both the medial and lateral heads when injecting the 3 sites
- Avoid going too distal so that the tendinous area is not inadvertently injected
- Gastrocnemius is thinner than the soleus, so consider needle depth carefully

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®
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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

Soleus

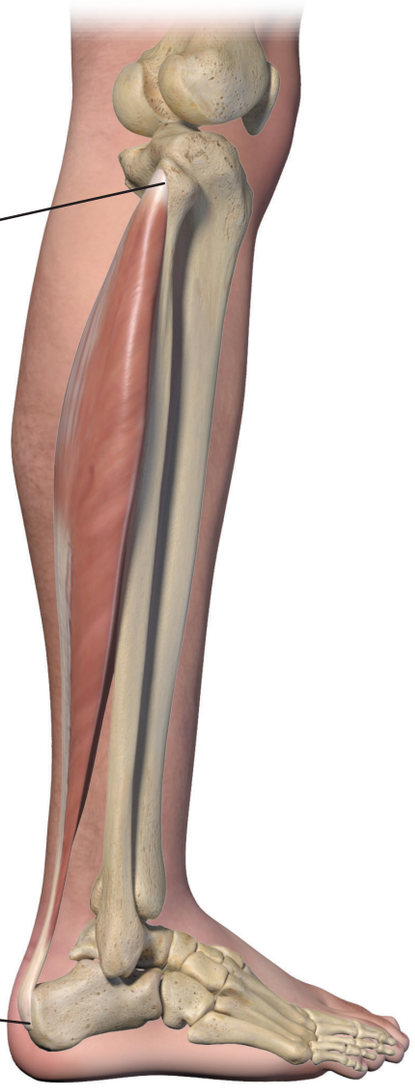
▶ BOTOX® dose: 75 Units divided in 3 sites

Muscle action[14]

Involved in plantarflexion

Proximal attachments

Posterior surface of the head and proximal quarter of the shaft of the fibula and the soleal line and middle third of the medial border of the tibia



Distal attachment

Posterior surface of calcaneus by calcaneal tendon

Other muscles involved in plantarflexion

- Gastrocnemius
- Tibialis posterior
- Flexor digitorum longus
- Flexor hallucis longus
- Fibularis longus*

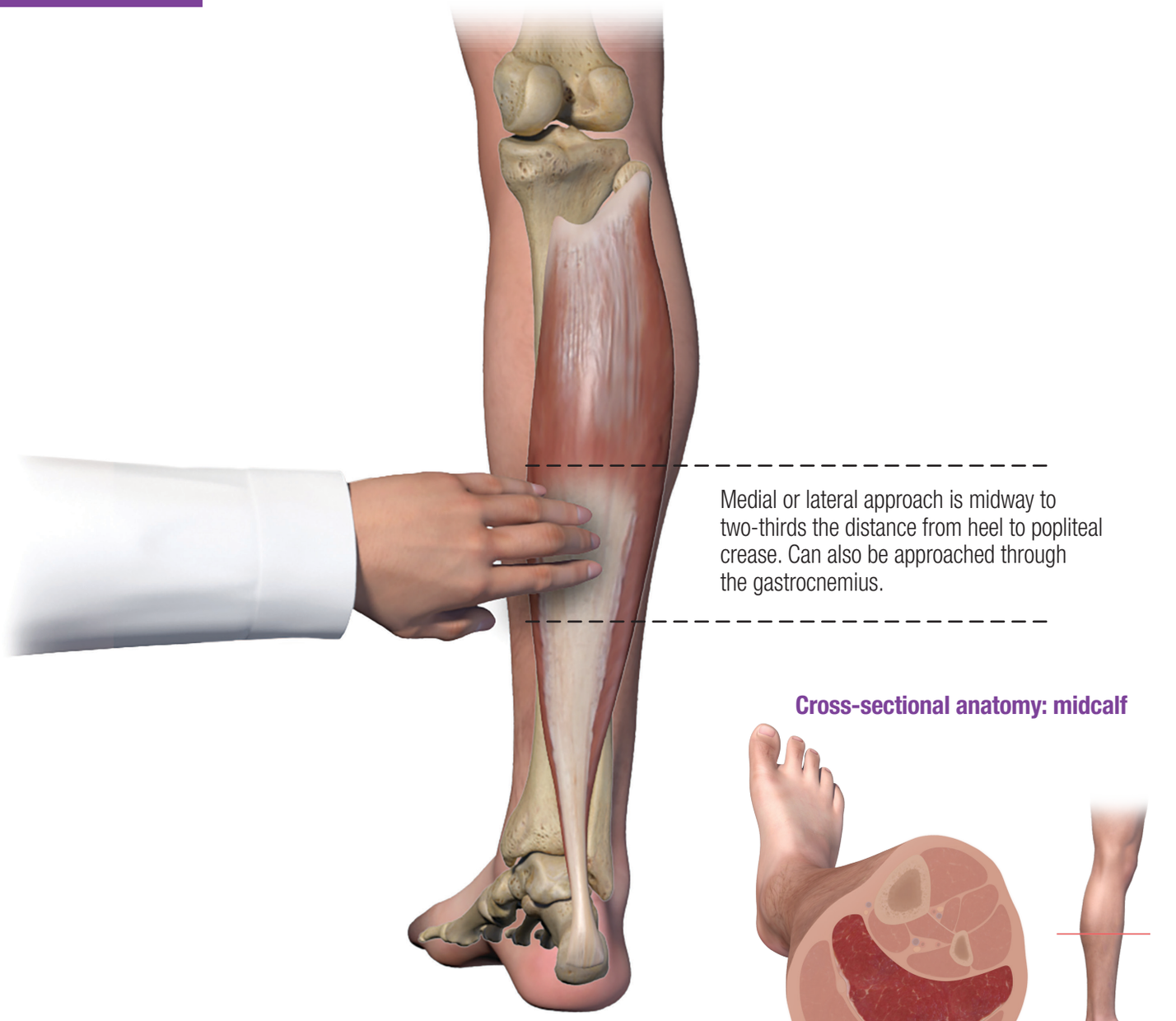
*For anatomical reference only.

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.

Soleus (continued)

Localization[21]



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

Please see additional Important Safety Information throughout.

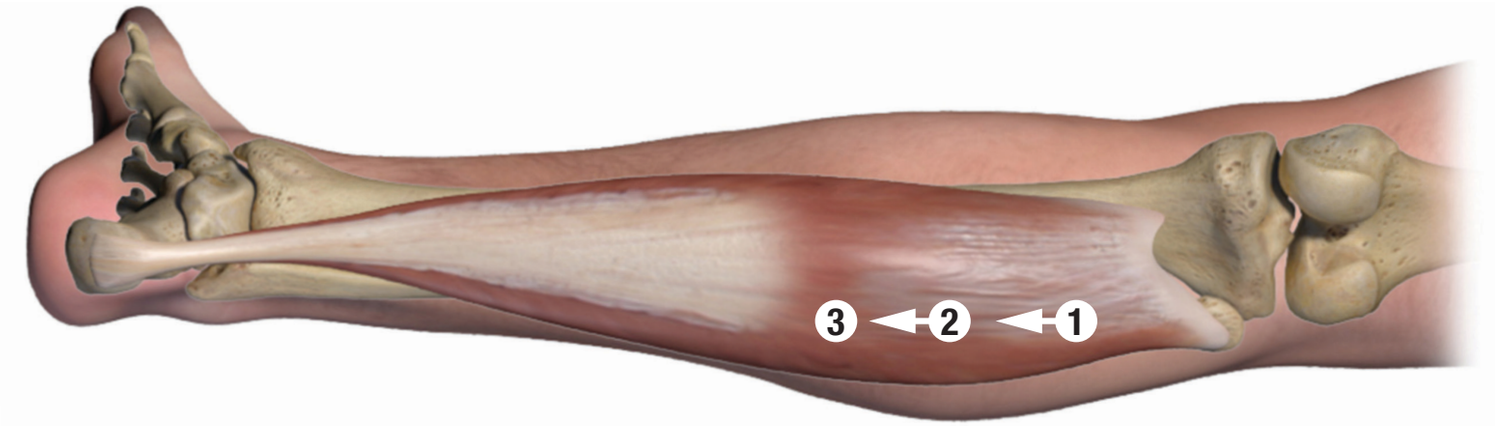
BOTOX® onabotulinumtoxinA injection

Soleus (continued)

Ultrasound

EMG/E-Stim

Injection considerations



Dots represent injection sites.

- Soleus and gastrocnemius muscles make up the triceps surae and should be thought of as a complex
- Position patient prone when possible
  - Activate the muscle with the knee flexed and have the patient plantarflex
- The soleus is deep and distal to the gastrocnemius, slightly lateral to the midline down the long axis of the leg
- Consider following a straight line from proximal to distal when injecting the 3 sites
- Consider advancing the needle to avoid further skin punctures
- Avoid going too distal to avoid the tendinous area. Stay above the midcalf

BOTOX®
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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.

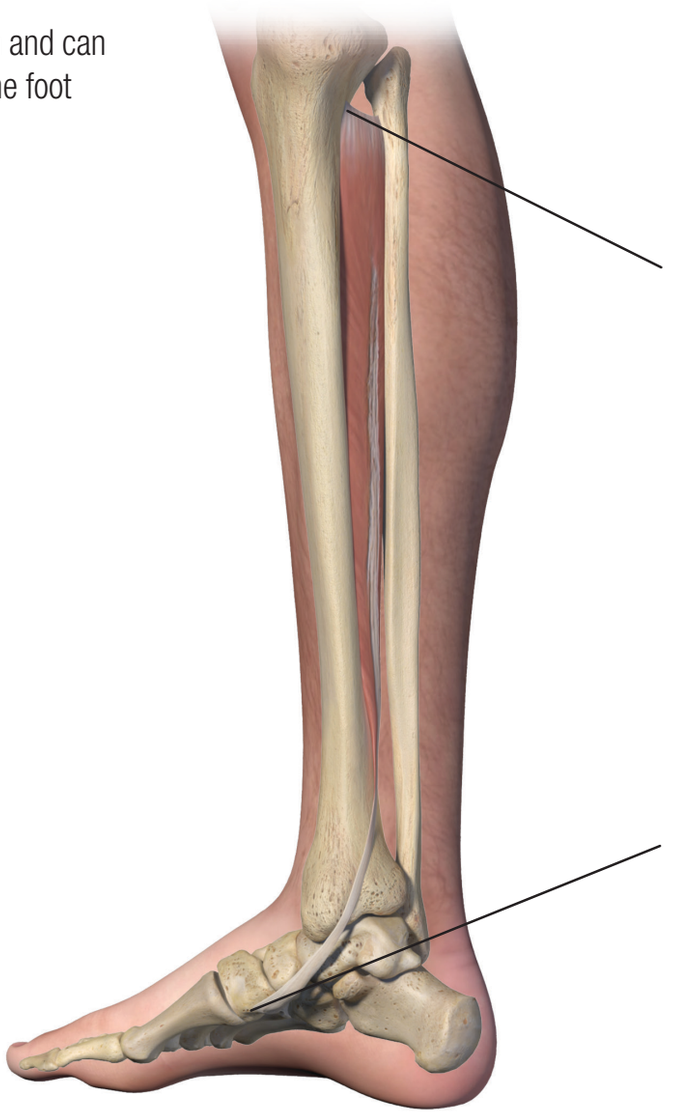
BOTOX® onabotulinumtoxinA injection

Tibialis posterior

▶ BOTOX® dose: 75 Units divided in 3 sites

Muscle action[14, 16]

Involved in plantarflexion and can also invert and adduct the foot



Proximal attachments

Posterior surfaces of the tibia and fibula, inferior to the soleal line

Distal attachments

Tuberosity of navicular, medial, and intermediate cuneiforms, and bases of second, third, and fourth metatarsals

Other muscles involved in plantarflexion and/or foot inversion

- Gastrocnemius (plantarflexion only)
- Soleus (plantarflexion only)
- Flexor digitorum longus[15]
- Flexor hallucis longus[15]
- Fibularis longus (plantarflexion only)*
- Tibialis anterior (foot inversion only)*

*For anatomical reference only.

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

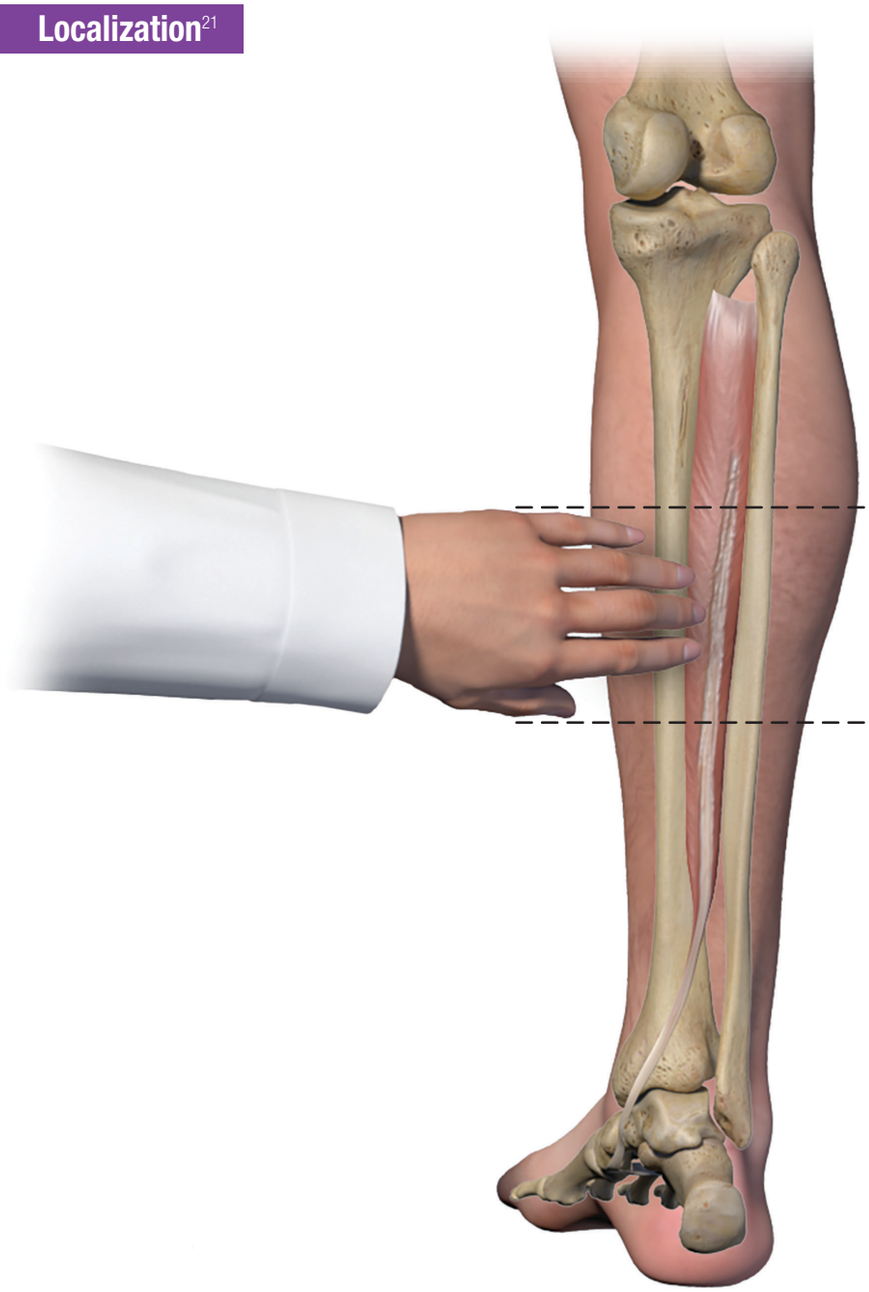
Hypersensitivity Reactions

Serious and/or immediate hypersensitivity reactions have been reported. These reactions include anaphylaxis, serum sickness, urticaria, soft-tissue edema, and dyspnea.

Please see additional Important Safety Information throughout.

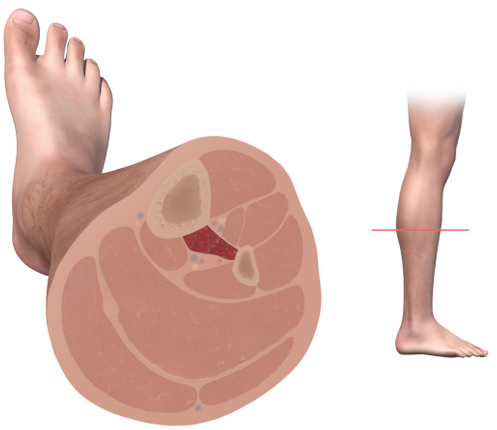
Tibialis posterior (continued)

Localization[21]



Medial approach is midway between heel and popliteal crease, just posterior to the tibia (and interosseous membrane, which will avoid nerves and vessels near this structure).

Cross-sectional anatomy: midcalf



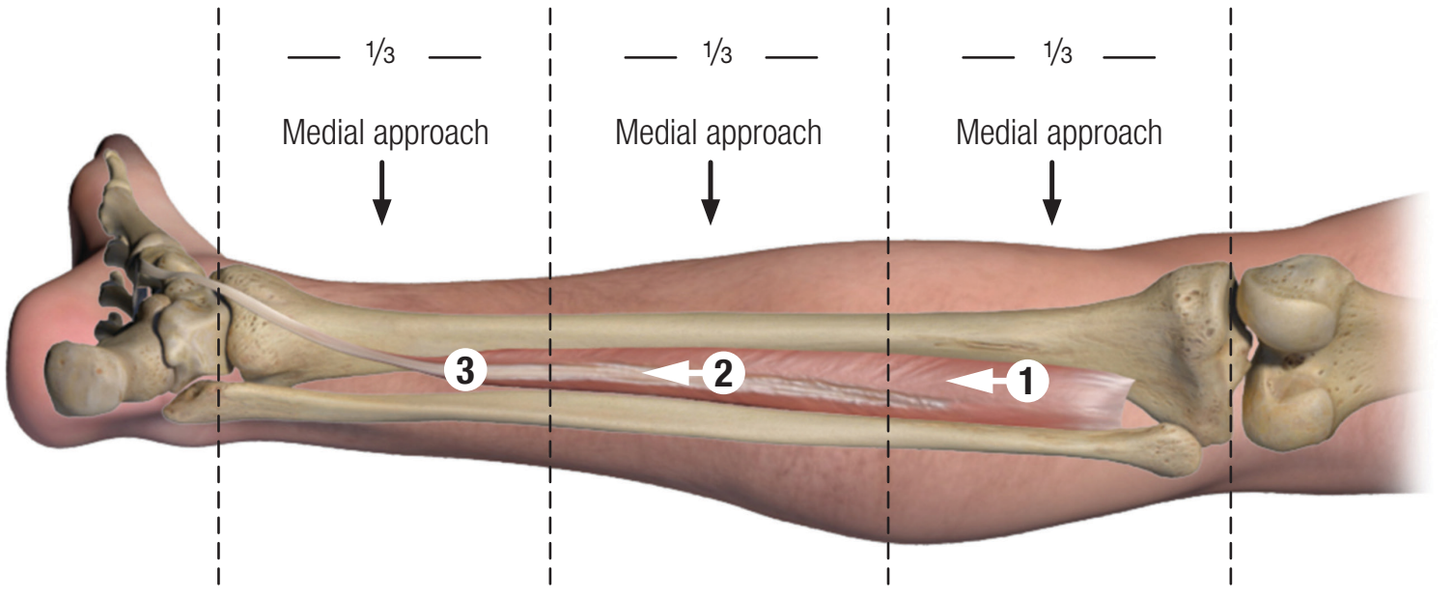
IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Hypersensitivity Reactions (continued)
If such a reaction occurs, further injection of BOTOX should be discontinued and appropriate medical therapy immediately instituted. One fatal case of anaphylaxis has been reported in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

Please see additional Important Safety Information throughout.

Tibialis posterior (continued)

Ultrasound EMG/E-Stim

Injection considerations



Dots represent injection sites.

- Position the patient supine with their leg extended, when possible
  - Recommend using established guidance techniques as the muscle may be difficult to locate
- This muscle runs the length of the tibia, so divide the leg into thirds
- Consider even distribution from proximal to distal when injecting the 3 sites
- Use a medial approach to avoid the neurovascular bundle

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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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.

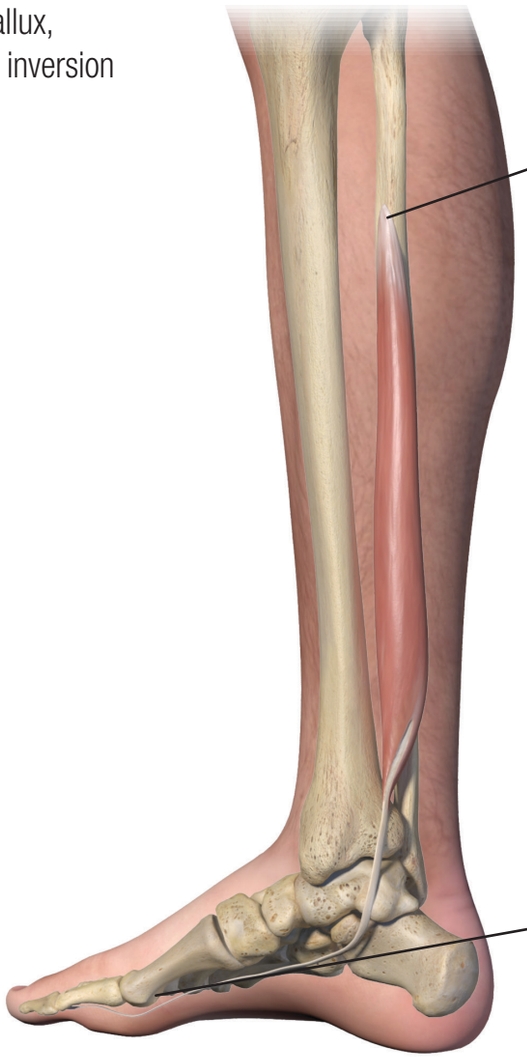
BOTOX® onabotulinumtoxinA injection

Flexor hallucis longus

▶ BOTOX® dose: 50 Units divided in 2 sites

Muscle action[14, 17]

Involved in flexion of hallux, plantarflexion, and foot inversion



Proximal attachments

Distal two-thirds of the posterior surface of the fibula (adjacent interosseous membrane and the posterior crural intermuscular septum, and fascia covering tibialis posterior)

Distal attachments

Bases of distal phalanx of hallux

Other muscles involved in plantarflexion and/or foot inversion

- Gastrocnemius (plantarflexion only)
- Soleus (plantarflexion only)
- Tibialis posterior[14]
- Flexor digitorum longus[15]
- Fibularis longus (plantarflexion only)*
- Tibialis anterior (foot inversion only)*

*For anatomical reference only.

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

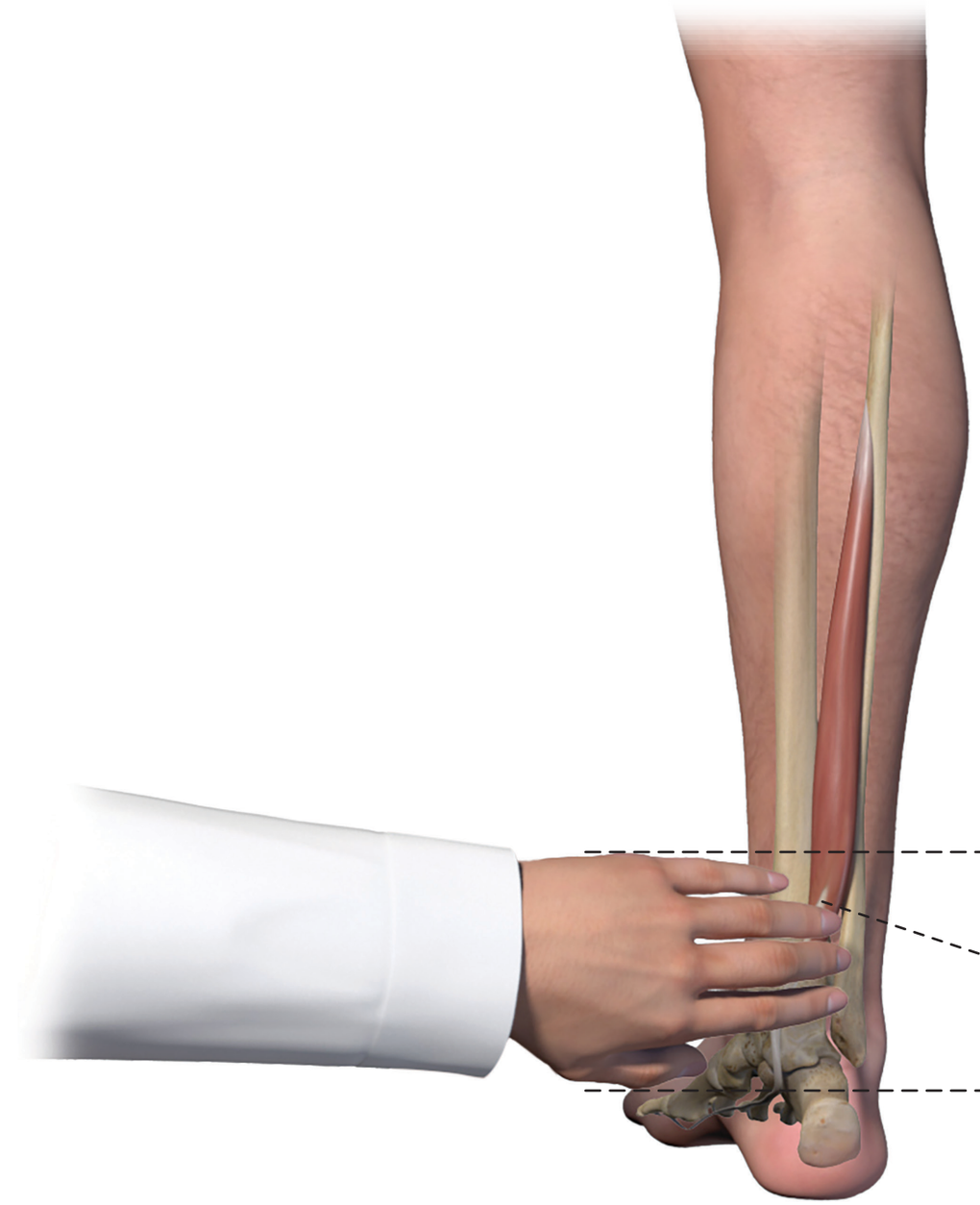
Dysphagia and Breathing Difficulties

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.

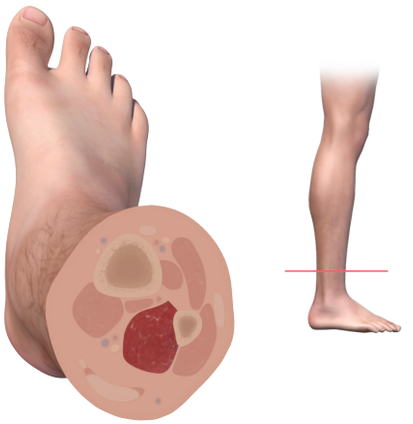
Please see additional Important Safety Information throughout.

Flexor hallucis longus (continued)

Localization[21]



Cross-sectional anatomy: distal calf



Take a posterior/lateral approach at one-third the distance from heel to popliteal crease and posterior to the fibula.

*For anatomical reference only.

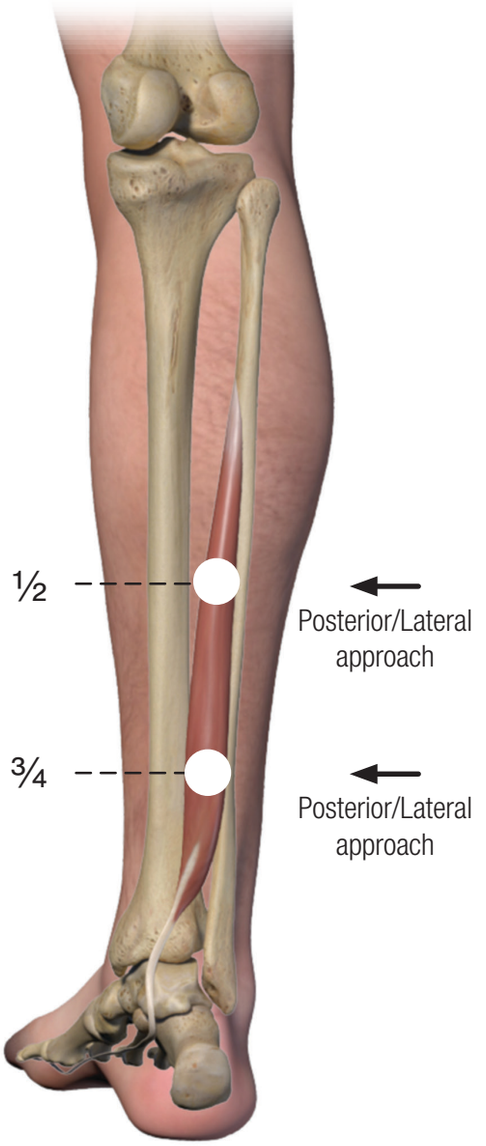
Flexor hallucis longus (continued)

Ultrasound EMG/E-Stim

Injection considerations

Dots represent injection sites.

- Position the patient supine, when possible
- This muscle starts at the lateral side of the leg and comes across the medial side at the ankle, but closer to the tendon than the bone
- Based on the anatomical structure, consider a lateral approach
- Consider targeting one-third to two-thirds proximal, respectively, to the lateral malleolus, one-third of the way up from the back of the heel to the knee when injecting the 2 sites
  - Consider placing the needle midway to three-fourths distally down the leg
- Inject this muscle when the great toe has flexion spasticity



IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Pulmonary Effects of BOTOX in Patients With Compromised Respiratory Status Treated for Spasticity
Patients with compromised respiratory status treated with BOTOX for spasticity should be monitored closely.

Please see additional Important Safety Information throughout.

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

Bronchitis and Upper Respiratory Tract Infections in Patients Treated for Spasticity

Bronchitis was reported more frequently as an adverse reaction in adult patients treated for upper limb spasticity with BOTOX (3% at 251 Units to 360 Units total dose) compared to placebo (1%). In adult patients with reduced lung function treated for upper limb spasticity, upper respiratory tract infections were also reported more frequently as adverse reactions in patients treated with BOTOX (11% at 360 Units total dose; 8% at 240 Units total dose) compared to placebo (6%). In adult patients treated for lower limb spasticity, upper respiratory tract infections were reported more frequently as an adverse reaction in patients treated with BOTOX (2% at 300 Units to 400 Units total dose) compared to placebo (1%).

Please see additional Important Safety Information throughout.

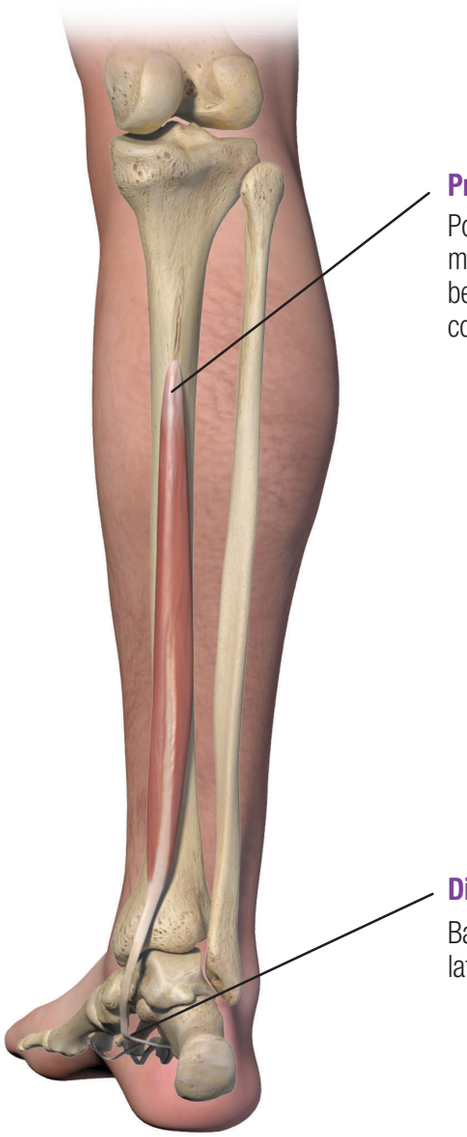
BOTOX® onabotulinumtoxinA injection

Flexor digitorum longus

▶ BOTOX® dose: 50 Units divided in 2 sites

Muscle action[14, 17]

Involved in flexion of lateral 4 digits, plantarflexion, and foot inversion



Proximal attachment

Posterior surface of the tibia medial to tibialis posterior and just below the soleal line (and fascia covering tibialis posterior)

Distal attachments

Bases of distal phalanges of lateral 4 digits

Other muscles involved in plantarflexion and/or foot inversion

- Gastrocnemius (plantarflexion only)
- Soleus (plantarflexion only)
- Tibialis posterior[16]
- Flexor hallucis longus[17]
- Fibularis longus (plantarflexion only)*
- Tibialis anterior (foot inversion only)*

*For anatomical reference only.

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

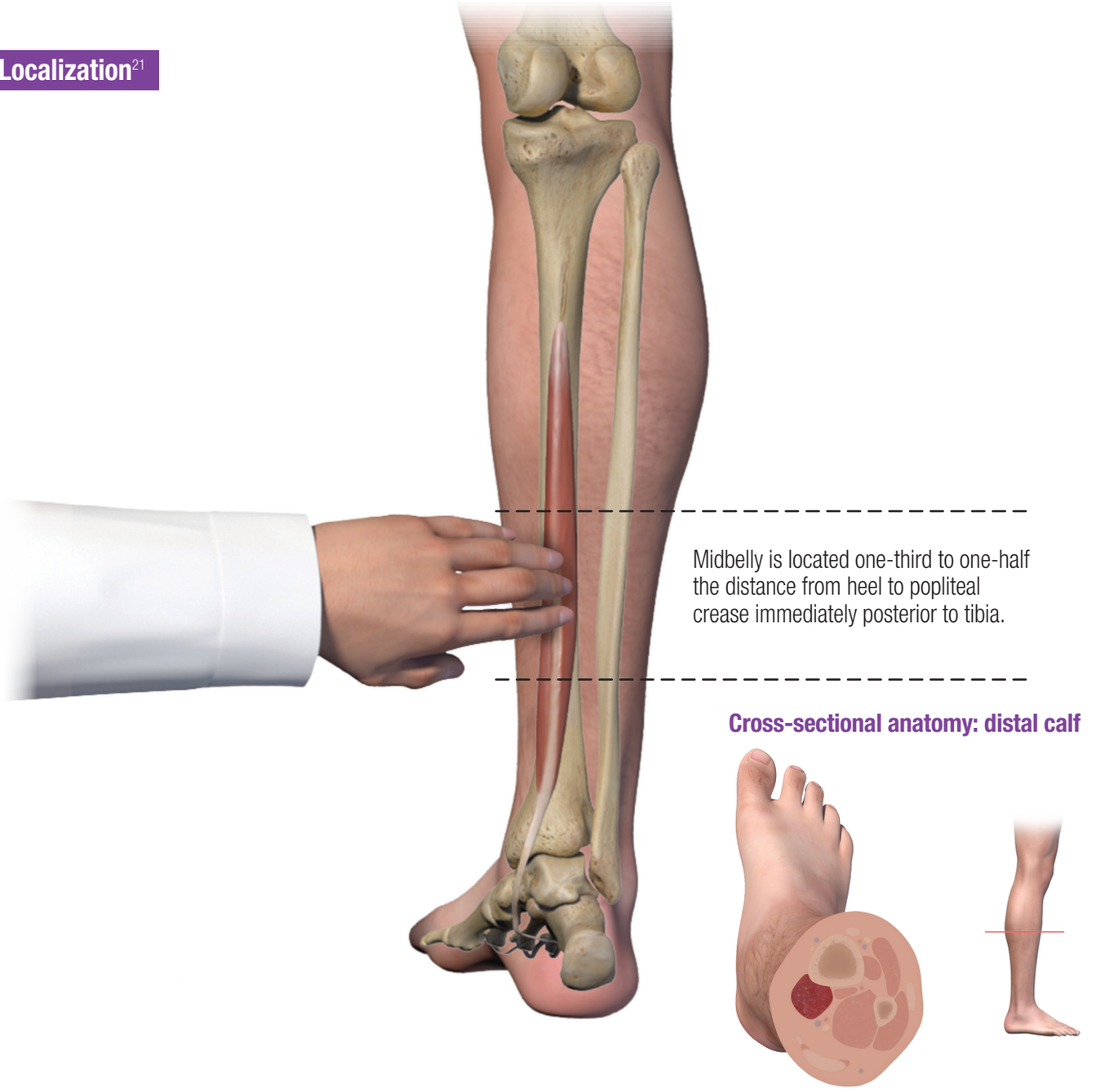
Human Albumin and Transmission of Viral Diseases

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.

Flexor digitorum longus (continued)

Localization[21]



IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS

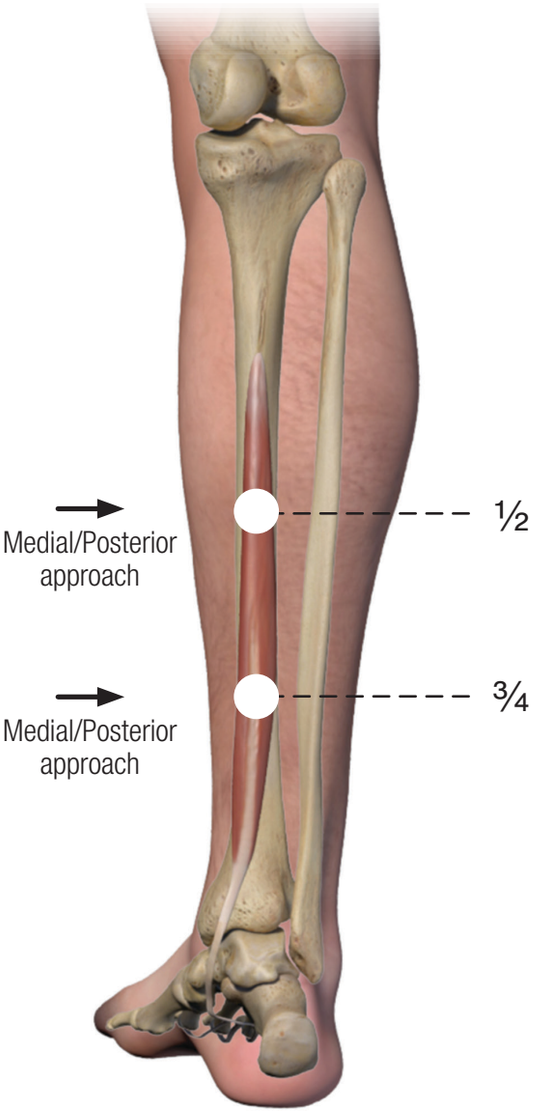
Adverse reactions to BOTOX for injection are discussed in greater detail in the following sections: *Boxed Warning*, *Contraindications*, and *Warnings and Precautions*.

Please see additional Important Safety Information throughout.

Flexor digitorum longus (continued)

Ultrasound EMG/E-Stim

Injection considerations



Dots represent injection sites.

- The patient can be positioned supine, prone, or sitting
- This muscle starts at the medial part of the leg and continues laterally to the foot
- Have patients bend their toes while using EMG to help localize the muscle. With E-Stim you want them to relax the muscle, not bend their toes
- Consider targeting one-half and three-fourths distally down the leg when injecting the 2 sites

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Adult Upper Limb Spasticity
The most frequently reported adverse reactions following injection of BOTOX for upper limb spasticity include pain in extremity, muscular weakness, fatigue, nausea, and bronchitis.

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

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IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Adult Lower Limb Spasticity
The most frequently reported adverse reactions following injection of BOTOX for lower limb spasticity include arthralgia, back pain, myalgia, upper respiratory tract infection, and injection-site pain.

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Dilution and reconstitution

Follow general dilution instructions for BOTOX® vials (100 Units and 200 Units)[4]

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/4 mL or 100 Units/2 mL with preservative-free 0.9% Sodium Chloride Injection, USP (see table 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 a refrigerator (2°C to 8°C) 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 2°C to 8°C or 36°F to 46°F) for up to 36 months

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

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.

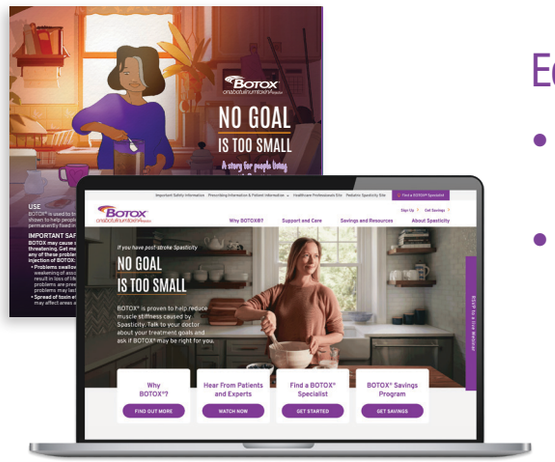
Disconnect the injection syringe from the vial and attach an appropriate needle for injection. A 25- to 30-gauge needle may be used for superficial muscles, and a longer 22-gauge needle may be used for deeper musculature.

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
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

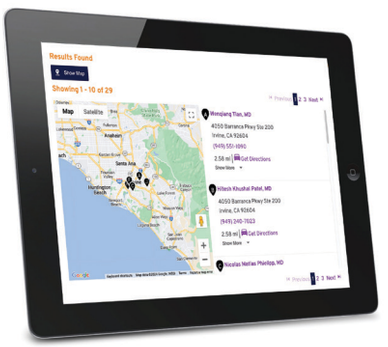
Resources available to help patients/caregivers



Education

- An informational brochure is available for patients/caregivers to educate them about Adult Spasticity and BOTOX®
- Additional resources and information are available on the BOTOX® patient website

Tell patients/caregivers to visit BOTOXSpasticity.com



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)
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

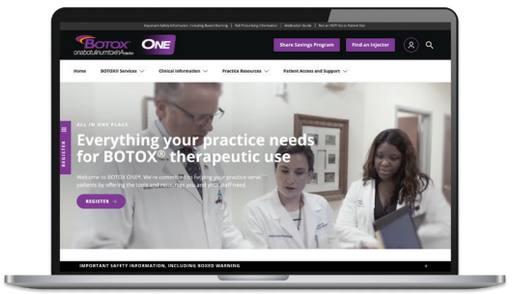
BOTOX®
onabotulinumtoxinA injection

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 Adult Spasticity 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)
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.

References:
1. Simpson DM, Hallet M, Ashman EJ, et al. Practice guideline update summary: Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache: Report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. 2016;86(19):1818-1826. 2. Verduzco-Gutierrez M, Raghavan P, Pruente J, et al. AAPM&R consensus guidance on spasticity and management. *PM&R*. 2024;16(8):864-887. 3. Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): a patient centered approach to grading evidence in the medical literature. *J am Board Fam Pract*. 2004;17(1):59-67. 4. BOTOX® Prescribing Information, November 2023. 5. Data on file, Allergan; Clinical Study Report GSK112958. 6. Data on file, AbbVie; Clinical Study Report BTX108509. 7. Data on file, AbbVie; Clinical Study Report GSK207660. 8. Data on file, AbbVie; ULS Summary of Clinical Safety. 9. Data on file, AbbVie; R&D Update. 10. Data on file, AbbVie, March 2021; Botulinum Toxin Peer Reviewed Publications. 11. Abo M, Shigematsu T, Hara H, et al. Efficacy and safety of onabotulinumtoxinA 400 Units in patients with post-stroke upper limb spasticity: final report of a randomized, double-blind, placebo-controlled trial with an open-label extension phase. *Toxins (Basel)*. 2020;12(2):127. 12. Esquenazi A, Wien TH, Ward AB, et al. Optimal muscle selection for onabotulinumtoxinA injections in poststroke lower-limb spasticity: a randomized trial. *Am J Phys Med Rehabil*. 2019;98(5):360-368. 13. Patel AT, Ward AB, Geis C, Jost WH, Liu C, Dimitrova R. Impact of early intervention with onabotulinumtoxinA treatment in adult patients with post-stroke lower limb spasticity: results from the double-blind, placebo-controlled, phase 3 REFLEX study. *J Neural Trans (Vienna)*. 2020;127(2):1619-1629. 14. Standring S, ed. *Gray's Anatomy: The Anatomical Basis of Clinical Practice*. 41st ed. Churchill Livingstone; 2016. 15. Benson DC, Miao KH, Varacallo M. Anatomy, shoulder and upper limb, hand flexor pollicis longus muscle. In: *StatPearls*. StatPearls Publishing; July 24, 2023. 16. Richardson M. Muscle atlas: tibialis posterior. University of Washington. Accessed 2024. http://rad.washington.edu/muscle-atlas/tibialis posterior/. 17. Murdock CJ, Munjal A, Agyeman K. Anatomy, bony pelvis and lower limb, calf flexor hallucis longus muscle. In: *StatPearls*. StatPearls Publishing; October 5, 2021.18. 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. Blackwell Science; 2003:158-191. 19. Alter KE, Karp BI. Ultrasound guidance for botulinum neurotoxin chemodenervation procedures. *Toxins (Basel)*. 2017;10(1):18. 20. Perotto AO. *Anatomical Guide for the Electromyographer: The Limbs and Trunk*. 5th ed. Charles C Thomas Publisher, Ltd; 2011. 21. Odderson IR, ed. *Botulinum Toxin Injection Guide*. Demos Medical Publishing, LLC; 2008.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS

Spread of Toxin Effect

See *Boxed Warning*.

Please see additional Important Safety Information throughout.

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

US-BNO-250052 04/2025 030733