BOTOX®
onabotulinumtoxinA injection

Injection Workbook for **Pediatric Spasticity**

Functional Anatomy, BOTOX® Treatment Considerations, and Injector Resources

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 inside.

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

Introduction

This workbook is designed to enhance your understanding of functional anatomy and explore treatment considerations for Pediatric Spasticity patients that you may encounter during a BOTOX® training program.

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.

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Clinical data summary for BOTOX® in Pediatric Spasticity

Proven efficacy across 2 pivotal studies[1]

Randomized, multicenter, double-blind, placebo-controlled studies in pediatric patients 2 to 17 years old

Study 1: Pediatric Upper Limb Spasticity (ULS)		
Patients	**BOTOX® Dosage**	**Co-Primary Endpoints**
N = 234 **BOTOX® (n = 155)** **Placebo (n = 79)**	3 Units/kg (n = 78)	Mean change from baseline in MAS* principal muscle group (elbow/wrist score), Weeks 4 and 6 average
	6 Units/kg (n = 77)	Mean CGI† score (Weeks 4 and 6 average)

*MAS = Modified Ashworth Scale.

†CGI = Clinical Global Impression of Overall Change by Physician.

BOTOX® provided significant improvements in MAS change from baseline at all time points compared to placebo

- Mean change of -1.92 (BOTOX® 3 Units/kg) and -1.87 (BOTOX® 6 Units/kg) vs -1.21 for placebo (elbow or wrist flexors, weeks 4 and 6 average; $P < .05$)

CGI scores numerically favored BOTOX® over placebo, although the difference was not statistically significant

- Mean CGI score of 1.88 (BOTOX® 3 Units/kg) and 1.87 (BOTOX® 6 Units/kg) vs 1.66 for placebo (weeks 4 and 6 average)

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

Please see additional Important Safety Information throughout.

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

Study 2: Pediatric Lower Limb Spasticity (LLS)		
Patients	**BOTOX® Dosage**	**Co-Primary Endpoints**
N = 381 **BOTOX® (n = 252)** **Placebo (n = 129)**	4 Units/kg (n = 125)	Mean change from baseline in MAS ankle score (Weeks 4 and 6 average)
	8 Units/kg (n = 127)	Mean CGI score (Weeks 4 and 6 average)

BOTOX® provided improvements in MAS ankle score at all time points compared to placebo

- Mean change of -1.01 (BOTOX® 4 Units/kg) and -1.06 (BOTOX® 8 Units/kg) vs -0.80 for placebo ($P < .05$), weeks 4 and 6 average

Improvements in mean CGI score were observed at all time points up to week 12

- Mean CGI score of 1.49 and 1.65 ($P < .05$, weeks 4 and 6 average) for the 4 Units/kg and 8 Units/kg doses, respectively

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Lack of Interchangeability Between Botulinum Toxin Products
The potency Units of BOTOX are specific to the preparation and assay method utilized. They are not interchangeable with other preparations of botulinum toxin products and, therefore, Units of biological activity of BOTOX cannot be compared to nor converted into Units of any other botulinum toxin products assessed with any other specific assay method.

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

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

Proven safety across 2 pivotal studies[1]

Adverse reactions in Study 1: Pediatric ULS

Adverse Reactions	BOTOX® 6 Units/kg (n = 77) %	BOTOX® 3 Units/kg (n = 78) %	Placebo (n = 79) %
Infections and infestations			
Upper respiratory tract infection[a]	17	10	9
General disorders and administration site conditions			
Injection-site pain	4	3	1
Gastrointestinal disorders			
Nausea	4	0	0
Constipation	3	0	1
Respiratory, thoracic, and mediastinal disorders			
Rhinorrhea	4	0	1
Nasal congestion	3	0	1
Nervous system disorders			
Seizure[b]	5	1	0

[a]Includes upper respiratory tract infection and viral upper respiratory tract infection.
[b]Includes seizure and partial seizure.

Adverse reactions reported by ≥ 2% of BOTOX® 6 Units/kg treated patients and more frequently than in placebo-treated patients in a pediatric upper limb spasticity double-blind, placebo-controlled clinical trial. 78 patients were treated with 3 Units/kg of BOTOX®, and 77 patients received 6 Units/kg to a maximum dose of 200 Units of BOTOX®, and were compared to 79 patients who received placebo. Patients were followed for an average of 91 days after injection.

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

Serious Adverse Reactions With Unapproved Use

Serious adverse reactions, including excessive weakness, dysphagia, and aspiration pneumonia, with some adverse reactions associated with fatal outcomes, have been reported in patients who received BOTOX injections for unapproved uses. In these cases, the adverse reactions were not necessarily related to distant spread of toxin, but may have resulted from the administration of BOTOX to the site of injection and/or adjacent structures. In several of the cases, patients had 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.

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

Adverse reactions in Study 2: Pediatric LLS

Adverse Reactions	BOTOX® 8 Units/kg (n = 128) %	BOTOX® 4 Units/kg (n = 126) %	Placebo (n = 128) %
General disorders and administration site conditions			
Injection-site erythema	2	0	0
Injection-site pain	2	2	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain	2	0	1
Injury, poisoning, and procedural complications			
Ligament sprain	2	1	0
Skin abrasion	2	0	0
Metabolism and nutrition disorders			
Decreased appetite	2	0	0

Adverse reactions reported by ≥ 2% of BOTOX® 8 Units/kg treated patients and more frequent than in placebo-treated patients in a pediatric lower limb spasticity, double-blind, placebo-controlled clinical trial. 126 patients were treated with 4 Units/kg of BOTOX®, and 128 patients received 8 Units/kg to a maximum dose of 300 Units of BOTOX®, and were compared to 128 patients who received placebo. Patients were followed for an average of 89 days after 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. 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

Injection insights and considerations

General considerations

- The recommended dilution rate is 2:1, meaning put 4 mL of saline into a 200-Unit vial or 2 mL 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
- Utilize muscle localization guidance to help ensure proper needle placement
  - 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
- Talk through the injection session step by step, explaining what may be experienced (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
  - Consider discussing the option of cold spray or conscious sedation with parents, if necessary

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 muscle localization guidance
- Verify the needle is securely fastened to the injection syringe
- Consider the type of needle/syringe to minimize the chance of the needle popping out during the injection
- Consider using *Luer Lock* syringes to prevent the leakage of BOTOX® during the injection
- Consider lining up the bevel of the needle with the gradations on the syringe so the bevel is facing upward; this will help you read the syringe when injecting
- Consider discussing the option of cold spray to numb the injection site(s)
- Explain that some injection sites may be more sensitive than others so the pain level can vary with each injection

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

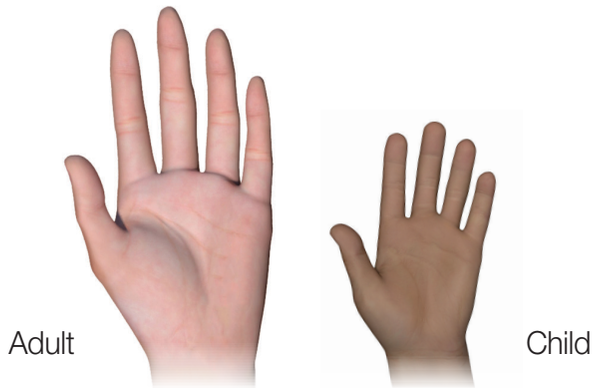
Please see additional Important Safety Information throughout.

Injection insights and considerations (continued)

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.

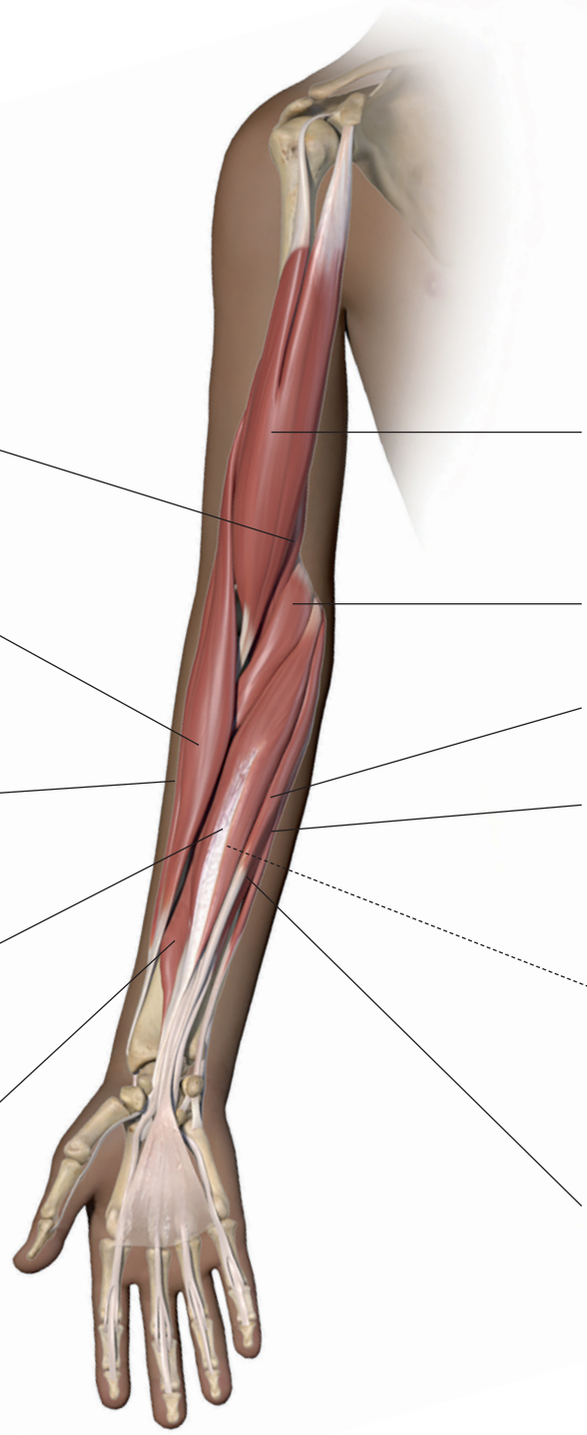


All measurements used for pediatric muscle localization are proportional and refer to a child's hand/finger

BOTOX® onabotulinumtoxinA injection

Main muscles involved in Pediatric ULS

Muscles listed in purple are those approved for BOTOX® injection[1]



Brachialis
1-2 Units/kg
divided in 2 sites

Brachioradialis
0.5-1 Unit/kg
divided in 2 sites

Extensor carpi radialis longus*

Flexor carpi radialis
1-2 Units/kg
divided in 2 sites

Flexor pollicis longus*

Biceps brachii
1.5-3 Units/kg
divided in 4 sites

Pronator teres*

Palmaris longus*

Flexor carpi ulnaris
1-2 Units/kg
divided in 2 sites

Flexor digitorum profundus (hidden)
0.5-1 Unit/kg
divided in 2 sites

Flexor digitorum superficialis (sublimis)
0.5-1 Unit/kg
divided in 2 sites

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

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

Upper Respiratory Tract Infections in Patients Treated for Spasticity

In pediatric patients treated for upper limb spasticity, upper respiratory tract infections were reported more frequently as an adverse reaction in patients treated with BOTOX (17% at 6 Units/kg and 10% at 3 Units/kg) compared to placebo (9%). In pediatric patients treated for lower limb spasticity, upper respiratory tract infection was not reported with an incidence greater than placebo.

Please see additional Important Safety Information throughout.

BOTOX® onabotulinumtoxinA injection

Main muscles involved in Pediatric ULS (continued)

Approved muscles and BOTOX® doses for common postures[1]

Posture	Muscle	BOTOX® Dose
Flexed Elbow	Biceps brachii	1.5 Units/kg-3 Units/kg divided in 4 sites
	Brachialis	1 Unit/kg-2 Units/kg divided in 2 sites
	Brachioradialis	0.5 Unit/kg-1 Unit/kg divided in 2 sites
Flexed Wrist/Fingers	Flexor carpi radialis	1 Unit/kg-2 Units/kg divided in 2 sites
	Flexor carpi ulnaris	1 Unit/kg-2 Units/kg divided in 2 sites
	Flexor digitorum profundus	0.5 Unit/kg-1 Unit/kg divided in 2 sites
	Flexor digitorum superficialis (sublimis)	0.5 Unit/kg-1 Unit/kg divided in 2 sites

The recommended dose for treating Pediatric ULS is 3-6 Units/kg divided among the affected muscles

The total dose of BOTOX® administered per treatment session in the upper limb should not exceed 6 Units/kg or 200 Units, whichever is lower

When treating both lower limbs or the upper and lower limbs in combination, the total dose should not exceed the lower of 10 Units/kg body weight or 340 Units in a 3-month interval

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.

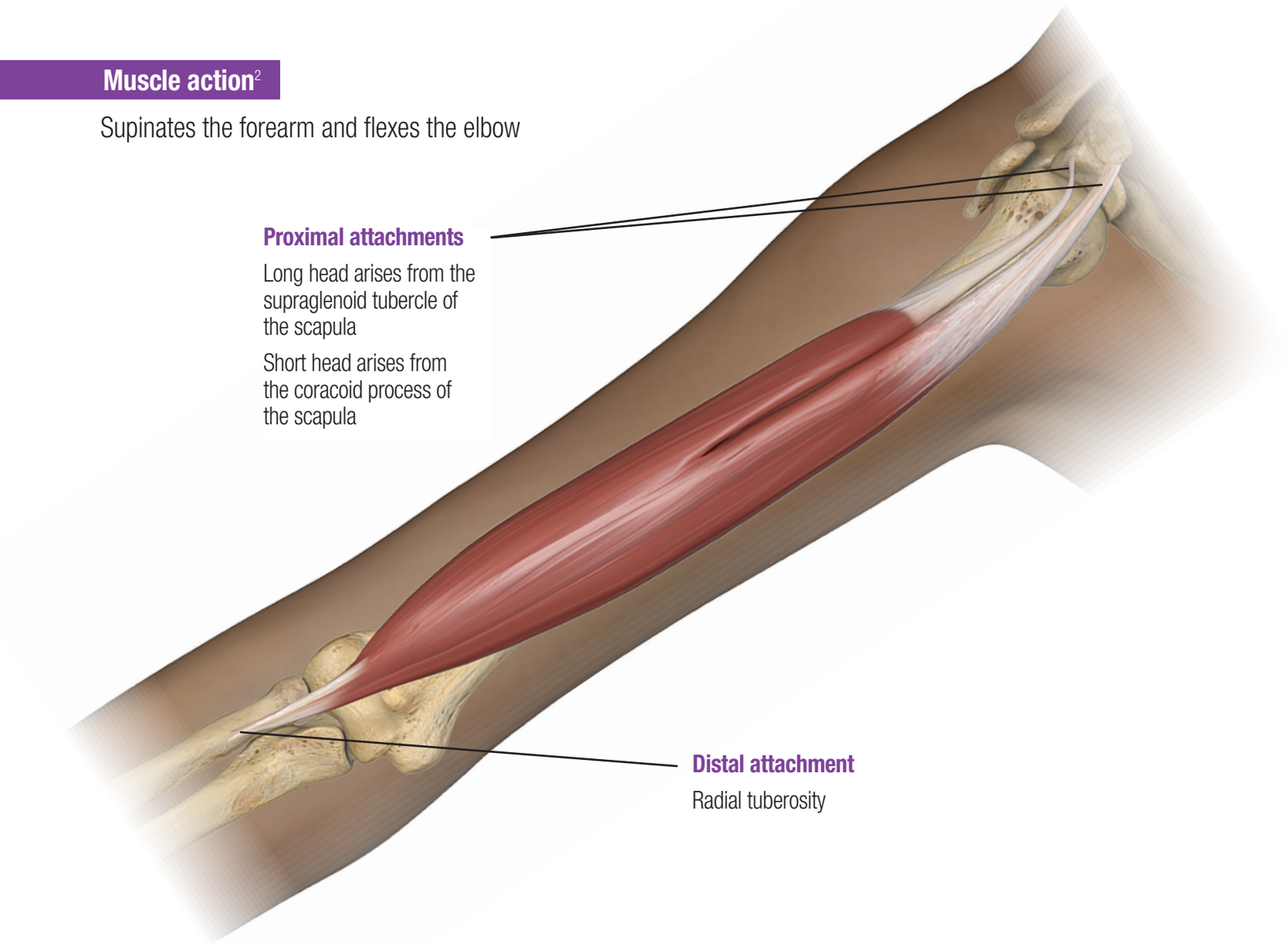
BOTOX® onabotulinumtoxinA injection

Biceps brachii

▶ BOTOX® dose: 1.5-3 Units/kg divided in 4 sites

Muscle action[2]

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.

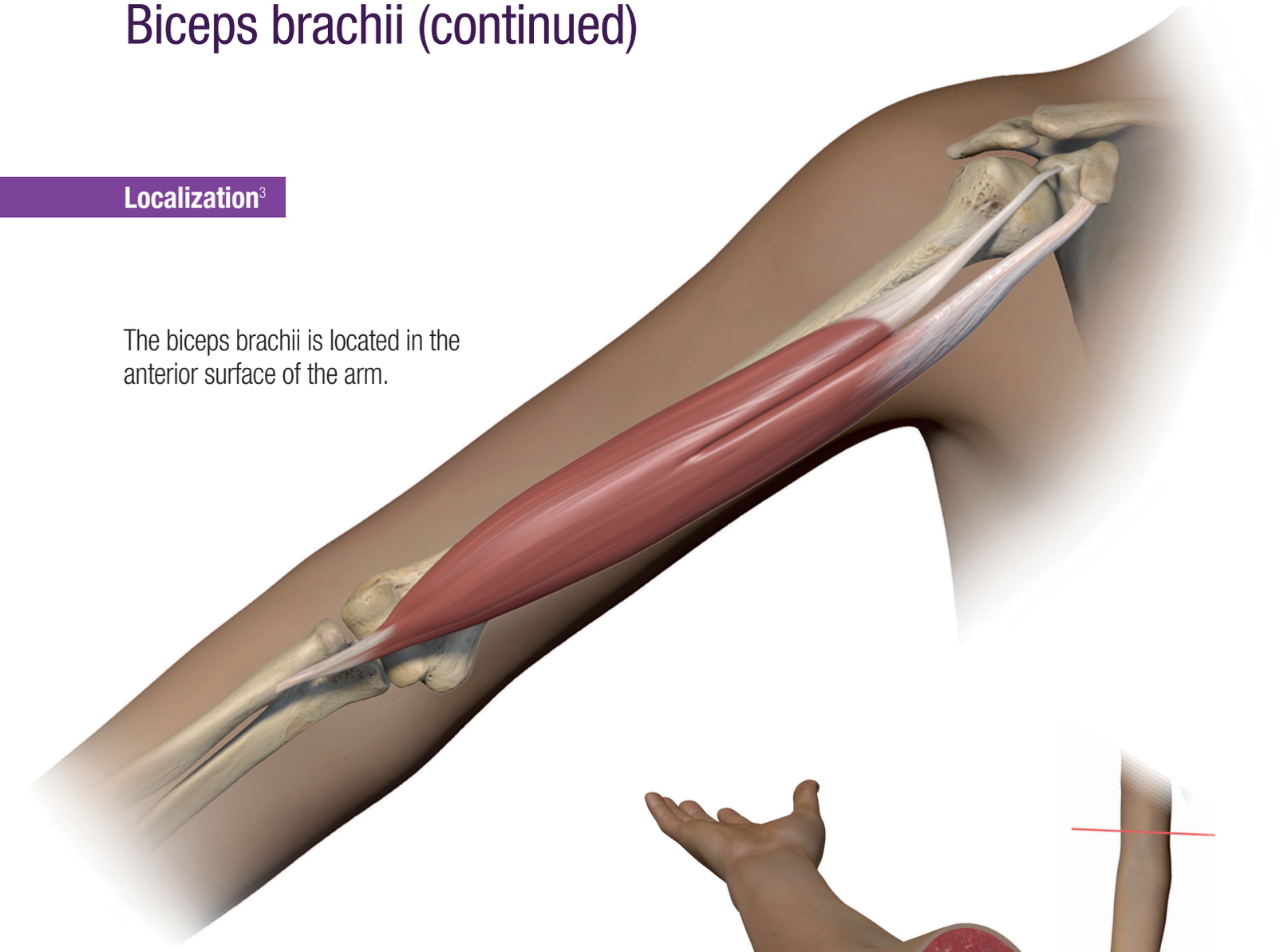
IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS
Adverse reactions to BOTOX for injection are discussed in greater detail in the following sections: *Boxed Warning*, *Contraindications*, and *Warnings and Precautions*.

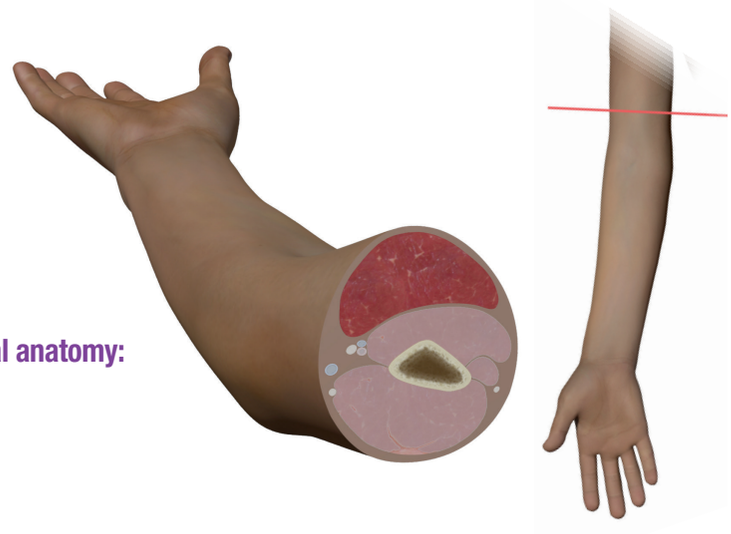
Please see additional Important Safety Information throughout.

Biceps brachii (continued)

Localization[3]

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





Cross-sectional anatomy: upper arm

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Pediatric Upper Limb Spasticity
The most frequently reported adverse reactions following injection of BOTOX in pediatric upper limb spasticity include upper respiratory tract infection (includes upper respiratory tract infection and viral upper respiratory tract infection), injection-site pain, nausea, constipation, rhinorrhea, nasal congestion, and seizure (includes seizure and partial seizure).

Please see additional Important Safety Information throughout.

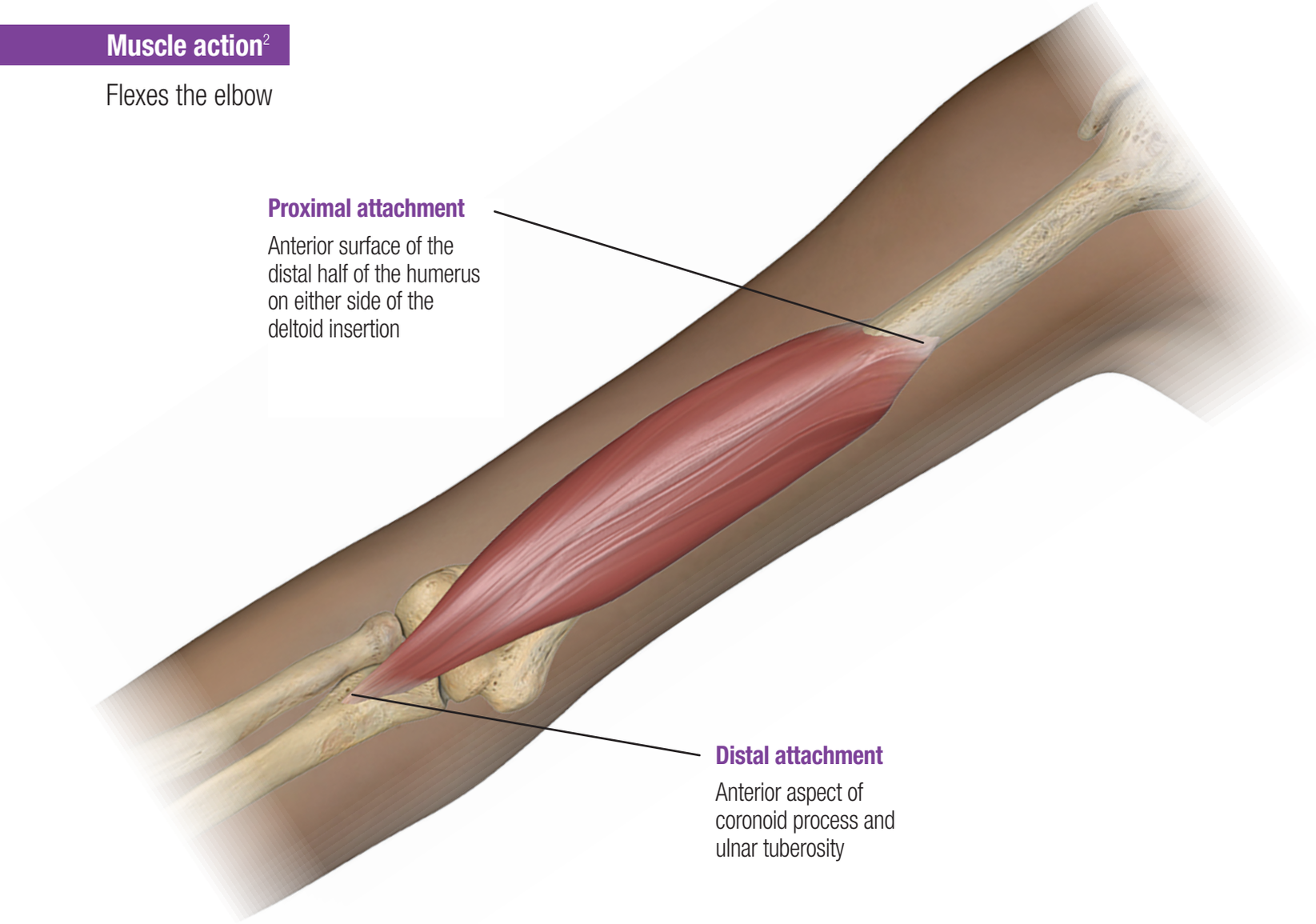
BOTOX® onabotulinumtoxinA injection

Brachialis

▶ BOTOX® dose: 1-2 Units/kg divided in 2 sites

Muscle action[2]

Flexes the elbow



Other muscles involved in elbow flexion

- Biceps brachii
- Brachioradialis
- Pronator teres*

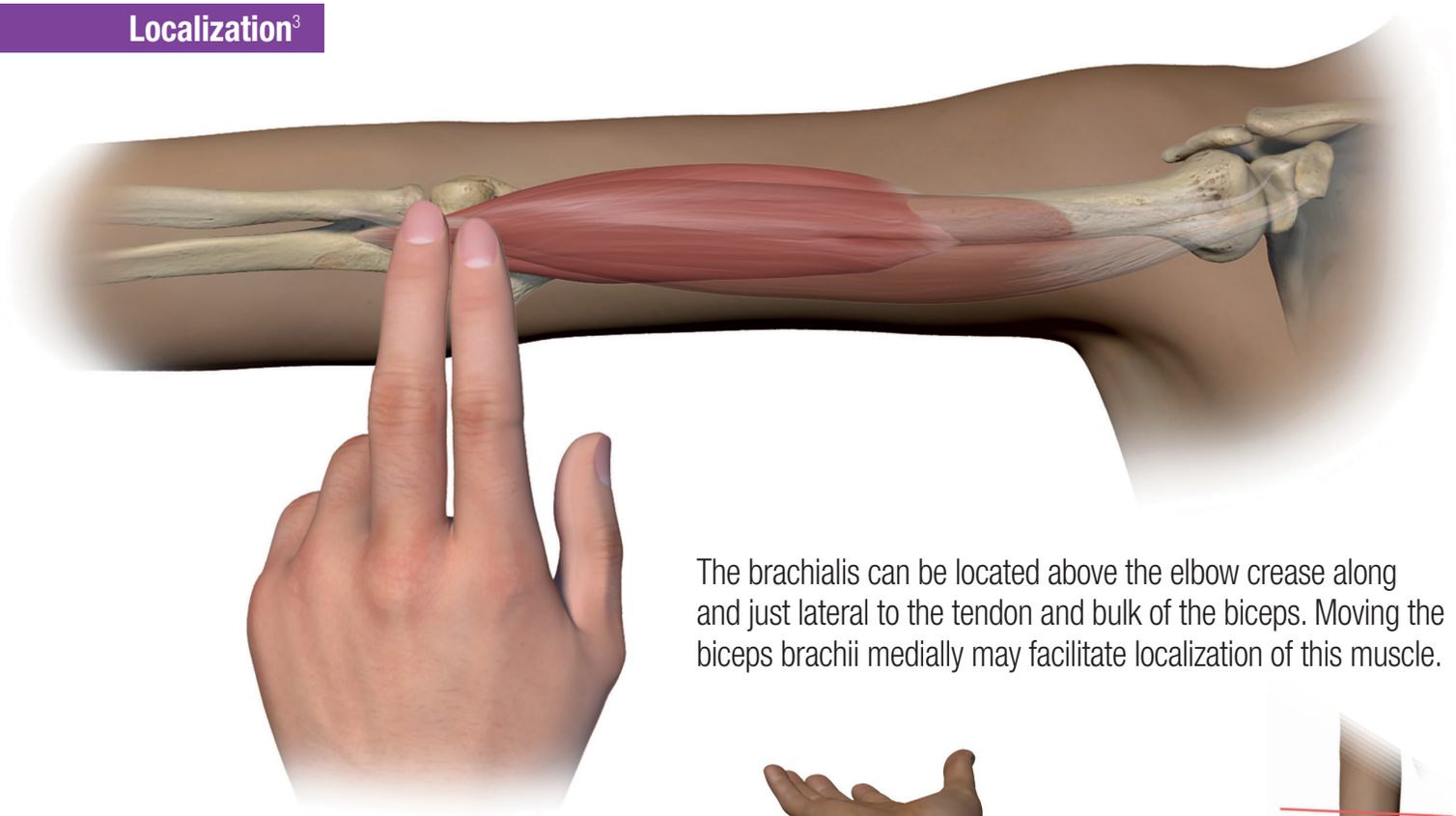
*For anatomical reference only.

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Pediatric Lower Limb Spasticity
The most frequently reported adverse reactions following injection of BOTOX in pediatric lower limb spasticity include injection-site erythema, injection-site pain, oropharyngeal pain, ligament sprain, skin abrasion, and decreased appetite.

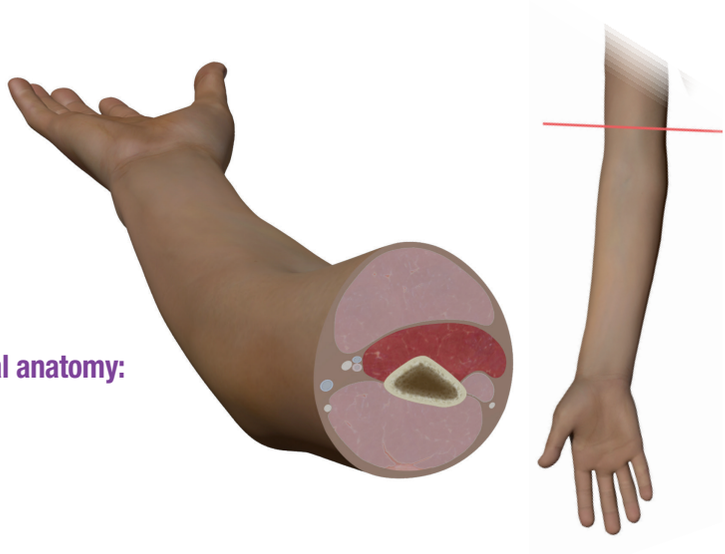
Please see additional Important Safety Information throughout.

Brachialis (continued)

Localization[3]



The brachialis can be located above the elbow crease along and just lateral to the tendon and bulk of the biceps. Moving the biceps brachii medially may facilitate localization of this muscle.



Cross-sectional anatomy: upper arm

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.

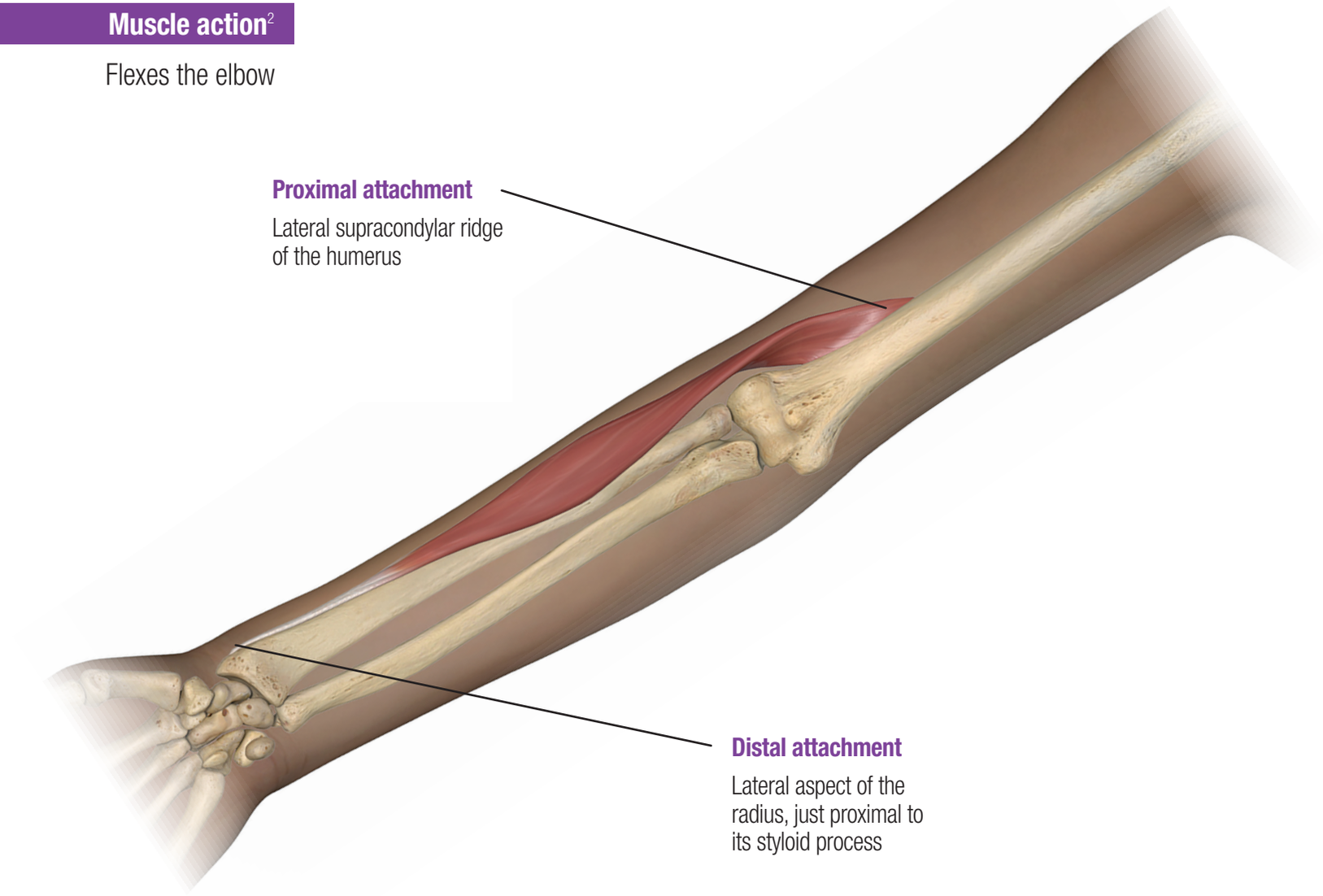
BOTOX® onabotulinumtoxinA injection

Brachioradialis

▶ BOTOX® dose: 0.5-1 Unit/kg divided in 2 sites

Muscle action[2]

Flexes the elbow



Other muscles involved in elbow flexion

- Biceps brachii
- Brachialis
- Pronator teres*

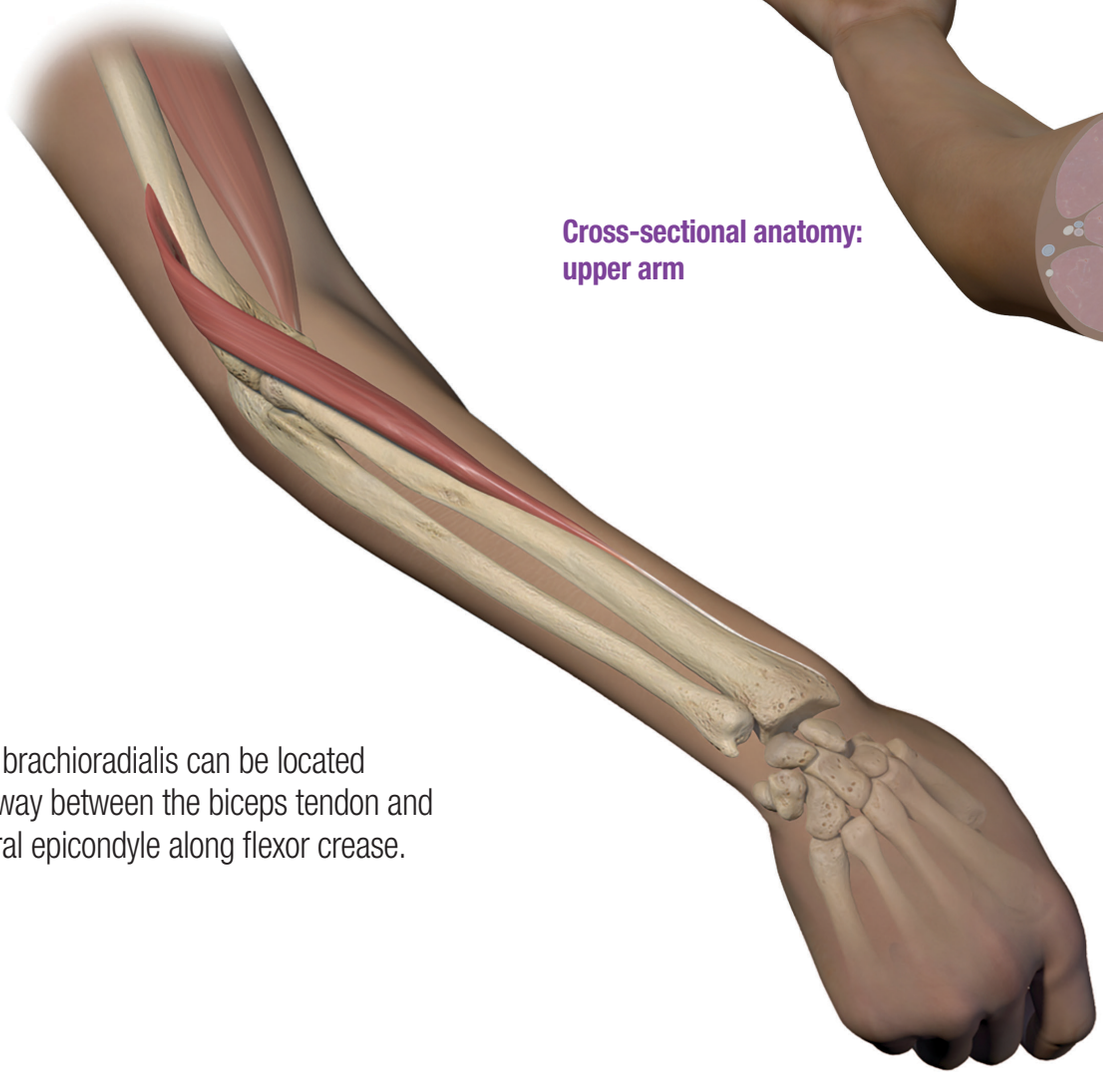
*For anatomical reference only.

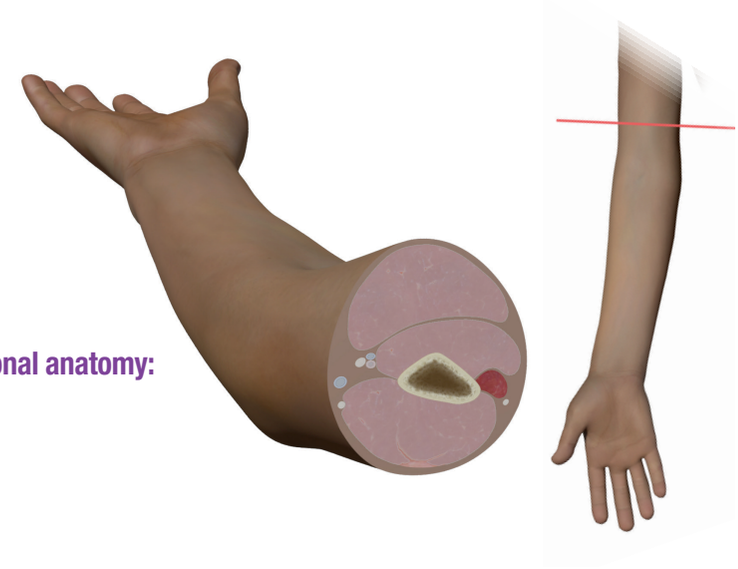
IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Postmarketing Experience (continued)
There have been spontaneous reports of death, sometimes associated with dysphagia, pneumonia, and/or other significant debility or anaphylaxis, after treatment with botulinum toxin. There have also been reports of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes.

Please see additional Important Safety Information throughout.

Brachioradialis (continued)

Localization[3]





Cross-sectional anatomy: upper arm

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

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

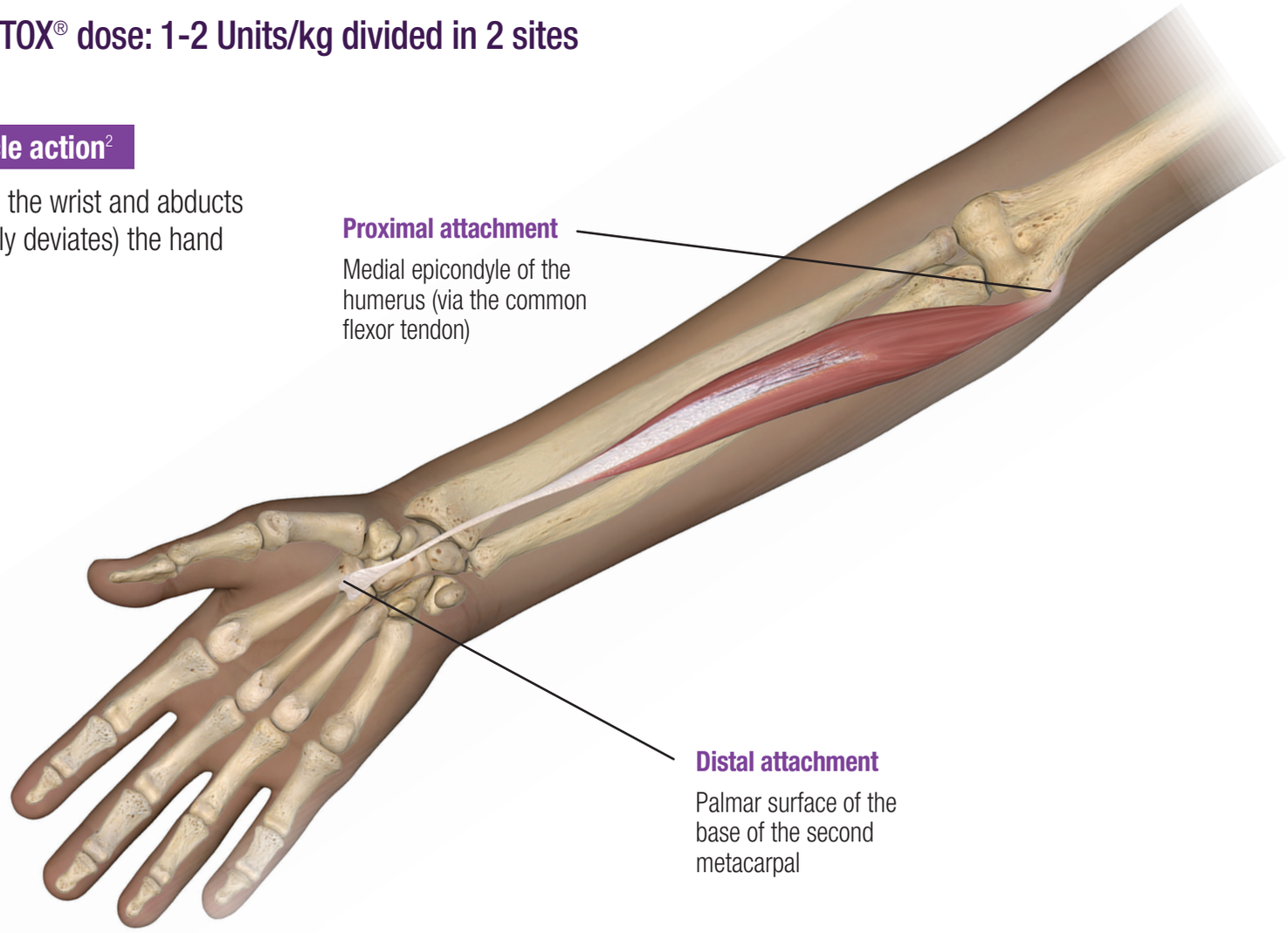
BOTOX® onabotulinumtoxinA injection

Flexor carpi radialis

▶ BOTOX® dose: 1-2 Units/kg divided in 2 sites

Muscle action[2]

Flexes the wrist and abducts (radially deviates) the hand



Other muscles involved in wrist flexion/abduction

- Flexor carpi ulnaris (flexion only)
- Flexor digitorum profundus (flexion only)
- Flexor digitorum superficialis (sublimis) (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)[4,*]

*For anatomical reference only.

IMPORTANT SAFETY INFORMATION (continued)
DRUG INTERACTIONS

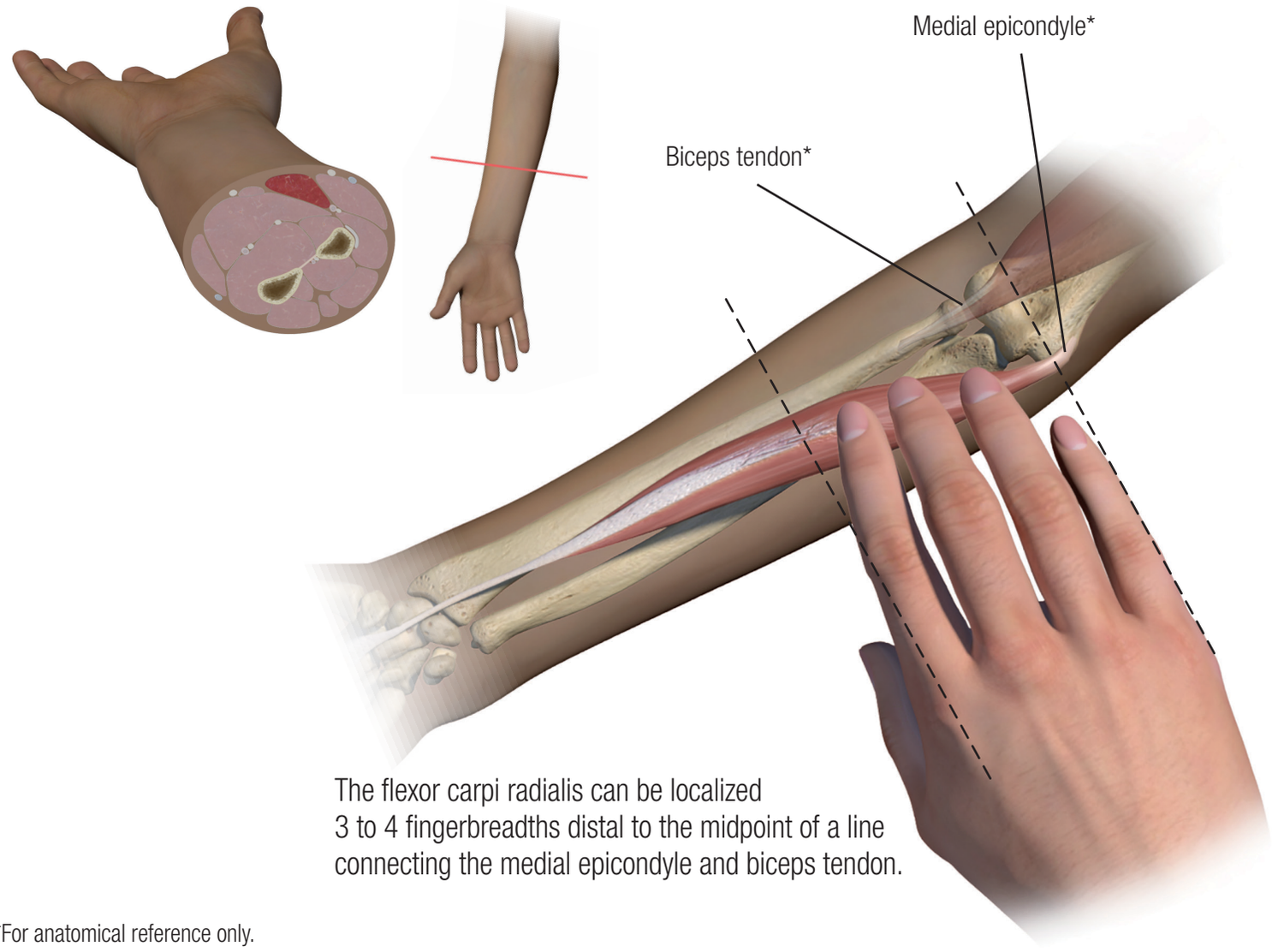
Co-administration of BOTOX and other agents interfering with neuromuscular transmission (eg, aminoglycosides, curare-like compounds) should only be performed with caution as the effect of the toxin may be potentiated. Use of anticholinergic drugs after administration of BOTOX may potentiate systemic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

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

Flexor carpi radialis (continued)

Localization[3]

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)
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.

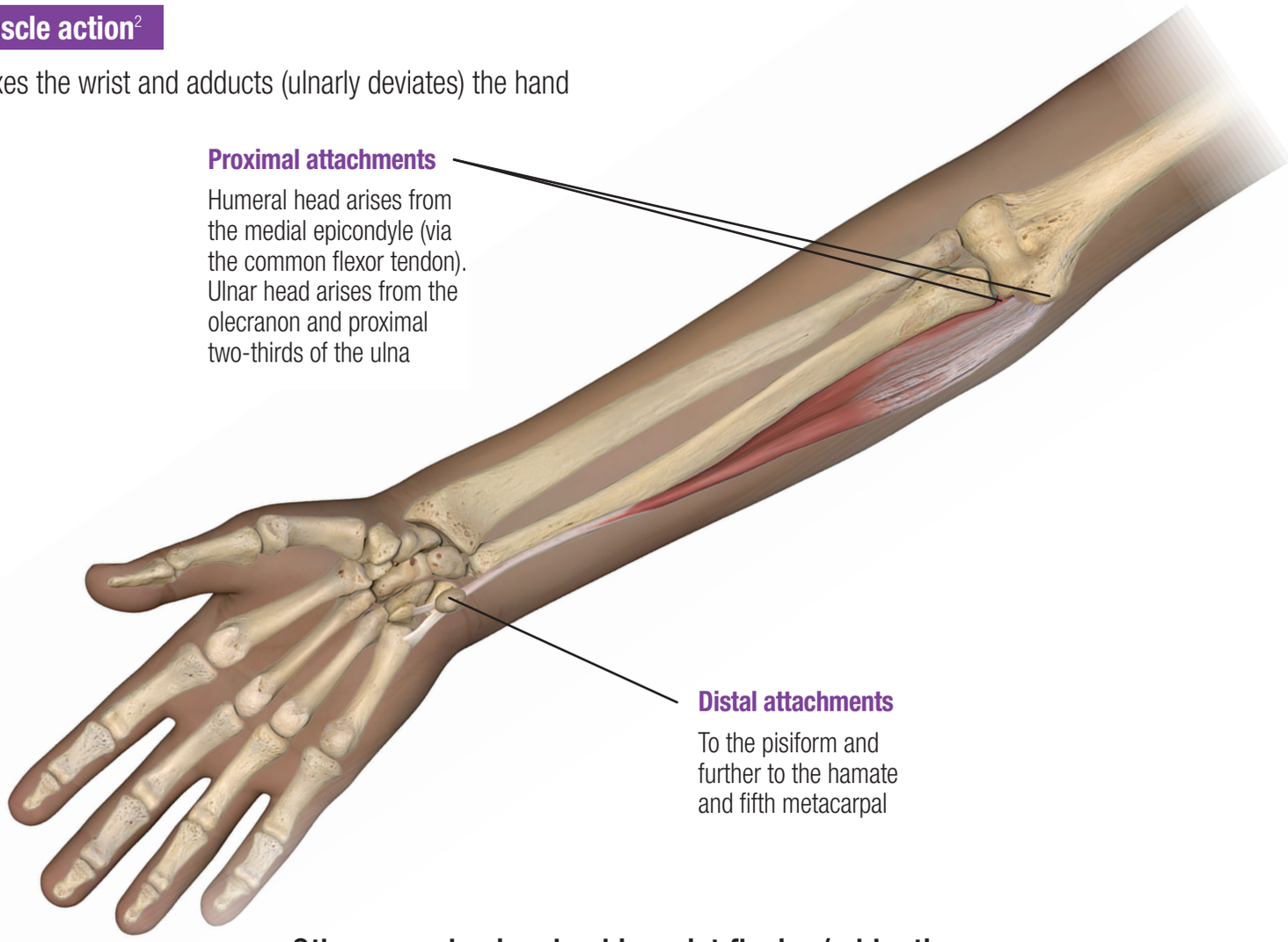
BOTOX® onabotulinumtoxinA injection

Flexor carpi ulnaris

▶ BOTOX® dose: 1-2 Units/kg divided in 2 sites

Muscle action[2]

Flexes the wrist and adducts (ulnarly deviates) the hand



Other muscles involved in wrist flexion/adduction

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

*For anatomical reference only.

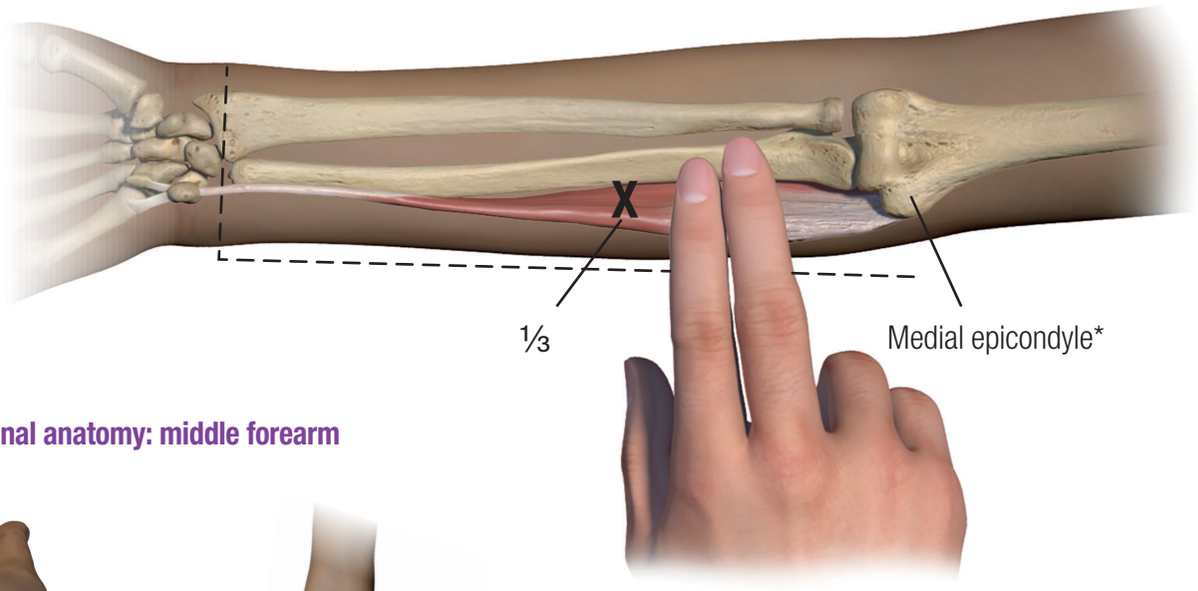
IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS
Spread of Toxin Effect
See *Boxed Warning*.

Please see additional Important Safety Information throughout.

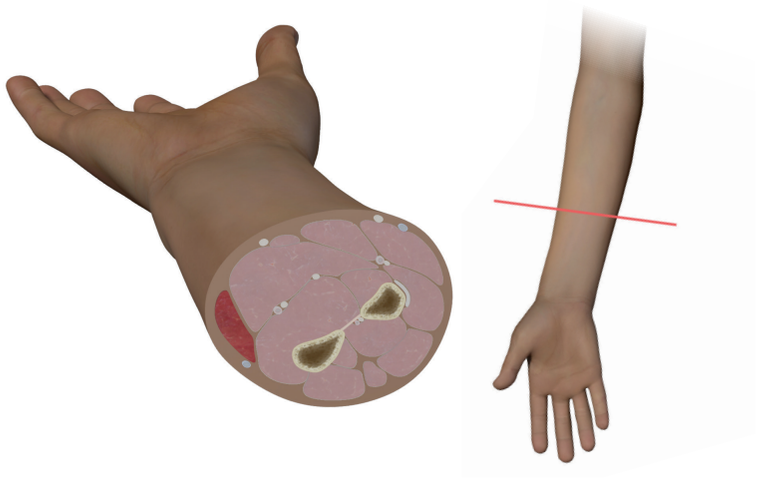
Flexor carpi ulnaris (continued)

Localization[3]

The flexor carpi ulnaris can be located at one-third the distance from the medial epicondyle to the wrist. Flexing the forearm (if possible) may facilitate localization of this muscle.



Cross-sectional anatomy: middle forearm



*For anatomical reference only.

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

Flexor digitorum superficialis (sublimis)

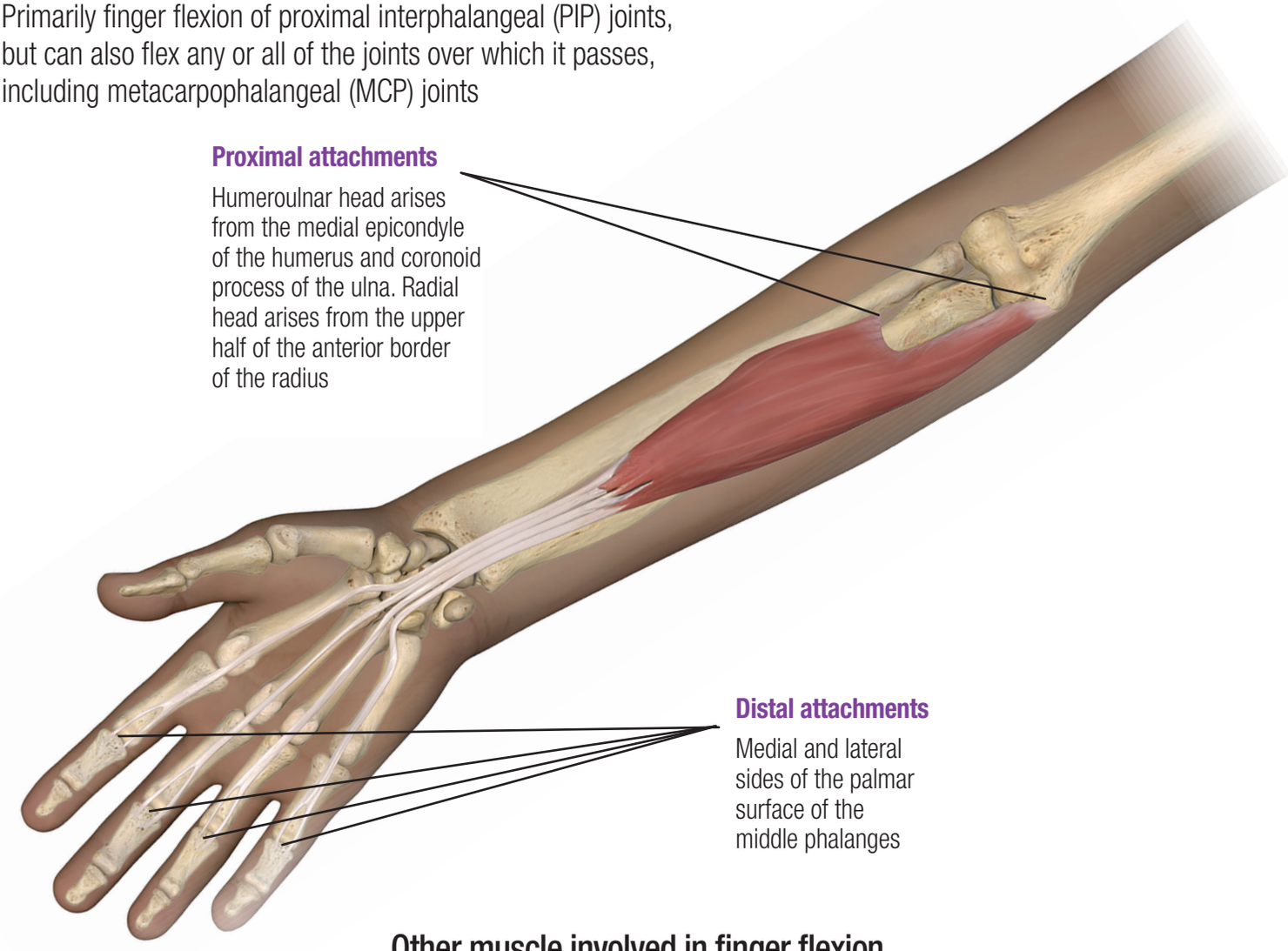
▶ BOTOX® dose: 0.5-1 Unit/kg divided in 2 sites

Muscle action[2]

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 upper half of the anterior border of the radius



Distal attachments

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

Other muscle involved in finger flexion

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

*For anatomical reference only.

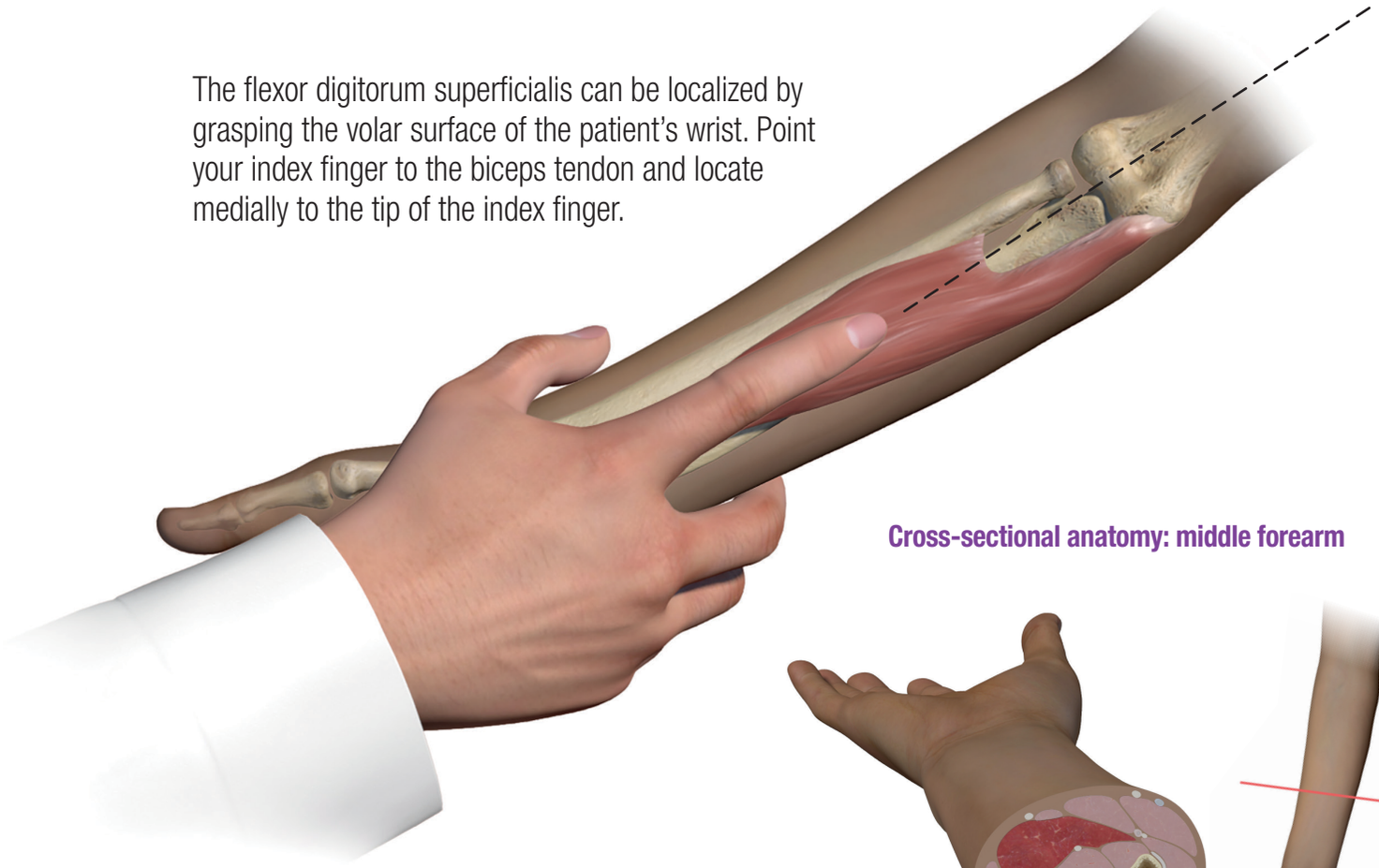
IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Serious Adverse Reactions With Unapproved Use
Serious adverse reactions, including excessive weakness, dysphagia, and aspiration pneumonia, with some adverse reactions associated with fatal outcomes, have been reported in patients who received BOTOX injections for unapproved uses. In these cases, the adverse reactions were not necessarily related to distant spread of toxin, but may have resulted from the administration of BOTOX to the site of injection and/or adjacent structures.

Please see additional Important Safety Information throughout.

Flexor digitorum superficialis (sublimis) (continued)

Localization[3]

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

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.

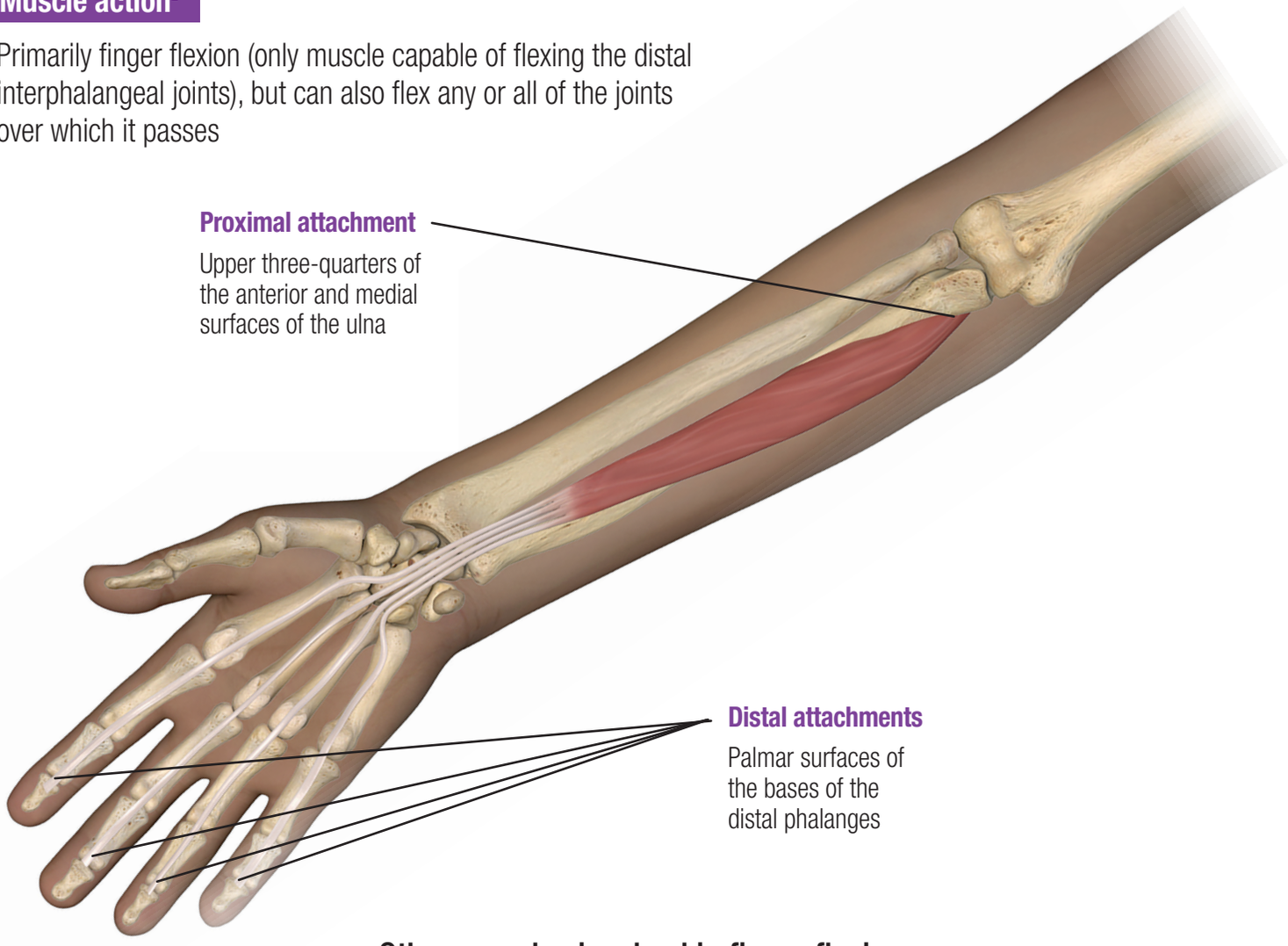
BOTOX® onabotulinumtoxinA injection

Flexor digitorum profundus

▶ BOTOX® dose: 0.5-1 Unit/kg divided in 2 sites

Muscle action[2]

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)*

*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.

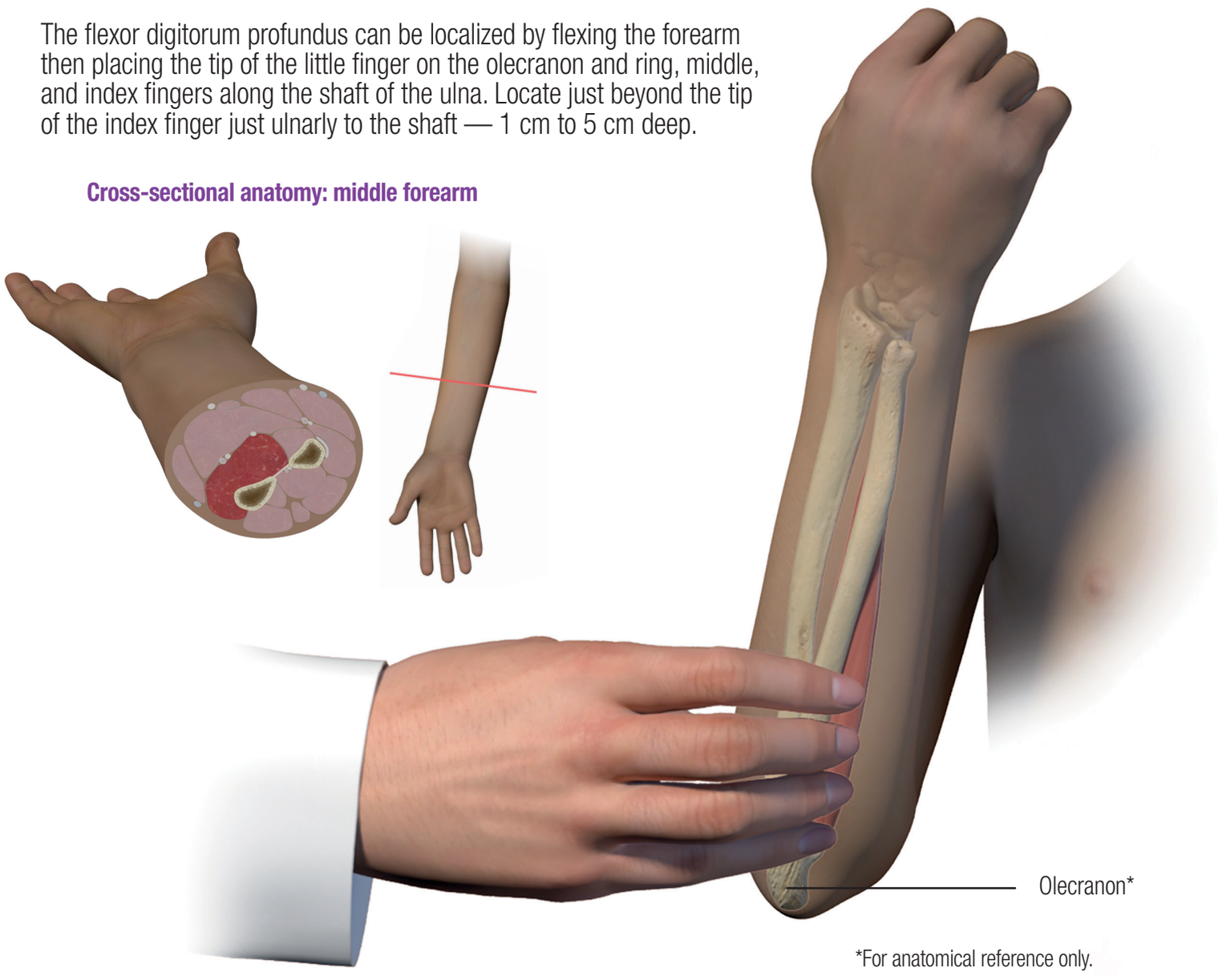
Please see additional Important Safety Information throughout.

Flexor digitorum profundus (continued)

Localization[3]

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)

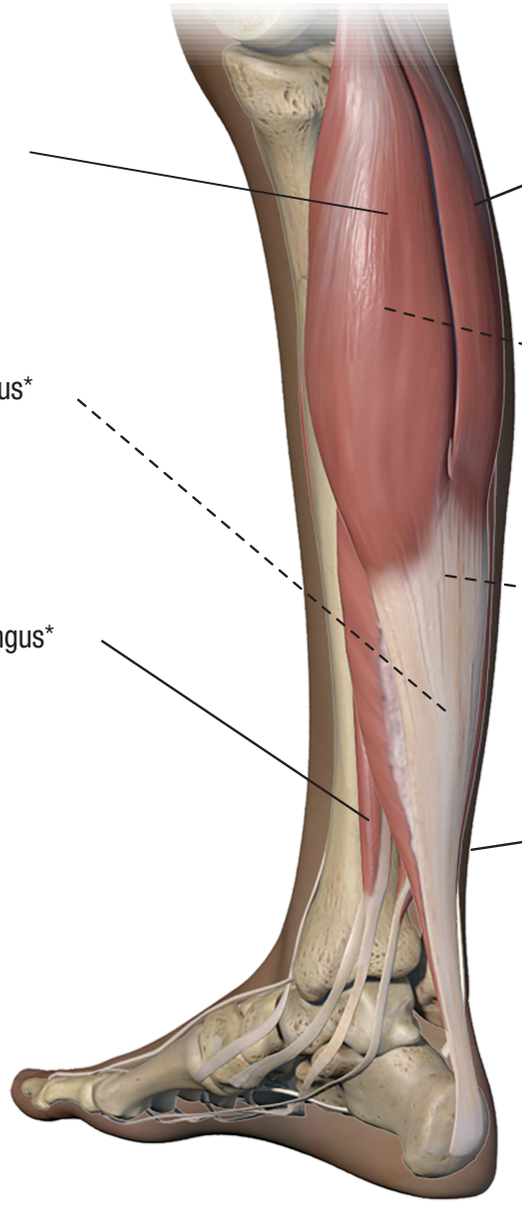
Increased Risk of Clinically Significant Effects With Preexisting Neuromuscular Disorders

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.

Main muscles involved in Pediatric LLS

Muscles listed in purple are those approved for BOTOX® injection[1]



Gastrocnemius (medial head)
1-2 Units/kg divided in 2 sites

Flexor hallucis longus* (hidden)

Flexor digitorum longus*

Gastrocnemius (lateral head)
1-2 Units/kg divided in 2 sites

Tibialis posterior (hidden)
1-2 Units/kg divided in 2 sites

Soleus (hidden)
1-2 Units/kg divided in 2 sites

Fibularis longus*

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

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

Main muscles involved in Pediatric LLS (continued)

Approved muscles and BOTOX® doses for flexed ankle[1]

Muscle	BOTOX® Dose
Gastrocnemius (medial head)	1 Unit/kg-2 Units/kg divided in 2 sites
Gastrocnemius (lateral head)	1 Unit/kg-2 Units/kg divided in 2 sites
Soleus	1 Unit/kg-2 Units/kg divided in 2 sites
Tibialis posterior	1 Unit/kg-2 Units/kg divided in 2 sites

The recommended dose for treating Pediatric LLS is 4-8 Units/kg divided among the affected muscles

The total dose of BOTOX® administered per treatment session in the lower limb should not exceed 8 Units/kg or 300 Units, whichever is lower

When treating both lower limbs or the upper and lower limbs in combination, the total dose should not exceed the lower of 10 Units/kg body weight or 340 Units in a 3-month interval

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.

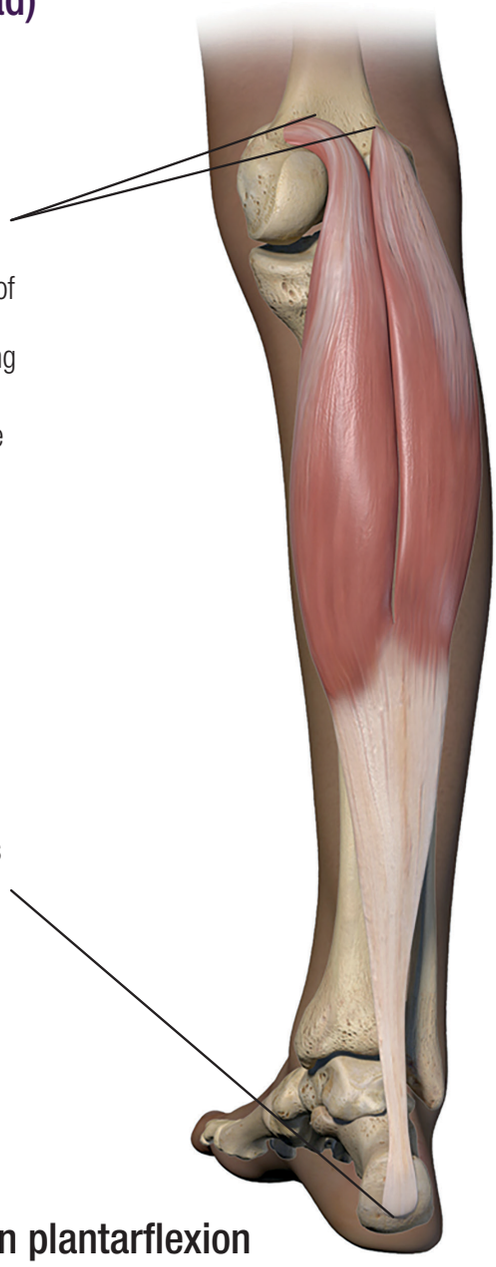
BOTOX® onabotulinumtoxinA injection

Gastrocnemius

▶ BOTOX® dose: 1-2 Units/kg divided in 2 sites (medial head) and 1-2 Units/kg divided in 2 sites (lateral head)

Muscle action[2]

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)
WARNINGS AND PRECAUTIONS (continued)

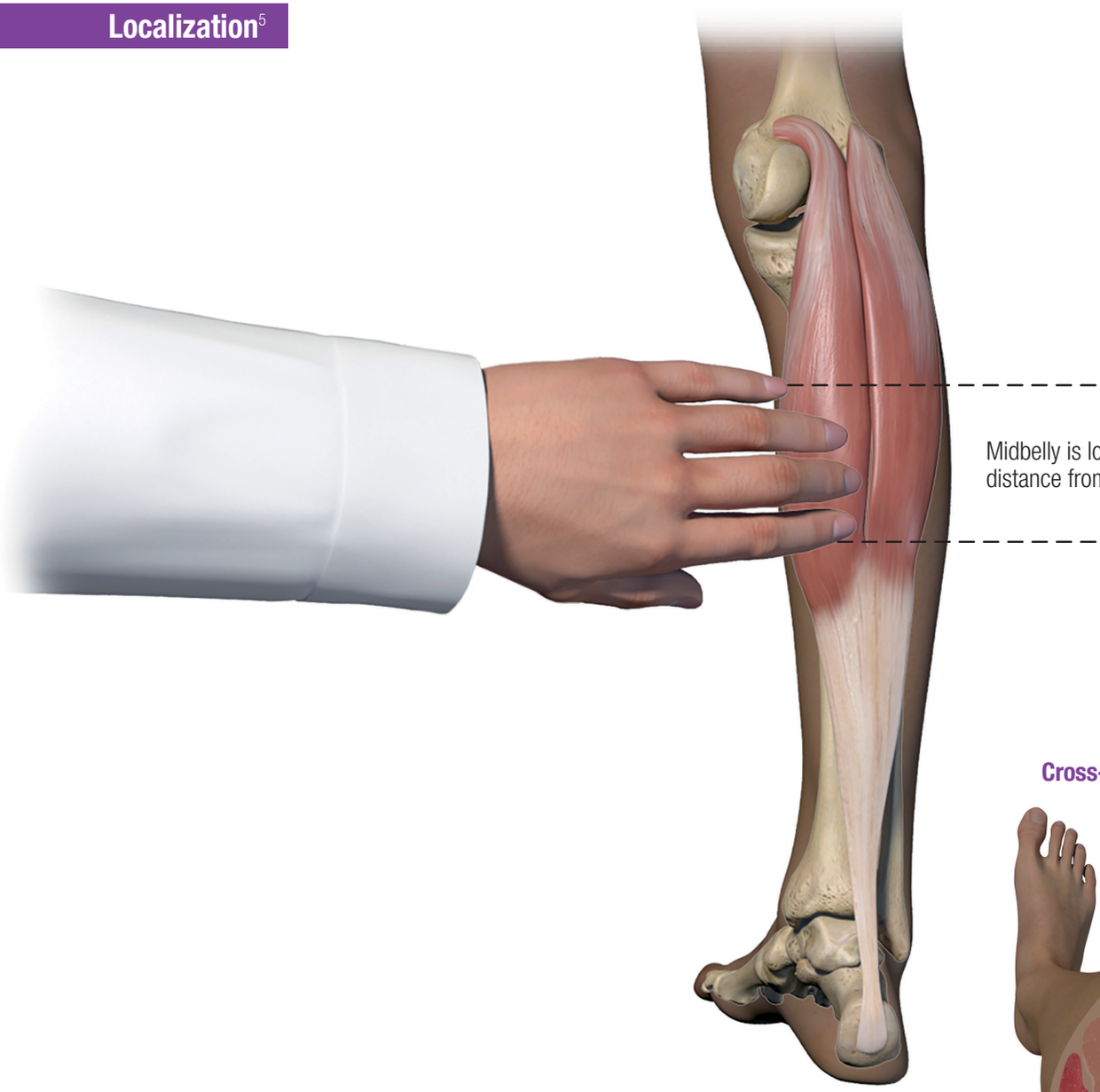
Upper Respiratory Tract Infections in Patients Treated for Spasticity

In pediatric patients treated for upper limb spasticity, upper respiratory tract infections were reported more frequently as an adverse reaction in patients treated with BOTOX (17% at 6 Units/kg and 10% at 3 Units/kg) compared to placebo (9%). In pediatric patients treated for lower limb spasticity, upper respiratory tract infection was not reported with an incidence greater than placebo.

Please see additional Important Safety Information throughout.

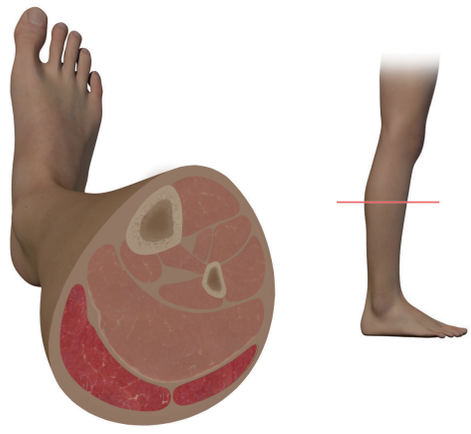
Gastrocnemius (continued)

Localization[5]



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

Cross-sectional anatomy: midcalf



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.

BOTOX®
onabotulinumtoxinA injection

Soleus

▶ BOTOX® dose: 1-2 Units/kg divided in 2 sites

Muscle action[2]

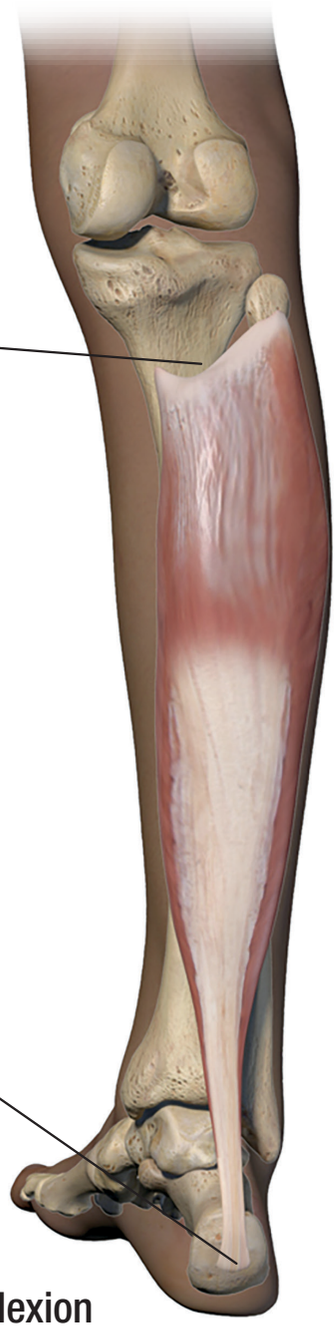
Involved in plantarflexion

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*

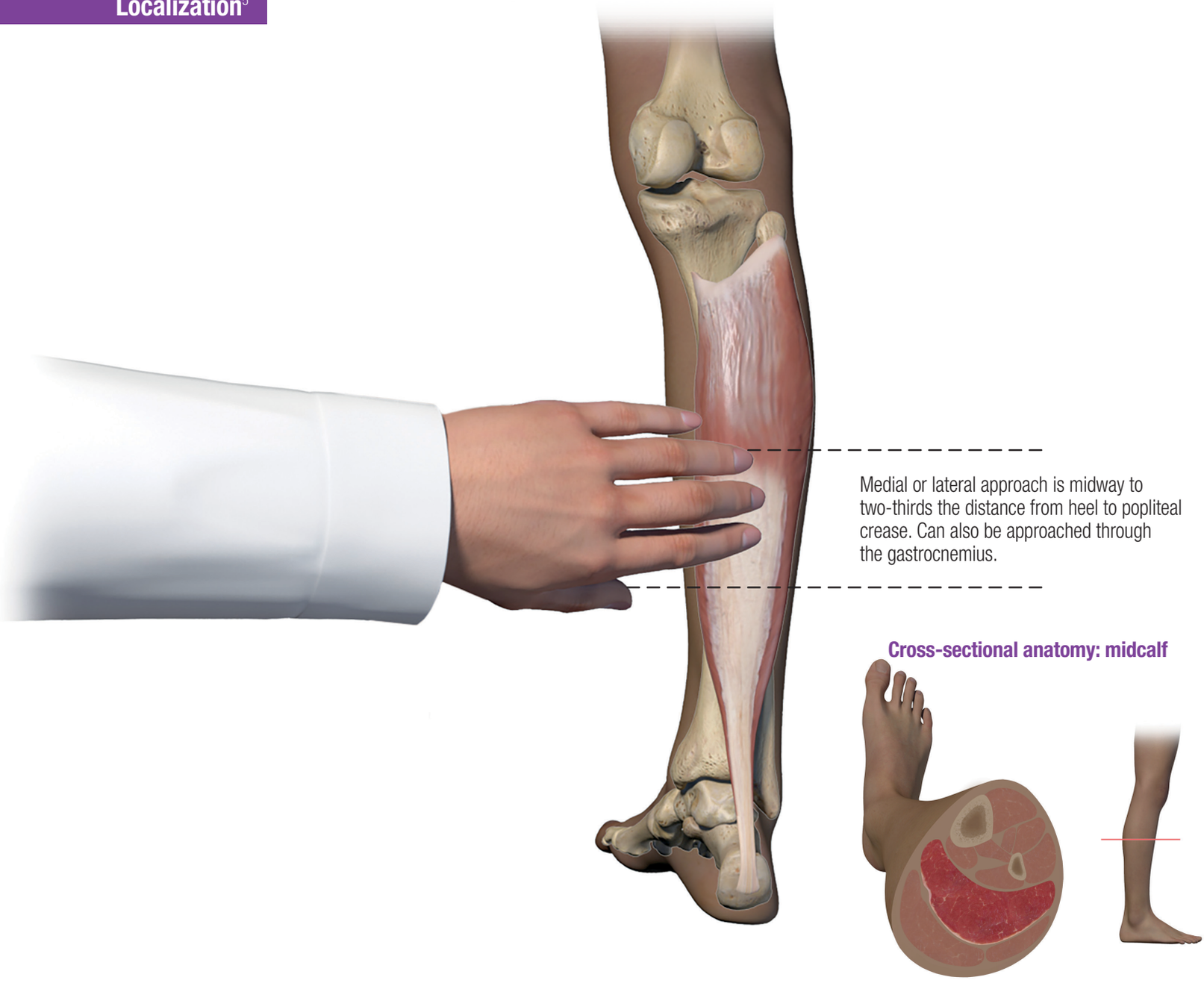
*For anatomical reference only.

IMPORTANT SAFETY INFORMATION (continued)
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.

Soleus (continued)

Localization[5]



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

Tibialis posterior

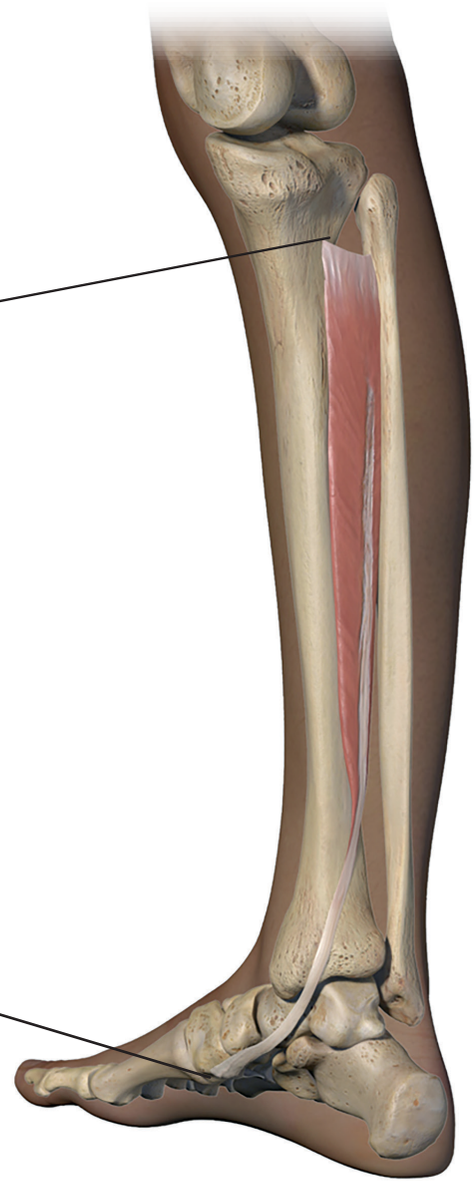
▶ BOTOX® dose: 1-2 Units/kg divided in 2 sites

Muscle action[2,6]

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 attachment

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[7,*]
- Flexor hallucis longus[7,*]
- Fibularis longus (plantarflexion only)*
- Tibialis anterior (foot inversion only)*

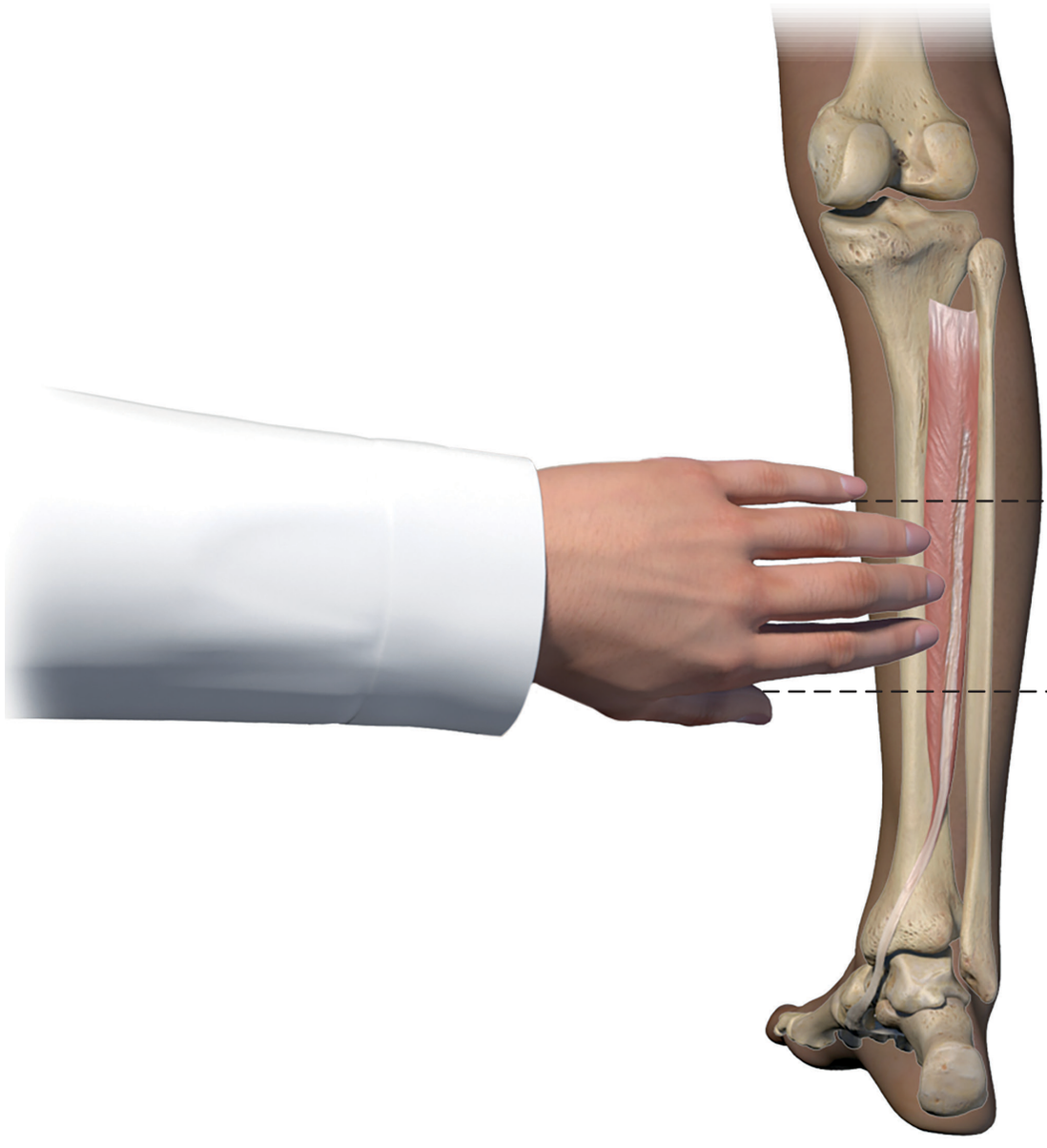
*For anatomical reference only.

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Pediatric Upper Limb Spasticity
The most frequently reported adverse reactions following injection of BOTOX in pediatric upper limb spasticity include upper respiratory tract infection (includes upper respiratory tract infection and viral upper respiratory tract infection), injection-site pain, nausea, constipation, rhinorrhea, nasal congestion, and seizure (includes seizure and partial seizure).

Please see additional Important Safety Information throughout.

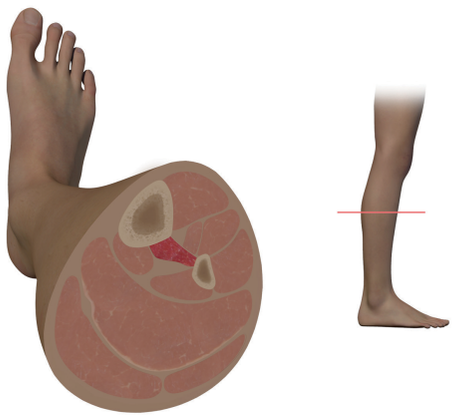
Tibialis posterior (continued)

Localization[5]



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)
ADVERSE REACTIONS (continued)
Pediatric Lower Limb Spasticity
The most frequently reported adverse reactions following injection of BOTOX in pediatric lower limb spasticity include injection-site erythema, injection-site pain, oropharyngeal pain, ligament sprain, skin abrasion, and decreased appetite.

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)[1]

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

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

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

- The recommended dilution is 200 Units/4 mL or 100 Units/2 mL with preservative-free 0.9% Sodium Chloride Injection, USP (see tables above)
- Administer the 200-Unit vial or 100-Unit vial of BOTOX® within 24 hours after reconstitution in the vial
- Unused reconstituted BOTOX® should be stored within 24 hours after reconstitution in the vial
- BOTOX® vials are for single-dose only. Discard any unused portion
- Unopened vials of BOTOX® should be stored in a refrigerator (between 2ºC to 8ºC or 36ºF to 46ºF) 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 (not shown). Then, tilt the vial at a 45° angle and 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.

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
  - Supplies for conscious sedation and/or local anesthetic, if necessary
- 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 parents of scheduled injections

References:
1. BOTOX® Prescribing Information, August 2022. **2.** Standring S, ed. *Gray's Anatomy*: *The Anatomical Basis of Clinical Practice.* 41st ed. Churchill Livingstone; 2016. **3.** Perotto AO. *Anatomical Guide for the Electromyographer: The Limbs and Trunk.* 5th ed. Charles C Thomas Publisher, Ltd; 2011. **4.** Washington University School of Medicine in St. Louis. Peripheral nerve surgery: a resource for surgeons. Extensor pollicis longus. Washington University School of Medicine in St. Louis website. http://nervesurgery.wustl.edu/ap/hand/radial/deepbranch/Pages/ExtensorPollicisLongus.aspx. Accessed December 2, 2022. **5.** Odderson IR, ed. *Botulinum Toxin Injection Guide.* Demos Medical Publishing, LLC; 2008. **6.** Richardson M. Muscle atlas: Tibialis posterior. University of Washington website. http://rad.washington.edu/muscle-atlas/tibialis-posterior/. Accessed December 2, 2022. **7.** Murdock CJ, Munjal A, Agyeman K. Anatomy, Bony Pelvis and Lower Limb, Calf Flexor Hallucis Longus Muscle. In: *StatPearls.* StatPearls Publishing; April 15, 2020.

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.

BOTOX® onabotulinumtoxinA injection

BOTOX ONE®

- Videos and e-lectures on:
  - Injection technique
  - Muscle localization
  - Functional anatomy
  - Reconstitution
- Downloadable patient education and office materials

Register at BOTOXONE.com

Parent Brochure for Pediatric Spasticity

- Educates parents about Pediatric Spasticity and how BOTOX® may help
- Provides information on available resources and support

Contact your Account Specialist for this brochure

Peer-to-Peer Training

- Several different programs are available for BOTOX® injection training, including Expert-On-Demand, preceptorships, and proctorships
- Expert-On-Demand is a 30- to 45-minute video conference with an experienced BOTOX® injector who can address specific training needs

Contact your Account Specialist for more information

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

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)

ALLERGAN® MEDICAL INFORMATION LINE

1-800-678-1605

PATIENT SAVINGS PROGRAM

For commercially insured patients: BOTOXSavingsProgram.com

PROFESSIONAL EDUCATION & 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, 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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