Indication

Spasticity

BOTOX® 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 about BOTOX® inside.
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
- Safety and efficacy data from clinical trials and additional data and insights on muscle/dose selection and treatment initiation strategies
- Dilution and reconstitution guidelines

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

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IMPORTANT SAFETY INFORMATION (continued)

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

WARNINGS AND PRECAUTIONS

Spread of Toxin Effect
See Boxed Warning.

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

Please see additional Important Safety Information about BOTOX® on following pages.
Integrate multiple approaches when assessing Adult Spasticity

**Upper limb spasticity**

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

**Lower limb spasticity**

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

*Nonambulatory patients were excluded from the BOTOX® lower limb spasticity clinical trial.
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?
- Are contraindicated 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 about BOTOX® on following pages.
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)

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.
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.

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**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 about BOTOX® on following pages.
Clinical presentation in upper limb (continued)

Flexed elbow, pronated forearm

Biceps brachii
Brachialis
Brachioradialis
Pronator teres (hidden)

Pronator quadratus (hidden)

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).
Clinical presentation in upper limb (continued)

Flexed elbow, supinated forearm

Biceps brachii
Brachialis
Brachioradialis

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 about BOTOX® on following pages.
Clinical presentation in upper limb (continued)

Flexed wrist

- Flexor carpi radialis
- Flexor digitorum superficialis (sublimis)
- Palmaris longus tendon*
- Flexor digitorum profundus (hidden)
- Flexor carpi ulnaris
- Flexor pollicis longus

*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.
Clinical presentation in upper limb (continued)

**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 about BOTOX® on following pages.*
Clinical presentation in upper limb (continued)

Thumb in palm

Flexor pollicis longus

Opponens pollicis (hidden)

Flexor pollicis brevis

Adductor pollicis

Abductor pollicis brevis*

*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 about BOTOX® on following pages.
Clinical presentation in upper limb (continued)

Intrinsic plus hand

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*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.
Clinical presentation in lower limb

Flexed ankle, flexed toes

*For anatomical reference only.
**Clinical presentation in lower limb (continued)**

*Flexed knee; flexed ankle*

- **Tibialis posterior** (hidden)
- **Soleus**
- **Flexor digitorum longus**
- **Flexor hallucis longus**
- **Gastrocnemius (medial and lateral heads)†**

*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)**

**WARNINGS AND PRECAUTIONS (continued)**

**Human Albumin and Transmission of Viral Diseases**

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

Please see additional Important Safety Information about BOTOX® on following pages.
Clinical presentation in lower limb (continued)

Inverted/supinated foot

Tibialis posterior

Tibialis anterior (hidden)*

*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 about BOTOX® on following pages.
Clinical presentation in lower limb (continued)
Clinical presentation in lower limb (continued)

Flexed toes

Flexor digitorum longus

Flexor hallucis longus

Flexor hallucis brevis*

Flexor digiti minimi brevis (hidden)*

Flexor digitorum brevis*

*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.
Clinical presentation in lower limb (continued)

Equinovarus foot, flexed toes

- Tibialis posterior
- Flexor hallucis longus
- Flexor digitorum longus
- Flexor digitorum brevis*
- Flexor hallucis brevis*
- Flexor digiti minimi brevis (hidden)*

*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 about BOTOX® on following pages.
### Adult ULS

**Proven efficacy and dosing across 7 pivotal studies**

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of Patients</th>
<th>Baseline Ashworth Score*</th>
<th>BOTOX® Dosage</th>
<th>Labeled End Points</th>
</tr>
</thead>
</table>
| 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)<sup>b</sup> |
| 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)<sup>b</sup> |
| 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)<sup>c</sup> |
| 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])<sup>d</sup> |
| 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)<sup>e</sup> and Clinical Global Impression (CGI)<sup>d</sup> |
| 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)<sup>a</sup> |

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).

---

*Includes original, expanded, and modified Ashworth Scales.

<sup>a</sup>Primary endpoint at Week 6.

<sup>b</sup>Primary endpoint at Week 4.

<sup>c</sup>Secondary endpoint at Week 6.

<sup>d</sup>Other endpoint at Week 6.
Adult LLS

<table>
<thead>
<tr>
<th>Study 7</th>
<th>Number of Patients</th>
<th>Baseline MAS</th>
<th>BOTOX® Dosage</th>
<th>Labeled End Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 468</td>
<td>BOTOX® (n = 233)</td>
<td>Ankle ≥ 3</td>
<td>300 Units to 400 Units</td>
<td>Mean change from baseline in ankle flexor score (modified Ashworth Scale)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Placebo (n = 235)</td>
<td></td>
<td></td>
<td></td>
<td>Mean Physician Global Assessment of Response (CGI)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Co-primary endpoint: Average of scores at Weeks 4 and 6.

**BOTOX® provided significant improvements in muscle tone in Adult Spasticity**

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

*Includes original, expanded, and modified Ashworth Scales.

**IMPORTANT SAFETY INFORMATION (continued)**

**ADVERSE REACTIONS (continued)**

**Postmarketing Experience**

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

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

**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 the accompanying BOTOX® full Prescribing Information, including Boxed Warning and Medication Guide.
Clinical data summary for BOTOX® in Adult Spasticity (continued)

Proven safety profile across 7 pivotal studies

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.

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>BOTOX® 251-360 Units (N = 115) %</th>
<th>BOTOX® 150-250 Units (N = 188) %</th>
<th>BOTOX® &lt; 150 Units (N = 54) %</th>
<th>Placebo (N = 182) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal disorder</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Infections and infestations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronchitis</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>6</td>
<td>5</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Muscular weakness</td>
<td>0</td>
<td>4</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

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.

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.
## Adult LLS (Study 7)

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>BOTOX(^\circledast) (N = 231) %</th>
<th>Placebo (N = 233) %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Musculoskeletal and connective tissue disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthralgia</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Back pain</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Myalgia</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><strong>Infections and infestations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><strong>General disorders and administration site conditions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection-site pain</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

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

### IMPORTANT SAFETY INFORMATION (continued)

#### WARNINGS AND PRECAUTIONS

**Spread of Toxin Effect**
See Boxed Warning.

**Lack of Interchangeability Between Botulinum Toxin Products**
The potency Units of BOTOX\(^\circledast\) 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\(^\circledast\) cannot be compared to nor converted into Units of any other botulinum toxin products assessed with any other specific assay method.

Please see additional Important Safety Information about BOTOX\(^\circledast\) on following pages.
Key guiding principles for BOTOX® treatment

OPTIMIZING MUSCLE/DOSE SELECTION

Use patient goals, clinical presentation, and additional insights to develop a more strategic approach

- Prioritize selections to help meet goals and manage postures
- Consider the patient’s medical profile and history, particularly time since stroke
- Select muscle-dose combinations that are appropriate based on the patient’s spasticity

SETTING PROPER GOALS AND TREATMENT EXPECTATIONS

Agree on specific and realistic goals to help guide the course of care considering:

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

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

- BOTOX® is not a cure. It helps reduce the severity of 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
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

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.

Increased Risk of Clinically Significant Effects With Preexisting Neuromuscular Disorders

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

Dysphagia and Breathing Difficulties

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

Please see additional Important Safety Information about BOTOX® on following pages.
Adopt evidence-based muscle selection patterns for your Adult Spasticity patients

In a post-hoc subgroup analysis, Adult LLS patients 2+ years post-stroke saw ankle MAS improvement from BOTOX® treatment when injected in both ankle and toe flexors.3

Mandatory Ankle Muscles Only (BOTOX® 300 Units)

<table>
<thead>
<tr>
<th>Time Since Stroke</th>
<th>Ankle MAS Mean Change From Baseline (weeks 4 and 6 average)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 24 Months</td>
<td>n = 37</td>
</tr>
<tr>
<td>&gt; 24 Months</td>
<td>n = 67</td>
</tr>
</tbody>
</table>

\[ \Delta = -0.1 \]
\[ P = 0.968 \]

BOTOX® (n = 233)

Placebo (n = 235)

Mandatory Ankle Muscles + FHL* + FDL† (BOTOX® 400 Units)

<table>
<thead>
<tr>
<th>Time Since Stroke</th>
<th>Ankle MAS Mean Change From Baseline (weeks 4 and 6 average)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 24 Months</td>
<td>n = 27</td>
</tr>
<tr>
<td>&gt; 24 Months</td>
<td>n = 35</td>
</tr>
</tbody>
</table>

\[ \Delta = -0.70 \]
\[ P = 0.001 \]

BOTOX® injections (300 Units) into the ankle flexors alone in patients ≤ 2 years post-stroke was sufficient to provide significant ankle MAS improvements.3

BOTOX® injections (400 Units) into both ankle and toe flexors in patients > 2 years post-stroke provided significant ankle MAS improvements.3

LIMITATIONS
- 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

STUDY DESIGN
- Post-hoc analysis of the double-blind phase of the BOTOX® pivotal study for Adult LLS (REFLEX)
- 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
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.

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%).

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

Please see additional Important Safety Information about BOTOX® on following pages.
Consider evidence-based treatment initiation strategies for your Adult Spasticity patients

In a post-hoc subgroup analysis, Adult LLS patients treated with BOTOX® within 2 years post-stroke saw significant ankle MAS improvements

LIMITATIONS

• 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)

• 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)

STUDY DESIGN

• Post-hoc analysis of the BOTOX® pivotal study for Adult LLS (REFLEX)
  • 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
In the same study, patients treated with BOTOX® within 2 years post-stroke also saw significant CGI improvements

**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.

**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.

**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 about BOTOX® on following pages.
# Muscles by posture in Adult Spasticity

<table>
<thead>
<tr>
<th>Posture</th>
<th>Muscles</th>
<th>[Upper limb spasticity]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Flexed elbow</strong></td>
<td>• Biceps brachii</td>
<td>• Brachioradialis</td>
</tr>
<tr>
<td></td>
<td>• Brachialis</td>
<td>• Pronator teres</td>
</tr>
<tr>
<td><strong>Pronated/supinated forearm</strong></td>
<td>• Biceps brachii (supination)</td>
<td>• Pronator teres (pronation)</td>
</tr>
<tr>
<td></td>
<td>• Supinator (supination)*</td>
<td>• Pronator quadratus (pronation)</td>
</tr>
<tr>
<td><strong>Flexed wrist</strong></td>
<td>• Flexor carpi radialis</td>
<td>• Flexor digitorum profundus</td>
</tr>
<tr>
<td></td>
<td>• Flexor carpi ulnaris</td>
<td>• Flexor pollicis longus</td>
</tr>
<tr>
<td></td>
<td>• Flexor digitorum superficialis (sublimis)</td>
<td>• Palmaris longus*</td>
</tr>
<tr>
<td><strong>Flexed fingers</strong></td>
<td>• Flexor digitorum superficialis (sublimis)</td>
<td>• Lumbricals</td>
</tr>
<tr>
<td></td>
<td>• Flexor digitorum profundus</td>
<td>• Interossei</td>
</tr>
<tr>
<td><strong>Thumb in palm</strong></td>
<td>• Flexor pollicis longus</td>
<td>• Adductor pollicis</td>
</tr>
<tr>
<td></td>
<td>• Flexor pollicis brevis</td>
<td>• Abductor pollicis brevis*</td>
</tr>
<tr>
<td></td>
<td>• Opponens pollicis</td>
<td></td>
</tr>
<tr>
<td><strong>Intrinsic plus hand</strong></td>
<td>• Lumbricals</td>
<td>• Abductor digiti minimi*</td>
</tr>
<tr>
<td></td>
<td>• Interossei</td>
<td>• Flexor digiti minimi*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Posture</th>
<th>Muscles</th>
<th>[Lower limb spasticity]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Flexed ankle</strong></td>
<td>• Gastrocnemius</td>
<td>• Flexor hallucis longus</td>
</tr>
<tr>
<td></td>
<td>• Soleus</td>
<td>• Flexor digitorum longus</td>
</tr>
<tr>
<td></td>
<td>• Tibialis posterior</td>
<td>• Fibularis longus*</td>
</tr>
<tr>
<td><strong>Flexed toes</strong></td>
<td>• Flexor hallucis longus</td>
<td>• Flexor digitorum brevis*</td>
</tr>
<tr>
<td></td>
<td>• Flexor hallucis brevis*</td>
<td>• Flexor digiti minimi brevis*</td>
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<tr>
<td></td>
<td>• Flexor digitorum longus</td>
<td>• Fibularis longus*</td>
</tr>
<tr>
<td><strong>Inverted/supinated foot</strong></td>
<td>• Tibialis posterior</td>
<td>• Flexor hallucis longus</td>
</tr>
<tr>
<td></td>
<td>• Tibialis anterior*</td>
<td>• Flexor digitorum longus</td>
</tr>
<tr>
<td><strong>Equinovarus foot</strong></td>
<td>• Gastrocnemius</td>
<td>• Tibialis posterior</td>
</tr>
<tr>
<td></td>
<td>• Soleus</td>
<td></td>
</tr>
</tbody>
</table>

*For anatomical reference only.

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

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

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

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

- 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)

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 the accompanying BOTOX® full Prescribing Information, including Boxed Warning and Medication Guide.
## 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
- 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

## 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

This information provides suggestions and considerations for injection training but does not constitute professional medical advice.
Ensure your office is ready for your first BOTOX® injections

- Set up an Allergan® account for BOTOX® ordering (1-800-811-4148)
- Ensure there is a refrigerator to store BOTOX® vials
- Make sure materials have been ordered:
  - 100- and/or 200-Unit BOTOX® vials
  - 25- to 30-gauge needles for superficial muscles
  - 22-gauge needles for deeper muscles
  - 21-gauge, 2-inch needles for reconstitution
  - 1-mL syringes for injections
  - Appropriately sized syringes for reconstitution
  - Single-use vials of preservative-free, 0.9% sodium chloride (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)

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

Please see additional Important Safety Information about BOTOX® on following pages.
Consider using guidance techniques for BOTOX® injections

**EMG/E-Stim®**
- 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**
- 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
Main muscles involved in Adult Upper Limb Spasticity

Muscles listed in purple are those approved for BOTOX® injection

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

**IMPORTANT SAFETY INFORMATION (continued)**

**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 about BOTOX® on following pages.

---

**Biceps Brachii**
60-200 Units divided in 2-4 sites

**Brachialis**
30-50 Units divided in 1-2 sites

**Brachioradialis**
45-75 Units divided in 1-2 sites

**Extensor Carpi Radialis Longus***

**Flexor Carpi Radialis**
12.5-50 Units in 1 site

**Flexor Carpi Ulnaris**
12.5-50 Units in 1 site

**Flexor Pollicis Longus**
20 Units in 1 site

**Flexor Pollicis Brevis**
5-25 Units in 1 site

**Adductor Pollicis**
20 Units in 1 site

**Pronator Teres**
15-25 Units in 1 site

**Pronator Quadratus**
10-50 Units in 1 site

**Opponens Pollicis**
5-25 Units in 1 site

**Flexor Digitorum Profundus**
30-50 Units in 1 site

**Flexor Digitorum Superficialis**
30-50 Units in 1 site

**Interossei**
5-10 Units in 1 site per muscle

**Lumbricals**
5-10 Units in 1 site per muscle

---

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

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

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

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 about BOTOX® on following pages.
Biceps brachii (continued)

Injection considerations

- 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)

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

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

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

**Muscle action**

- 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
Brachialis (continued)

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

*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 about BOTOX® on following pages.
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

**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).

**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 about BOTOX® on following pages.
Brachioradialis

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

**Muscle action**

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
Brachioradialis (continued)

Localization

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)
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 about BOTOX® on following pages.
Brachioradialis (continued)

Injection considerations

Consider spacing the injection sites 2 cm apart and inserting the needle perpendicular to the muscle.

- 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.

Dots represent injection sites.

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

Human Albumin and Transmission of Viral Diseases

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

Please see additional Important Safety Information about BOTOX® on following pages.
Notes
**Pronator teres**

- **BOTOX® dose:** 15 Units to 25 Units in 1 site

**Muscle action**

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)**

**ADVERSE REACTIONS**

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

**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.
Pronator teres (continued)

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.

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 about BOTOX® on following pages.
Pronator teres (continued)

Injection considerations

- 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)
ADVERSE REACTIONS (continued)

Postmarketing Experience

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

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

Please see additional Important Safety Information about BOTOX® on following pages.
**Flexor carpi radialis**

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

**Muscle action**

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)
- 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)10,*

*For anatomical reference only.
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.
Injection considerations

- 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)
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 about BOTOX® on following pages.
Flexor carpi ulnaris

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

**Muscle action**

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.*
Flexor carpi ulnaris (continued)

Localization

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.

Cross-sectional anatomy: middle forearm

*For anatomical reference only.

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

Serious Adverse Reactions With Unapproved Use

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

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

**Hypersensitivity Reactions**

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

Please see additional Important Safety Information about BOTOX® on following pages.
Flexor digitorum superficialis (sublimis)

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

**Muscle action**
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)

**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)

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.

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 about BOTOX® on following pages.
Injection considerations

- 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)

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 about BOTOX® on following pages.
Notes
Flexor digitorum profundus

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

**Muscle action**

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.

**Proximal attachment**

Upper three-quarters of the anterior and medial surfaces of the ulna.

**Distal attachments**

Palmar surfaces of the bases of the distal phalanges.

**Other muscles involved in finger flexion**

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

*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 about BOTOX® on following pages.
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)**

**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 about BOTOX® on following pages.
Notes
Flexor pollicis longus

- **BOTOX® dose:** 20 Units (1 site)

**Muscle action**
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)
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)**

**Human Albumin and Transmission of Viral Diseases**

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

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

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.

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.

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 about BOTOX® on following pages.
Pronator quadratus

- **BOTOX® dose**: 10 Units to 50 Units in 1 site

**Muscle action**

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 muscles involved in forearm pronation**

- 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 about BOTOX® on following pages.
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.
Pronator quadratus (continued)

Injection considerations

- 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)
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 about BOTOX® on following pages.
Flexor pollicis brevis

- **BOTOX® dose:** 5 Units to 25 Units in 1 site

**Muscle action**

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
Flexor pollicis brevis (continued)

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.

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 the accompanying BOTOX® full Prescribing Information, including Boxed Warning and Medication Guide.
Injection considerations

- Advise the patient that this may be a painful injection
  - Consider using a 30-gauge needle
  - Consider utilizing a distractive strategy during injection (e.g., 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)

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 about BOTOX® on following pages.
Opponens pollicis

- **BOTOX® dose:** 5 Units to 25 Units in 1 site

**Muscle action**

Flexes the metacarpal bone of the thumb

**Proximal attachments**
- Flexor retinaculum and trapezium

**Distal attachment**
- Shaft of the first metacarpal bone

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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 about BOTOX® on following pages.
Opponens pollicis (continued)

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.

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

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

Please see additional Important Safety Information about BOTOX® on following pages.
Opponens pollicis (continued)

**Injection considerations**

- 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

**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*).

**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 about BOTOX® on following pages.*
Adductor pollicis

- **BOTOX® dose:** 20 Units (1 site)

**Muscle action**
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

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**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.
Adductor pollicis (continued)

Localization

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.

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 about BOTOX® on following pages.
Adductor pollicis (continued)

Injection considerations

- 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)

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

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

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

**Muscle action**

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)
Lumbricals (continued)

Localization

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.

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.

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.

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 about BOTOX® on following pages.
In the image, the text discusses the considerations for injecting the lumbricals and interossei muscles. Key points include:

- 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 (e.g., 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.
  - Using 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.
ADVERSE REACTIONS (continued)

Postmarketing Experience

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

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

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

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

**Muscle action**

**Dorsal group:** Abducts the 2nd, 3rd, and 4th digits toward a longitudinal axis that passes through the 3rd digit. Also contributes to MCP flexion

**Palmar group:** Adducts the 2nd, 4th, and 5th digits toward the longitudinal axis of the 3rd digit. Also contributes strongly to MCP flexion and weak IP extension

**Proximal attachments**

- **Dorsal group:** Adjacent sides of the metacarpals
- **Palmar group:** 2nd, 4th, and 5th metacarpals

**Distal attachments**

- **Dorsal group:** Proximal phalanges of 2nd through 4th digits
- **Palmar group:** Proximal phalanges of the respective digits

**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 about BOTOX® on following pages.

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Interossei (continued)

Localization

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).

1st palmar: Just ulnar to 2nd metacarpal
2nd palmar: Just radial to 4th metacarpal
3rd palmar: Just radial to 5th metacarpal

1st dorsal: Just radial to 2nd metacarpal
2nd dorsal: Just radial to 3rd metacarpal
3rd dorsal: Just ulnar to 3rd metacarpal
4th dorsal: Just ulnar to 4th metacarpal

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

Cross-sectional anatomy: hand (palmar arch)
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)

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 the accompanying BOTOX® full Prescribing Information, including Boxed Warning and Medication Guide.
Main muscles involved in Adult Lower Limb Spasticity

Muscles listed in purple are those approved for BOTOX® injection

Anterior view

- **Gastrocnemius (lateral head)**
  - 75 Units divided in 3 sites

- **Gastrocnemius (medial head)**
  - 75 Units divided in 3 sites

- **Tibialis Anterior**

- **Soleus (hidden)**
  - 75 Units divided in 3 sites

- **Extensor Hallucis Longus (hidden)**

- **Extensor Digitorum Longus**

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

IMPORTANT SAFETY INFORMATION (continued)

CONTRAINDICATIONS

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

Please see additional Important Safety Information about BOTOX® on following pages.
Approved Muscles Involved in Common Postures

**Ankle Flexors**
- Gastrocnemius
- Soleus
- Tibialis Posterior

**Toe Flexors**
- Flexor Digitorum Longus
- Flexor Hallucis Longus

---

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

**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*"
Gastrocnemius

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

**Muscle action**

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.
Gastrocnemius (continued)

Localization

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

Cross-sectional anatomy: midcalf

IMPORTANT SAFETY INFORMATION (continued)
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 about BOTOX® on following pages.
Gastrocnemius (continued)

Injection considerations

- 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)
WARNINGS AND PRECAUTIONS
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 about BOTOX® on following pages.
Notes
Soleus

- **BOTOX® dose:** 75 Units divided in 3 sites

**Muscle action**

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.*
Soleus (continued)

Medial or lateral approach is midway to two-thirds the distance from heel to popliteal crease. Can also be approached through the gastrocnemius.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Serious Adverse Reactions With Unapproved Use (continued)
In several of the cases, patients had pre-existing dysphagia or other significant disabilities. There is insufficient information to identify factors associated with an increased risk for adverse reactions associated with the unapproved uses of BOTOX®. The safety and effectiveness of BOTOX® for unapproved uses have not been established.

Please see additional Important Safety Information about BOTOX® on following pages.
Soleus (continued)

Injection considerations

- 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

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

Hypersensitivity Reactions

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

Increased Risk of Clinically Significant Effects With Preexisting Neuromuscular Disorders

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

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

- **BOTOX® dose:** 75 Units divided in 3 sites

**Muscle action**

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
- Flexor hallucis longus
- Fibularis longus (plantarflexion only)*
- Tibialis anterior (foot inversion only)*

*For anatomical reference only.
Tibialis posterior (continued)

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).

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 about BOTOX® on following pages.
Tibialis posterior (continued)

Injection considerations

- Position the patient supine with his/her 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)

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 about BOTOX® on following pages.
Flexor hallucis longus

- **BOTOX® dose:** 50 Units divided in 2 sites

**Muscle action**
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
- Flexor digitorum longus
- Fibularis longus (plantarflexion only)*
- Tibialis anterior (foot inversion only)*

*For anatomical reference only.
Take a posterior/lateral at one-third the distance from heel to popliteal crease and posterior to the fibula.

Achilles tendon (hidden)*

*For anatomical reference only.

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 about BOTOX® on following pages.
Flexor hallucis longus (continued)

- 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
Human Albumin and Transmission of Viral Diseases

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

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

- **BOTOX® dose:** 50 Units divided in 2 sites

**Muscle action**

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
- Flexor hallucis longus
- Fibularis longus (plantarflexion only)*
- Tibialis anterior (foot inversion only)*

*For anatomical reference only.
Cross-sectional anatomy: distal calf

Localisation

Midbelly is located one-third to one-half the distance from heel to popliteal crease immediately posterior to tibia.

Flexor digitorum longus (continued)

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.

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 about BOTOX® on following pages.
Flexor digitorum longus (continued)

Injection considerations

- 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 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 about BOTOX® on following pages.
Dilution and reconstitution

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

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<th>Dose per 1 mL syringe</th>
<th>Dose per 0.1 mL</th>
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*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
Reconstitution procedures

1. 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.

2. 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.

3. 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.

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

5. 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

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

Please see additional Important Safety Information about BOTOX® on following pages.
Resources available to help your patients access BOTOX®

Education

- An informational brochure is available for patients/caregivers to educate them about Adult Spasticity and BOTOX®
- In-office materials are available to help patients/caregivers understand what to expect with BOTOX® treatment

Patient Support

- The Find a BOTOX® Specialist tool helps patients seeking treatment find providers and practices
- Create and customize your profile with multiple options (e.g., 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

Sign up at BOTOXMedical.com

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 about BOTOX® on following pages.
Resources available to help clinicians and office staff

Peer-to-peer training

• Several different programs are available for BOTOX® injection training
  – Expert-On-Demand is a 30- to 45-minute video conference with an experienced BOTOX® injector who can address specific training needs
• Anatomical models offer the ability to practice localizing and injecting muscles for Adult Spasticity treatment

Contact your Allergan® Account Specialist to learn more about our training offerings

BOTOXAcademy.com

• Videos and e-lectures on: injection technique, functional anatomy, muscle localization, and reconstitution
• Downloadable patient education and office materials

Register at BOTOXAcademy.com to access these resources and more
References:


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 the accompanying BOTOX® full Prescribing Information, including Boxed Warning and Medication Guide.
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 AND RESOURCES
For injection training opportunities: Contact your Allergan® Account Specialist
For injection and reconstitution videos, plus downloadable patient education and more: BOTOXAcademy.com

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