BOTOX®
onabotulinumtoxinA injection

Injection Workbook for **Chronic Migraine**

Guidance for identifying appropriate BOTOX® candidates, the injection procedure, and discussing treatment with patients

Enhanced Learning!

This workbook features QR codes throughout that link to videos demonstrating anatomy and injection techniques relevant to specific injection sites. Scan this QR code to watch the injection administration video in its entirety.

INDICATION

Chronic Migraine

BOTOX® (onabotulinumtoxinA) for injection is indicated for the prophylaxis of headaches in adult patients with chronic migraine (≥15 days per month with headache lasting 4 hours a day or longer).

Limitations of Use

Safety and effectiveness have not been established for the prophylaxis of episodic migraine (14 headache days or fewer per month) in 7 placebo-controlled studies.

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® on the following pages.

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

Introduction

Take the next step in your education with this comprehensive guide to BOTOX® injections. Review Chronic Migraine diagnosis, anatomical assessment, injection technique, patient dialogue, and more.

Table of contents

*__COMPEL__ = **C**hronic Migraine **O**nabotulinu**M**toxinA **P**rolonged **E**fficacy open **L**abel.
†__CGRP mAb__ = **C**alcitonin **G**ene-**R**elated **P**eptide **m**onoclonal **A**nti**b**ody.
‡__PREEMPT__ = **P**hase 3 **RE**search **E**valuating **M**igraine **P**rophylaxis **T**herapy.

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 the following pages.

Anterior Injections

Posterior Injections

Insurance and Resources

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

No definitive serious adverse event reports of distant spread of toxin effect associated with BOTOX for chronic migraine at the labeled dose have been reported.

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

Notes

Migraine is a common, disabling primary headache disorder[1,*]

~**15%** of the US population reports having migraine or severe headaches[2,†]

~**75%** of patients did not receive a Chronic Migraine diagnosis[3,‡]

Migraine is the **2nd leading cause** of years lived with disability[4,§]

A severe migraine attack is ranked within the same disability category as **active psychosis** or **quadriplegia**[5]

The **American Headache Society** identifies the goals of a preventive therapy as reducing attack frequency, severity, duration, and disability[6]

*As defined in the ICHD-3.
†According to the 2015 National Health Interview Survey.[2]
‡Based on a study of Chronic Migraine patients (N = 512) who had sought evaluation from a healthcare professional (specialist or non-specialist) for their headaches.[3]
§After back pain, according to the 2016 Global Burden of Diseases, Injuries, and Risk Factors Study.[4]

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

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

Diagnosing migraine with and without aura[1]

Diagnostic Criteria

Migraine Without Aura

A. At least 5 attacks fulfilling criteria B-D

B. Headache attacks lasting 4-72 hours (when untreated or unsuccessfully treated)

C. Headache has at least 2 of the following 4 characteristics:

1. Unilateral location
2. Pulsating quality
3. Moderate or severe pain intensity
4. Aggravation with physical activity

D. During headache at least 1 of the following:

1. Nausea and/or vomiting
2. Photophobia and phonophobia

E. Not better accounted for by another ICHD-3 diagnosis

Migraine With Aura

A. At least 2 attacks fulfilling criteria B and C

B. One or more of the following fully reversible aura symptoms:

1. Visual
2. Sensory
3. Speech and/or language
4. Motor
5. Brainstem
6. Retinal

C. At least 3 of the following 6 characteristics:

1. At least 1 aura symptom spreads gradually over ≥ 5 minutes
2. Two or more aura symptoms occur in succession
3. Each individual aura symptom lasts 5-60 minutes
4. At least 1 aura symptom is unilateral
5. At least 1 aura symptom is positive
6. The aura is accompanied, or followed within 60 minutes, by headache

D. Not better accounted for by another ICHD-3 diagnosis

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 the following pages.

Chronic Migraine is a progressive disease with well-defined diagnosis criteria[1,7]

Chronic Migraine is defined by:

≥ 15 headache days per month

≥ 8 headache days are migraine days

≥ 4 hours of headache per day

Important considerations[1,8]

- Count days when a headache lasted fewer than 4 hours due to a successful acute treatment
- Criteria must be met for 3 months per the ICHD-3
  - Patients receive a diagnosis according to the headache frequency that they currently present or that they have presented within the last year

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 the following pages.

A disease with distinct characteristics[1,7,9]

	CHRONIC MIGRAINE	EPISODIC MIGRAINE
Definition	≥ 15 headache days per month; ≥ 8 headache days are associated with migraine; ≥ 4 hours of headache per day	≤ 14 headache days per month
Average headache duration per attack (without medication)[10,*]	65.1 hours	38.8 hours
MIDAS[†] Grade IV (≥ 21)[10,*]	79.1%	23.6%
Visit emergency room[10,*]	9.0% per year	5.4% per year
Anxiety[11,‡,§]	30.2%	18.8%
Depression[11,‡,§]	41.2%	25.6%
Obesity[11,‡,§]	25.5%	21.0%

KNOWN RISK FACTORS FOR PROGRESSION[12-15]

Nonmodifiable

- Structural changes in the brain
- Age
- Low education
- Low economic status
- Head trauma
- Sex
- Stress
- Chronic pain
- Depression/anxiety

Modifiable

- Attack frequency
- Obesity
- Medication overuse
- Inadequate symptomatic therapy
- Caffeine overuse
- Snoring
- Sleep apnea

*According to the International Burden of Migraine Study, a cross-sectional, Web-based observational survey; Chronic Migraine: n = 499; Episodic Migraine: n = 8227.[10]
[†]MIDAS = The Migraine Disability Assessment Test.
[‡]According to the American Migraine Prevalence and Prevention Study (AMPP), a longitudinal, population-based survey; Chronic Migraine: n = 655; Episodic Migraine: n = 11,249.[11]
[§]Incidence of comorbidity.

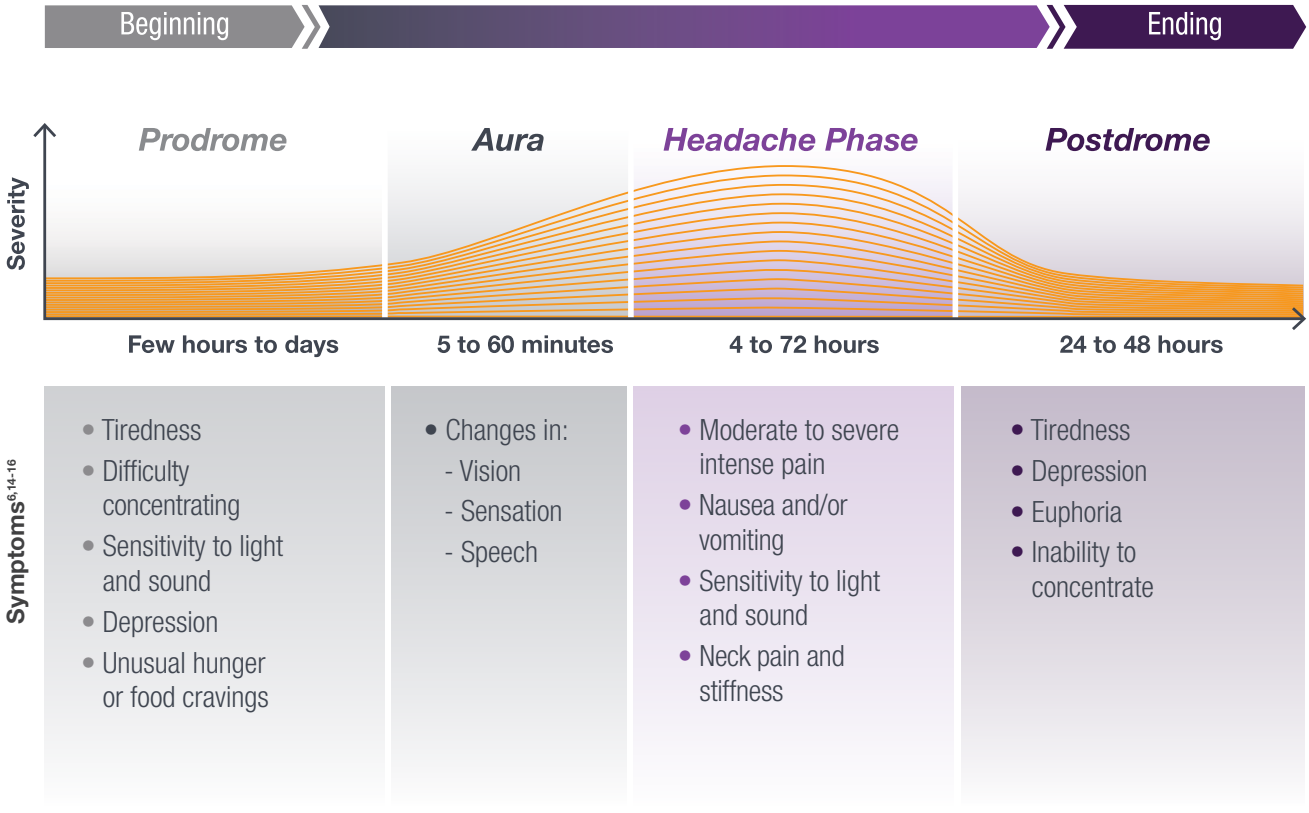
IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

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 the following pages.

The nature of migraine attacks may obscure a patient's true headache count and lead to a misdiagnosis

Phases of a migraine attack[1,9,16,17]



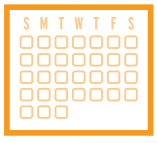
Patients may not count dull headaches that may accompany postdrome as part of their headache day tally because they are less severe. This could lead to underdiagnosis of Chronic Migraine.

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 the following pages.

The importance of a specific Chronic Migraine diagnosis

Possible reasons clinicians may misdiagnose:



Patients did not account for all their headache days **accurately**

Classifying some migraine attacks as tension type, leading to a diagnosis of **mixed headache disorder**[18]

Not accounting for headache features, leading to an **underdiagnosis** of headache days

Did You Know

"Patients may leave out milder headache days. To uncover their true disease burden, consider asking a patient, 'How many days per month do you NOT have a headache?'"

- US Headache Expert

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 the following pages.

A structured approach to dialogue can help facilitate an appropriate diagnosis

Getting to an appropriate diagnosis

1 UNCOVER TRUE HEADACHE FREQUENCY

Determine crystal clear (headache-free) days	Encourage patients to include postdrome as part of their headache day count

2 ASK TO UNDERSTAND DISABILITY

"How does your headache impact your life in work, family, and social settings?"	"If you didn't have any responsibilities, what would you be doing on a migraine day?"

3 DISTINGUISH MIGRAINE FEATURES

Type of migraine	Attack symptoms and if they are alleviated with acute medicine

4 CLEARLY COMMUNICATE A DIAGNOSIS

"You have Chronic Migraine, and you are not alone."	"I believe that you have Chronic Migraine, and it is having a significant impact on your life."

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*.

Chronic Migraine
The most frequently reported adverse reactions following injection of BOTOX for chronic migraine vs placebo include, respectively, neck pain (9% vs 3%); headache (5% vs 3%); eyelid ptosis (4% vs <1%); migraine (4% vs 3%); muscular weakness (4% vs <1%); musculoskeletal stiffness (4% vs 1%); bronchitis (3% vs 2%); injection-site pain (3% vs 2%); musculoskeletal pain (3% vs 1%); myalgia (3% vs 1%); facial paresis (2% vs 0%); hypertension (2% vs 1%); and muscle spasms (2% vs 1%).

Severe worsening of migraine requiring hospitalization occurred in approximately 1% of BOTOX treated patients in study 1 and study 2, usually within the first week after treatment, compared to 0.3% of placebo-treated patients.

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

The right communication style can help validate the patient's experience[19]

The LEAP approach is one way to help clinicians alleviate migraine disease stigma to achieve a more open, productive dialogue

ACTION	METHOD	SAMPLE DIALOGUE
Listen	• Employ active listening • Use a combination of open- and closed-ended questions • Elicit patient's agenda	"What brings you here today?"
Empathize	• Validate patient's experiences • Demonstrate concern for patient's distress	"I can see how it upsets you when people say that your migraine is just another headache."
Accept	• Be aware of how stigma can affect treatment • Accept the reality of the disease	"Chronic Migraine is a debilitating disease that is often misunderstood."
Partner	• Educate • Set realistic goals together • Empower patient to take responsibility for their disease management	"I understand that you want these symptoms to go away. There is no cure for Chronic Migraine yet, but if you could reduce the number of headache days, would that help?"

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 the following pages.

A comprehensive Chronic Migraine management plan may be needed

Considerations for a multidisciplinary approach in Chronic Migraine[20-22]

MANAGE MEDICATIONS

- Review medical history to determine which treatments the patient has tried in the past
- Ensure adequate prevention
  - Preventive medications include antidepressants, antiepileptics, beta-blockers, botulinum toxin, oral CGRP receptor antagonist, subcutaneous CGRP mAbs, and IV CGRP mAb*,†
- Assess acute medication use

CHANGE BEHAVIORS

- Biofeedback therapy
- Cognitive therapy

*__CGRP mAb__ = **C**alcitonin **G**ene-**R**elated **P**eptide **m**onoclonal **A**nti**b**ody.
†Not all products within each category are FDA approved for the prevention of migraine or Chronic Migraine.

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

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

ADJUST LIFESTYLES[20,21]

- Maintain a healthy diet
- Exercise regularly
- Limit caffeine
- Manage stress
- Attain a regular sleep pattern
- Stop smoking

ADDRESS COMORBIDITIES[20,21]

- Allergies/hay fever
- Sinusitis
- Depression
- High cholesterol
- High blood pressure
- Arthritis
- Chronic pain
- Anxiety
- Obesity

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

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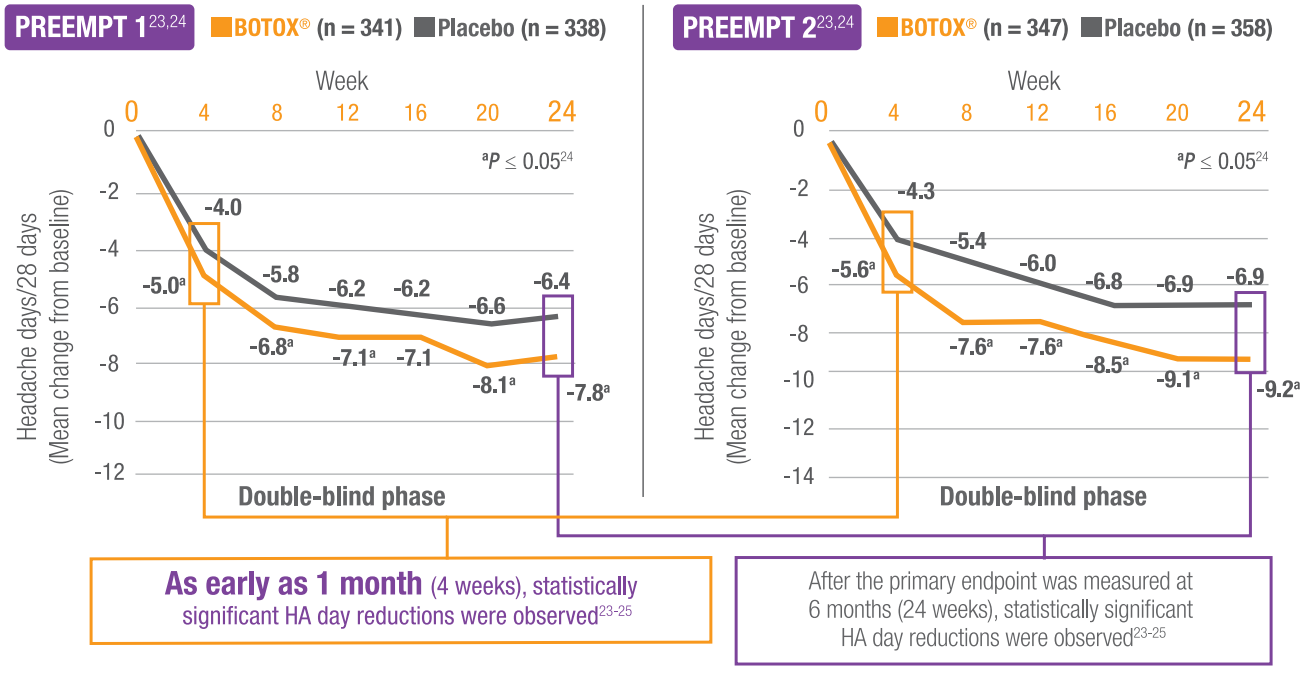
Notes

Proven prevention in Chronic Migraine with significant headache (HA) day reductions

8 to 9 fewer headache days per month from baseline at primary time point of week 24 (vs 6 to 7 with placebo)[23,24]

PREEMPT* 1 & 2



As early as 1 month (4 weeks), statistically significant HA day reductions were observed[23-25]

After the primary endpoint was measured at 6 months (24 weeks), statistically significant HA day reductions were observed[23-25]

- 8 to 9 fewer migraine/probable migraine days per month at 24 weeks (vs 6 to 7 with placebo)[23,24] (secondary endpoint)
  - Efficacy analyses occurred every 4 weeks (28 days). Week 4 was the first pre-specified efficacy evaluation time point, and week 24 was the primary endpoint[24]

Study design: PREEMPT 1 and 2 were randomized, double-blind, placebo-controlled studies (N = 1384) across 122 sites. Subjects included adult Chronic Migraine patients not using any concurrent headache prophylaxis and, during a 28-day baseline period, had ≥ 15 headache days lasting 4 hours or more, with ≥ 50% being migraine/probable migraine. Patients were allowed to use acute headache treatments during the study. Primary time point was 24 weeks. A headache day was defined as a calendar day per 28 days with ≥ 4 continuous hours of headache.[23,24]

DIALOGUE TIP: "**BOTOX®** results were based on patients receiving **2 treatments, 12 weeks** apart. If you don't get treated every 12 weeks, then you may not get the **full benefit** of the treatment."[23]

*PREEMPT = **P**hase 3 **RE**search **E**valuating **M**igraine **P**rophylaxis **T**herapy.

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

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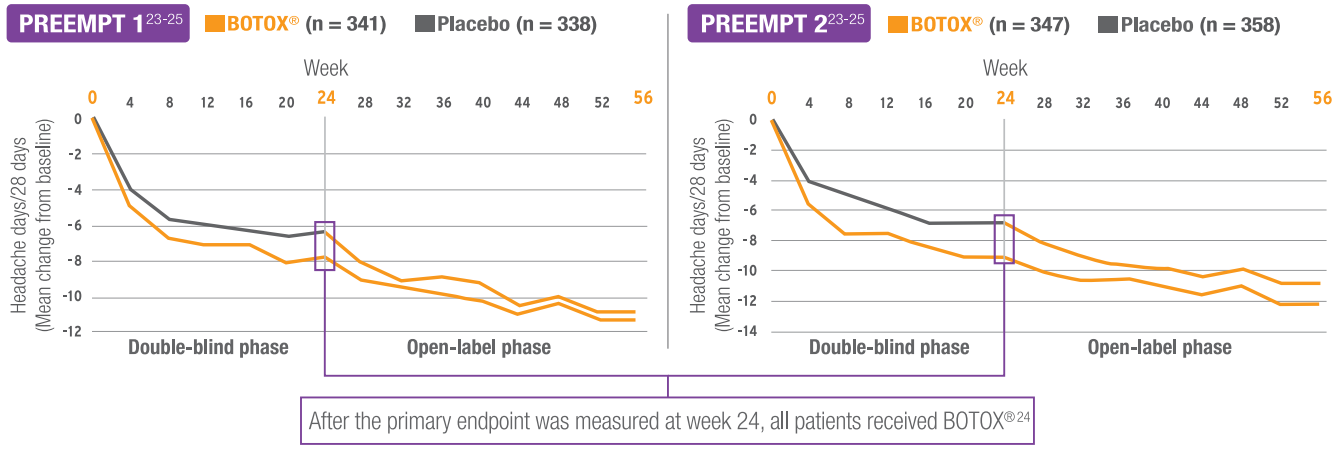
Starting with BOTOX® earlier showed results sooner[23-25]

Differences in headache day reductions were observed across 56 weeks in patients who received BOTOX® earlier† vs patients who received BOTOX® later[24,25,‡]

Open-Label Extension Phase of PREEMPT 1 & 2



Limitations: The open-label extension phase of the study was not blinded, not controlled, and included inherent self-selection bias for remaining in the trial. Results should be interpreted with these factors in mind and treatment differences cannot be regarded as statistically significant.

Study design: The open-label phase was an extension of the randomized, double-blind, placebo-controlled phases of PREEMPT 1 and 2. All patients received BOTOX® during this phase, which included 3 injection cycles.[24]

†Earlier = Patients who received BOTOX® in the 0- to 24-week double-blind and 24- to 56-week open-label phases.[24]
‡Later = Patients who received placebo in the 0- to 24-week double-blind phase and BOTOX® in the 24- to 56-week open-label phase.[24]

BOTOX® patient baseline data from PREEMPT trials showed notable headache burden[23,25]

	PREEMPT 1 (n = 341)	PREEMPT 2 (n = 347)
Headache days/month	20 days	19.9 days
Migraine/probable migraine days/month	19.1 days	19.2 days
Severe HIT-6§ scores	94.4%	92.5%

- Patients in PREEMPT trials were not allowed to use concurrent preventive medications[23,25]

§HIT-6 = Headache Impact Test-6.

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 the following pages.

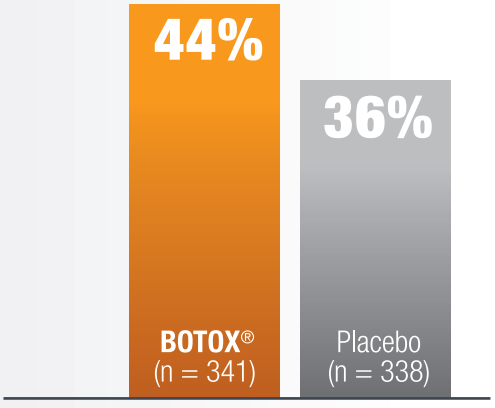
Responder rates for BOTOX® patients in PREEMPT* clinical trials (other endpoint)

Patients who achieved ≥ 50% reduction in headache days/month at week 24[24]

RESULTS

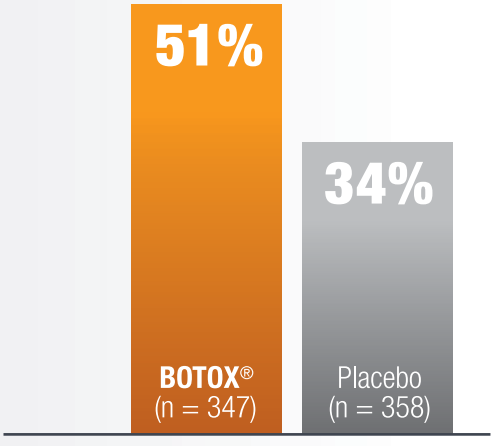
PREEMPT 1

Other endpoint: Percentage of patients with a ≥ 50% decrease from baseline in headache days (out of 100%)[24]



PREEMPT 2

Other endpoint: Percentage of patients with a ≥ 50% decrease from baseline in headache days (out of 100%)[24]



Limitation: The responder rate analyses were prespecified other endpoints in PREEMPT clinical trials and were not included as part of the hierarchical testing strategy or adjusted for multiplicity. Therefore, treatment differences cannot be regarded as statistically significant.[24]

See PREEMPT 1 and 2 Study Design on the following page.

*__PREEMPT__ = **P**hase 3 **RE**search **E**valuating **M**igraine **P**rophylaxis **T**herapy.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
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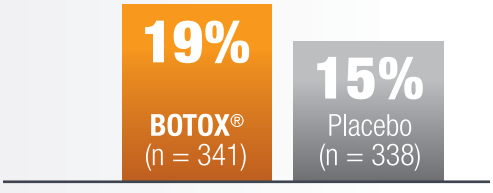
Please see additional Important Safety Information about BOTOX® on the following pages.

Patients who achieved ≥ 75% reduction in headache days/month at week 24[24]

RESULTS

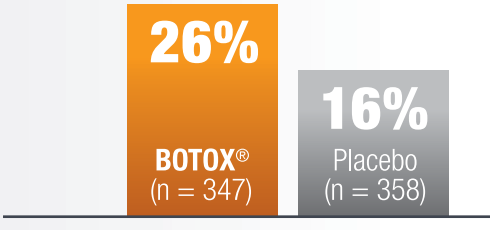
PREEMPT 1

Other endpoint: Percentage of patients with a ≥ 75% decrease from baseline in headache days (out of 100%)[24]



PREEMPT 2

Other endpoint: Percentage of patients with a ≥ 75% decrease from baseline in headache days (out of 100%)[24]



See Limitations of data on the previous page.

Study design: PREEMPT 1 and 2 were randomized, double-blind, placebo-controlled studies (N = 1384) across 122 sites. Subjects included adult Chronic Migraine patients not using any concurrent headache prophylaxis and, during a 28-day baseline period, had ≥ 15 headache days lasting 4 hours or more, with ≥ 50% being migraine/probable migraine. Patients were allowed to use acute headache treatments during the study. Primary time point was 24 weeks. A headache day was defined as a calendar day per 28 days with ≥ 4 continuous hours of headache.[23,24]

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 the following pages.

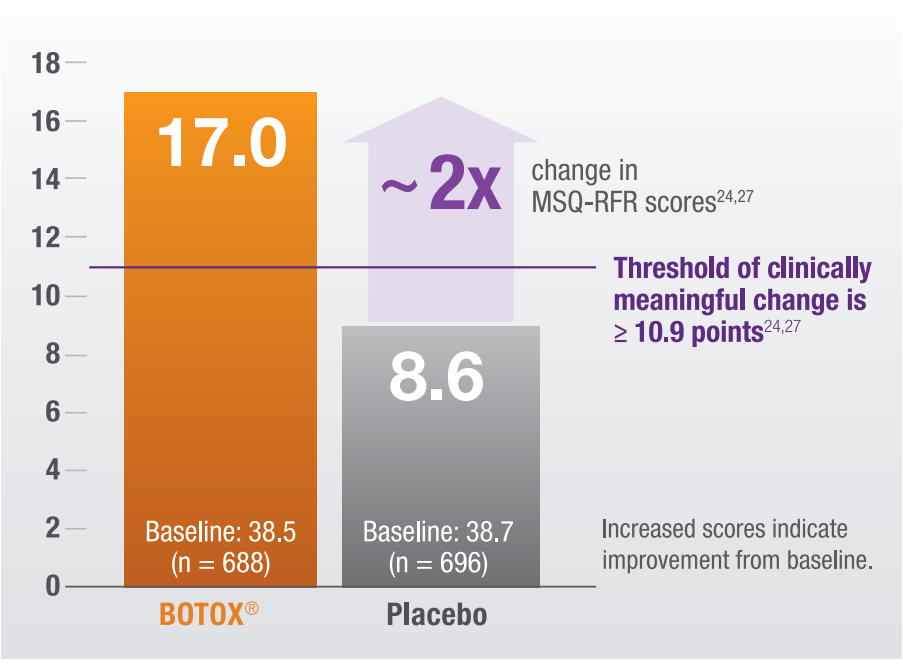
BOTOX® data beyond headache days (other endpoint)

MSQ-RFR* measures the degree to which performance of daily work and social activities is limited by migraine

Increased scores indicate improvement from baseline[26]

Pooled PREEMPT† 1[24] and PREEMPT 2[24]

Other endpoint: Change from baseline MSQ-RFR score at week 24



- ~ 2x change in MSQ-RFR scores from baseline vs placebo at 24 weeks[24,27]
- Threshold of clinically meaningful change (≥ 10.9 points) was met and surpassed at 17.0 points with BOTOX® vs 8.6 with placebo[24,27]

Limitations: MSQ-RFR change from baseline was a prespecified other endpoint in PREEMPT clinical trials and was not included as part of the hierarchical testing strategy or adjusted for multiplicity. Therefore, treatment differences cannot be regarded as statistically significant.[24,26]

MSQ-RFR v2.1 is a self-reported outcome instrument that measures the degree to which performance of daily activities is limited by migraine across these concepts[24,28-30]:
Work activities, relationships, focus, home activities, social activities, productivity, leisure activities, and energy levels.

The MSQ-RFR is a valuable tool for assessing the functional impact of migraine in clinical trials

- The MSQ version 2.1 is a 14-item patient-reported outcome instrument that measures the impact of migraine across 3 domains of a patient's migraine-related quality of life[24,28-30]:
  - RFR: 7 items assess how migraines limit daily social and work-related activities
  - Role function-preventive (RFP): 4 items assess how migraines prevent daily social and work-related activities
  - Emotional function (EF): 3 items assess emotions associated with migraine
- All 3 MSQ domains were assessed in the PREEMPT pivotal trials as prespecified other endpoints at week 24. This presentation focuses only on the RFR domain to assess participants' functional limitations attributable to migraine[24]
- Clinically meaningful change is considered ≥ 10.9 points from baseline[27]

*__MSQ-RFR__ = **M**igraine **S**pecific **Q**uality-of-Life Questionnaire **R**ole **F**unction-**R**estrictive.
†__PREEMPT__ = **P**hase 3 **RE**search **E**valuating **M**igraine **P**rophylaxis **T**herapy.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Dysphagia and Breathing Difficulties
Treatment with BOTOX and other botulinum toxin products can result in swallowing or breathing difficulties. Patients with preexisting swallowing or breathing difficulties may be more susceptible to these complications.

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

BOTOX® has an *established safety* profile

Most frequently reported adverse reactions[23,24,‡]

	BOTOX® (n = 687)	Placebo (n = 692)
Neck pain	9%	3%
Headache	5%	3%
Eyelid ptosis	4%	< 1%
Migraine	4%	3%
Muscular weakness	4%	< 1%
Musculoskeletal stiffness	4%	1%
Bronchitis	3%	2%
Injection-site pain	3%	2%
Musculoskeletal pain	3%	1%
Myalgia	3%	1%
Facial paresis	2%	0%
Hypertension	2%	1%
Muscle spasms	2%	1%

- 4% of BOTOX® patients discontinued pivotal trials due to adverse events (vs 1% for placebo)[23,24]
- Observed treatment-related adverse events were typically mild to moderate in severity[23,24]

Study design: PREEMPT 1 and 2 were randomized, double-blind, placebo-controlled studies (N = 1384) across 122 sites. Subjects included adult Chronic Migraine patients not using any concurrent headache prophylaxis and, during a 28-day baseline period, had ≥ 15 headache days lasting 4 hours or more, with ≥ 50% being migraine/probable migraine. Patients were allowed to use acute headache treatments during the study. Primary time point was 24 weeks. A headache day was defined as a calendar day per 28 days with ≥ 4 continuous hours of headache.[23,24]

DIALOGUE TIP: "The **most common BOTOX®** side effect was neck pain, which was experienced by 9 out of 100 patients (vs 3 out of 100 for placebo)."[23]

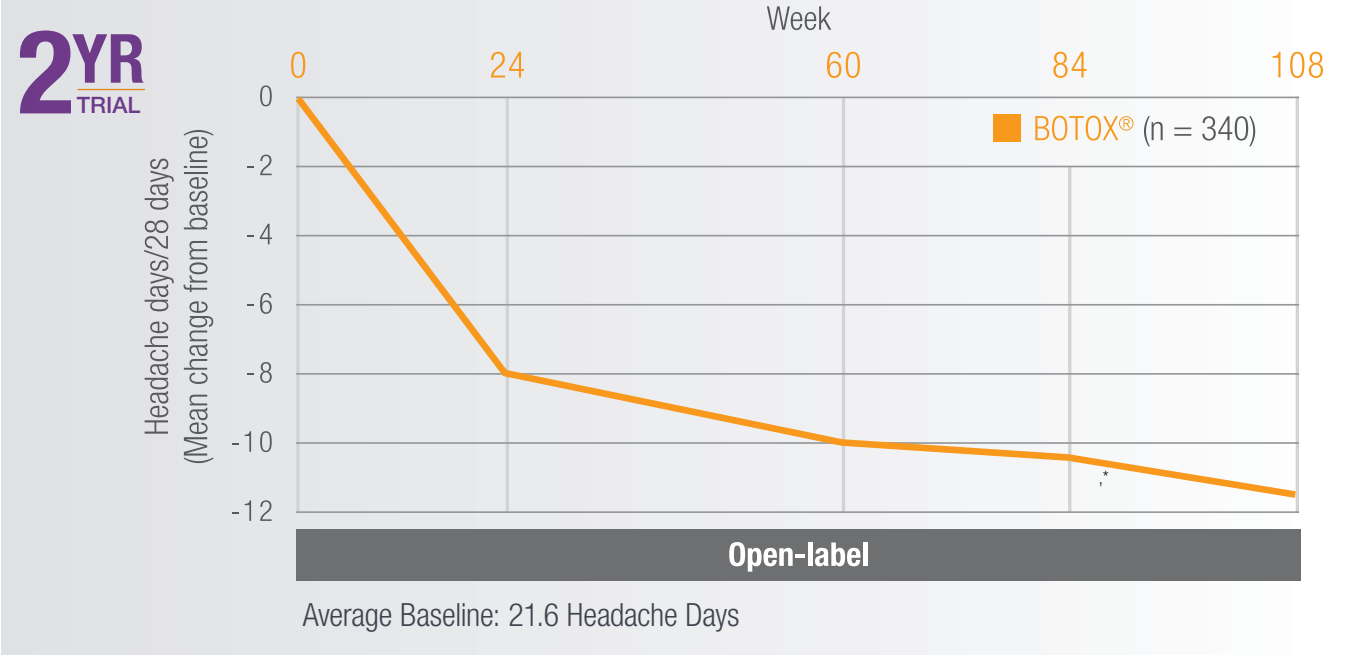
‡This does not cover all the possible serious side effects of BOTOX®. Please see the Important Safety Information, including Boxed Warning, and the full Prescribing Information and Medication Guide.

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

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

Long-term efficacy and safety were observed in the 2-year, open-label COMPEL* trial[24,31,32]

Results from COMPEL



- 8.0, 10.0, 10.5, and 11.6 fewer headache days per month from baseline at weeks 24, 60, 84, and 108, respectively[24]
- Data from the subgroup of patients who did not use an oral preventive medication anytime during the study are presented (n = 340)[24]
- Adverse events reported in COMPEL were: neck pain, eyelid ptosis, musculoskeletal stiffness, injection-site pain, headache, migraine, muscular weakness, facial paresis, and skin tightness[33]
- Adverse events from the COMPEL trial were consistent with those of the PREEMPT 1 and 2 trials[33]

Limitation: This nonrandomized, 2-year, open-label study has potential for bias due to no placebo or active comparator arm and low persistency rates given the duration[33]

- Considered the established efficacy and safety of BOTOX® for Chronic Migraine and determined it most appropriate to avoid giving patients placebo for the study duration because of the debilitating impact of the disease[33]

Study design: Open-label study (n = 716) in which enrolled patients received 155 Units of BOTOX® (31 sites in a fixed-site, fixed-dose protocol across 7 head/neck muscles over 12 weeks for 9 treatment cycles [108 weeks]). The primary endpoint was headache-day reduction at week 108. Missing headache days data were imputed using a modified last observation carried forward (mLOCF) methodology. 56% of patients enrolled received all 9 treatments, and 52% received all study treatments and attended the final follow-up visit.[33]

*__COMPEL__ = **C**hronic Migraine **O**nabotulinu**M**toxinA **P**rolonged **E**fficacy open **L**abel.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Human Albumin and Transmission of Viral Diseases
This product contains albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases and variant Creutzfeldt-Jakob disease (vCJD).

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

BOTOX® is PREDICTABLE with a legacy of ~15 years in Chronic Migraine[24,*]

There is only one BOTOX®

15 YEARS OF PATIENT IMPACT*

1+ million
Chronic Migraine patients treated
since FDA approval in 2010[24,†]

#1 prescribed
branded Chronic Migraine treatment[24,‡]

Most studied
preventive treatment
approved for Chronic Migraine[24,§]

*Since FDA approval in October 2010.[24]
†Cumulative data from October 2010 through June 2023.[24]
‡Based on IQVIA data from May 2018 to May 2024.[24]
§Based on a literature search for peer-reviewed publications on Chronic Migraine prevention and therapy.[24]

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

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

Notes

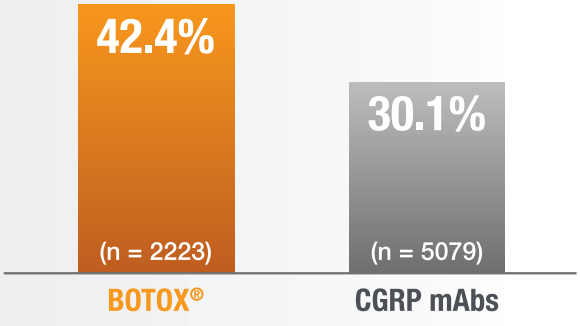
Real-world treatment persistence among adult Chronic Migraine patients based on a claims database analysis

Study 1: New initiators of Chronic Migraine preventive treatment: BOTOX® vs CGRP mAbs[24,*]

Proportion of patients persistent to therapy at 12 months

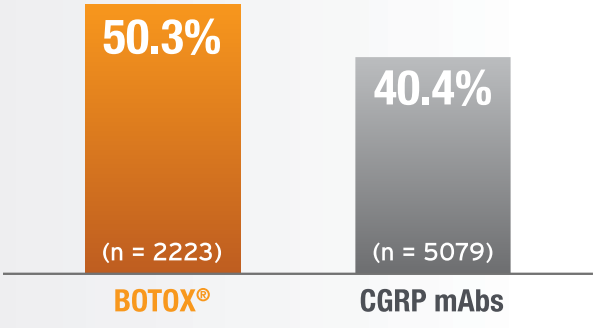
Persistence[24]:
No gap in claim for index medication
> **30 days**

Results for individual CGRP mAbs:
Aimovig® (erenumab) 30%, n = 1906
Ajovy® (fremanezumab) 25%, n = 1060
Emgality® (galcanezumab) 33%, n = 2090
Vyepti® (eptinezumab) 29%, n = 23



Persistence[24]:
No gap in claim for index medication
> **60 days (sensitivity analysis)**

Results for individual CGRP mAbs:
Aimovig® (erenumab) 40%, (n = 1906)
Ajovy® (fremanezumab) 34%, (n = 1060)
Emgality® (galcanezumab) 45%, (n = 2090)
Vyepti® (eptinezumab) 49%, (n = 23)



Limitations: Real-world persistence data should not be considered as a comparison of safety and efficacy. No conclusions regarding superiority to other treatments should be drawn.[34]
Impact of efficacy, safety, or other factors on persistence cannot be determined via administrative claims data.[34]
The presence of a claim for a filled prescription may not indicate actual use of the drug per its approved label.[34]
Healthcare claims data analyzed in this study may be subject to data errors (eg, miscoding).[34]
Due to the real-world nature of the data, patients may have been taking concomitant oral generic medications for migraine prophylaxis.[34]
The study design allowed for the addition of an index medication (BOTOX® or CGRP mAb) after the index date.[24]

Study Design for Study 1: This was a retrospective, observational, cohort study to assess persistence to therapy using patient-level data from the MarketScan Commercial Claims and Encounters, and Medicare Supplemental databases with an observational period from July 1, 2018 through December 31, 2022. This study included adults ≥ 18 years of age with a Chronic Migraine diagnosis prior to initiating BOTOX® or a CGRP mAb on or after January 1, 2019.[24]

Statistical Analysis: Persistence to therapy was adjusted for differences in the following baseline characteristics using logistic regression: age, gender, baseline health plan, region, Quan-Charlson Comorbidity Index, number of baseline acute and preventive medication classes, index year, number of migraine-related comorbidities, and index treatment provider.

*__CGRP mAb__ = **C**alcitonin **G**ene-**R**elated **P**eptide **m**onoclonal **A**nti**b**ody.

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*.

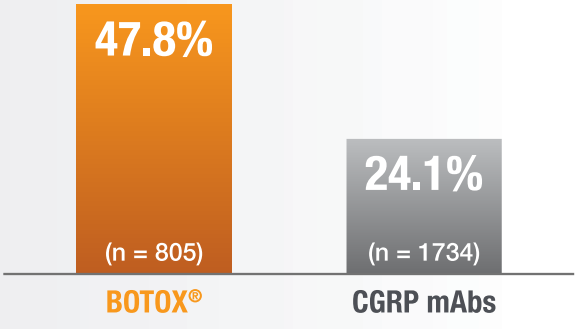
Please see additional Important Safety Information about BOTOX® on the following pages.

Study 2: Patterns among patients whose first branded preventive was a CGRP mAb then changed to BOTOX® vs another CGRP mAb[24]

Proportion of patients persistent to therapy at 12 months

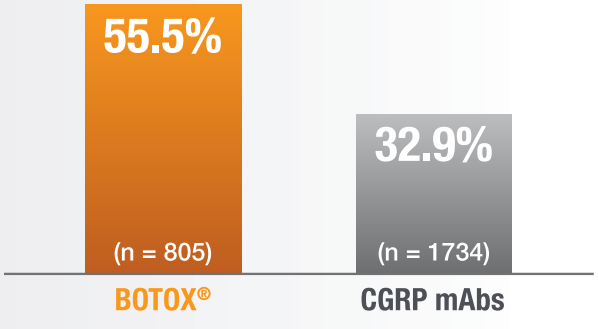
Persistence[24]:
No gap in claim for index medication
> **30 days**

Second-line CGRP mAb was measured as a class and not delineated by therapy.



Persistence[24]:
No gap in claim for index medication
> **60 days (sensitivity analysis)**

Second-line CGRP mAb was measured as a class and not delineated by therapy.



Limitations: Real-world persistence data should not be considered as a comparison of safety and efficacy. No conclusions regarding superiority to other treatments should be drawn.[34]
Impact of efficacy, safety, or other factors on persistence cannot be determined via administrative claims data.[34]
The presence of a claim for a filled prescription may not indicate actual use of the drug per its approved label.[34]
Healthcare claims data analyzed in this study may be subject to data errors (eg, miscoding).[34]
Due to the real-world nature of the data, patients may have been taking concomitant oral generic medications for migraine prophylaxis.[34]
The study design allowed for the addition of an index medication (BOTOX® or CGRP mAb) after the index date.[34]

Study Design for Study 2: This was a retrospective, observational, cohort study to assess persistence to therapy using patient-level data from the MarketScan Commercial Claims and Encounters, and Medicare Supplemental databases with an observational period from July 1, 2018 through December 31, 2022. This study included adults ≥ 18 years of age with a Chronic Migraine diagnosis prior to initiating either a CGRP mAb (eptinezumab, erenumab, galcanezumab, or fremanezumab) on or after January 1, 2019, and BOTOX® or a 2nd line CGRP mAb or after January 2, 2019.[24]

Statistical Analysis: Persistence to therapy was adjusted for differences in the following baseline characteristics using logistic regression: age, gender, baseline health plan, region, Quan-Charlson Comorbidity Index, number of baseline acute and preventive medication classes, index year, number of migraine-related comorbidities, and index treatment provider.

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Chronic Migraine
The most frequently reported adverse reactions following injection of BOTOX for chronic migraine vs placebo include, respectively, neck pain (9% vs 3%); headache (5% vs 3%); eyelid ptosis (4% vs <1%); migraine (4% vs 3%); muscular weakness (4% vs <1%); musculoskeletal stiffness (4% vs 1%); bronchitis (3% vs 2%); injection-site pain (3% vs 2%); musculoskeletal pain (3% vs 1%); myalgia (3% vs 1%); facial paresis (2% vs 0%); hypertension (2% vs 1%); and muscle spasms (2% vs 1%). Severe worsening of migraine requiring hospitalization occurred in approximately 1% of BOTOX treated patients in study 1 and study 2, usually within the first week after treatment, compared to 0.3% of placebo-treated patients.

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

Notes

BOTOX® is injected using the PRECISE PREEMPT* Protocol[23,35]

The only locally administered procedure delivered with purposeful fixed-site, fixed-dose injections into 7 head and neck muscle areas[23,35]

155-Unit dose[23]
(5 Units per injection site)

31 injection sites[23]
(across 7 specific head and neck muscle areas)

~10 minute procedure[24,†]

Retreatment every 12 weeks[23,‡]

Inhibits signaling

BOTOX® injections inhibit nerve and muscle communications by cleaving SNAP-25[23]

Choose BOTOX® for patients who you determine could benefit from a different mechanism of action (MoA).[23]

*__PREEMPT__ = **P**hase 3 **RE**search **E**valuating **M**igraine **P**rophylaxis **T**herapy.
†Based on the InCrowd Physician Survey to support BOTOX® for Chronic Migraine.
‡Retreatment after 24 weeks (2 treatments) should be determined per clinician's discretion.

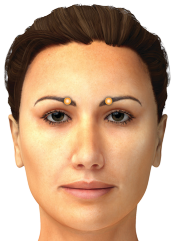
IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS (continued)
Postmarketing Experience
Adverse reactions that have been identified during postapproval use of BOTOX are discussed in greater detail in *Postmarketing Experience* (Section 6.3 of the Prescribing Information).

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.

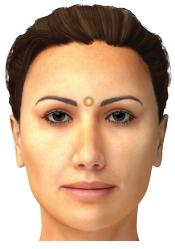
Please see additional Important Safety Information about BOTOX® on the following pages.

PREEMPT Protocol Injection Sites[23,25,‡]

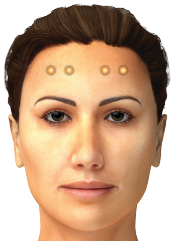
TOTAL DOSE: 155 Units divided between 31 sites across 7 specific head and neck muscle areas (5 Units at each site, fixed dose)[§]



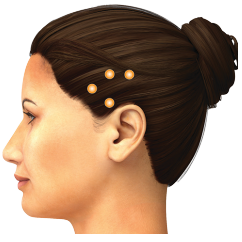
Corrugator
10 Units divided in 2 sites



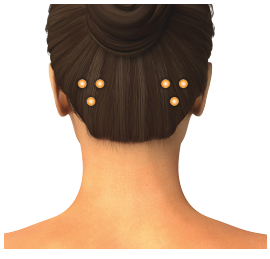
Procerus
5 Units in 1 site



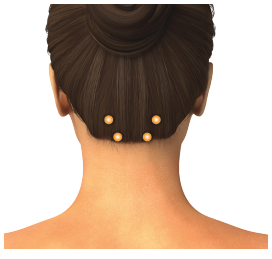
Frontalis
20 Units divided in 4 sites



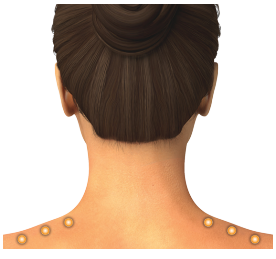
Temporalis
40 Units divided in 8 sites



Occipitalis
30 Units divided in 6 sites



Cervical paraspinals
20 Units divided in 4 sites



Trapezius
30 Units divided in 6 sites

Departures from the approved protocol may lead to efficacy results and adverse events different from those seen in the clinical trials.

The following section provides a step-by-step overview of the PREEMPT Protocol for BOTOX®.

[‡]Muscles and/or anatomical structures shown for anatomical reference only.
[§]Document and discard the 45-Unit wastage.

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

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

General injection considerations

SUPPLIES NEEDED

- One 200-Unit vial of BOTOX®
- One 21-gauge, 2-inch needle (for reconstitution)
- One 5-mL syringe
- Four 1-mL tuberculin syringes (for injection)
- At least four 30-gauge, 0.5-inch needles (for injection)
- One 10-mL single-use vial of preservative-free, 0.9% sodium chloride (saline)
- Alcohol swabs for cleaning the rubber stoppers on the saline and BOTOX® vials
- Gauze pads
- One pair of gloves
- Hazardous medical waste container
- For more information about reconstitution, please see page 40

STANDARD METHODS REGARDLESS OF AREA

- The volume of each injection will be 0.1 mL (equivalent to 5 Units)[7]
- Consider injecting in the most superficial aspect of the muscle
- Evaluate the anatomy, including relevant function, and the effects of treatment on these muscles
- Recognize unique anatomy, as no 2 patients are alike; focus on the muscle, not measurements, to adjust for individual anatomical variations
- Consider location, depth, and angle carefully, as the site of medication delivery may be different from the needle insertion point
  - Injection sites depicted in diagrams represent the delivery point of the medication

IMPORTANT SAFETY INFORMATION (continued)

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

Spread of Toxin Effect

See *Boxed Warning*.

No definitive serious adverse event reports of distant spread of toxin effect associated with BOTOX for chronic migraine at the labeled dose have been reported.

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

BEFORE INJECTION

- Verify the needle is securely fastened to the injection syringe
- Line up the bevel of the needle with the gradations on the syringe so the bevel is facing upward
  - This will help you more easily orient the bevel of the needle when injecting

DURING INJECTION

- Inject on 1 side first for bilateral injections, then proceed to the other side and repeat
- Consider changing needles frequently to reduce patient discomfort; consider using 1 needle per area or changing every 4 to 6 sites
- Inject with the bevel up, pointing away from the skin
- Consider holding the hub of the needle with 1 hand to ensure the needle does not twist
  - Push the plunger with the other hand to administer the medication
- Target the muscle—the needle should be inserted through the epidermis/dermis layer, which may feel more rigid when penetrated. The injection should be given just when there is a decrease in resistance, avoiding the periosteum. This decrease in resistance may be subdermal, not intramuscular

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

Lack of Interchangeability Between Botulinum Toxin Products

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

Serious Adverse Reactions With Unapproved Use

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

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

Patient assessment before injection*

Before any injections occur, patients should be evaluated for preexisting conditions that may be affected or exacerbated by treatment. If any conditions are found, the injector should inform and counsel the patient to help set expectations. Patients with preexisting conditions should be carefully assessed to determine if they are appropriate for injection.[36]

Pre-examination of the brow[36]

- ☑ **INSPECT:** Palpate the muscle to look for excessive soft tissue near the upper lid of the eye and lid drooping **(Figure 1)**.
- ☑ **ACTIVATE:** N/A
- ☑ **EXAMINE:** Ptosis may be a preexisting condition or may occur after BOTOX® treatment. Patients should be evaluated for both eyelid and brow ptosis. See the examples below in **Figures 2–5**.

Purposeful relaxation of the frontalis muscle by instructing patients to relax the frontalis muscle; frontalis compensatory activity and weakness will become evident.

Lid ptosis
Notice the asymmetry as a result of the drooping lid.[36,*]

Medial brow ptosis
Notice the medial brow depression and lateral brow elevation.[36,*]

Pseudoptosis
Notice the extra soft tissue around the eyelid and the misalignment of the lids.[36,*]

Full brow ptosis
Notice how the weakened frontalis muscle has depressed both the medial and lateral brow.[36,*]

*Muscles and/or anatomical structures shown for anatomical reference only.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Serious Adverse Reactions With Unapproved Use (continued)
The safety and effectiveness of BOTOX for unapproved uses have not been established.

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

Pre-examination of the forehead[36]

- ☑ **INSPECT:** Palpate the muscle to look for brow ptosis, possibly compensated by active frontalis muscles, of which the patient may be unaware.
- ☑ **ACTIVATE:** Ask the patient to activate the frontalis by raising and lowering the eyebrows **(Figure 6)**.
- ☑ **EXAMINE:** Observe the dynamic muscle activity and whether there is any compensatory mechanism keeping the eyelids open in the presence of brow weakness. See the examples below in **Figures 2–5**.

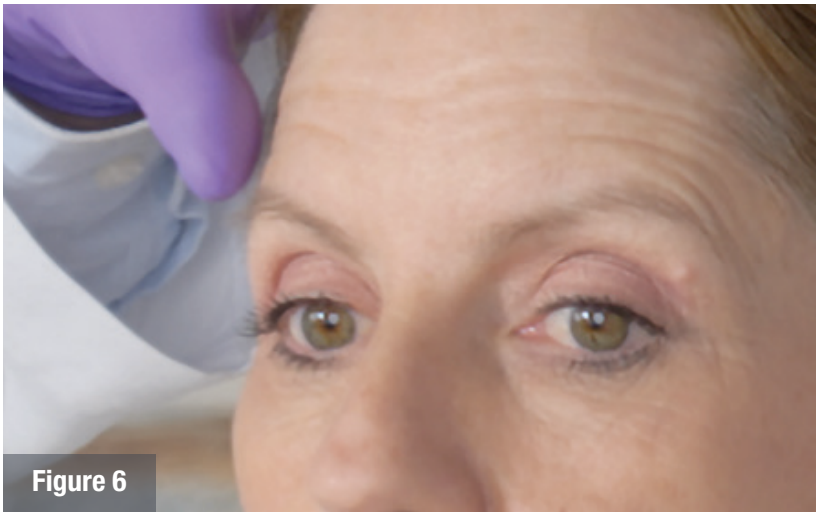


Figure 6

DIALOGUE TIP: "**BOTOX**® is locally administered, with **purposeful injections** across 7 head/neck muscle areas that may be associated with migraine (31 injections)."[23,35]

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 the following pages.

Patient assessment before injection* (continued)

Pre-examination of the neck[46]

☑ **INSPECT:** Neck pain and neck weakness may be present among Chronic Migraine patients. Inspect the patient for a head-forward position, which may indicate preexisting muscle weakness **(Figure 7A)**.[36]

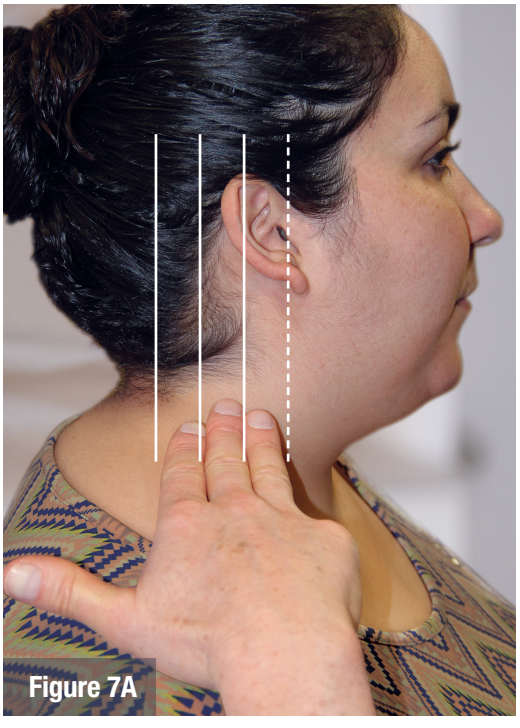


Figure 7A

Three-fingerbreadths head-forward position

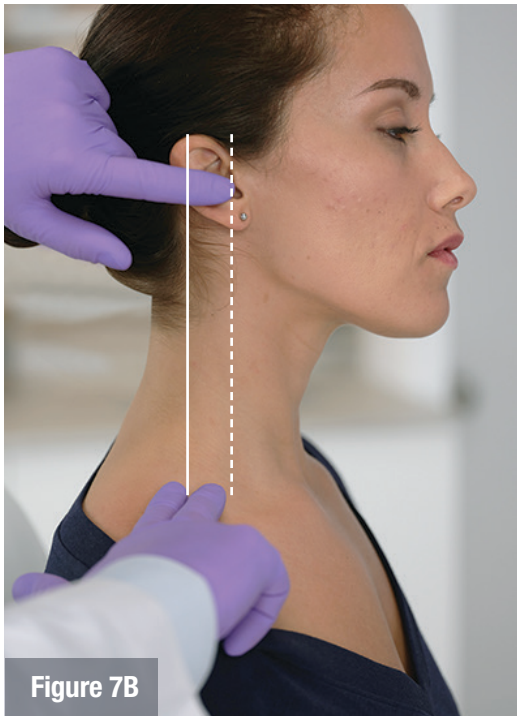


Figure 7B

Optimal head-forward position

! Prior to BOTOX® injections, consider pre-examining patients for pain sensitivity in the neck.

*Muscles and/or anatomical structures shown 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 the following pages.

- ☑ **ACTIVATE:** Ask the patient to stand in profile, with a neutral-spine position.[36]
- ☑ **EXAMINE:** Look for a plumb (vertical) line from the tragus and anterior ridge of the trapezius through the patient's center of gravity **(Figure 8)**. If the tragus is anterior to this line by 2 to 3 fingerbreadths, this may be abnormal **(Figure 7A)**.[36]

DIALOGUE TIP: "**BOTOX®** is given with **small needles**, which are about the thickness of 5 human hairs. The shallow injections may feel like tiny **pinches or pinpricks**."[24]

For more injection considerations for preexisting conditions, please refer to the specific injection site within the Anterior Injections or Posterior Injections tabs.

Figure 8†

†This is a hypothetical patient.

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

Reconstitution Information for BOTOX®

Supplies needed for the reconstitution procedure

- One 200-Unit vial of BOTOX® (onabotulinumtoxinA)
- One 21-gauge, 2-inch needle (for reconstitution)
- One 5-mL syringe
- Four 1-mL tuberculin syringes (for injection)
- At least four 30-gauge, 0.5-inch needles (for injection)
- One 10-mL single-use vial of preservative-free, 0.9% sodium chloride (saline)
- Alcohol swabs for cleaning the rubber stoppers on the saline and BOTOX® vials
- Gauze pads
- 1 pair of gloves
- Hazardous medical waste container

	Dilution[23]	
	Saline added (0.9% sodium chloride injection)	Resulting BOTOX® dose (Units per 0.1 mL)
100-Unit Vial	2 mL	5 Units
200-Unit Vial	4 mL	5 Units

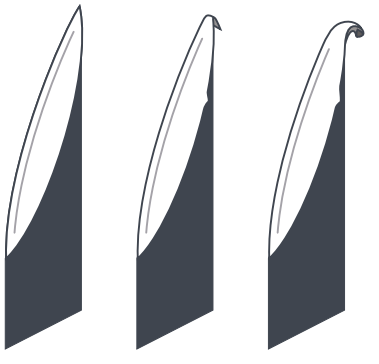
Resulting concentration is 5 Units per 0.1 mL.

- Upon completion of reconstitution, you will have 4 tuberculin syringes, each with 1 mL of BOTOX® and a 30-gauge, 0.5-inch needle attached

Order	Muscle	Total Recommended Dosage[23,*]
A	Corrugator†	10 Units divided in 2 sites
B	Procerus	5 Units in 1 site
C	Frontalis†	20 Units divided in 4 sites
D	Temporalis†	40 Units divided in 8 sites
E	Occipitalis†	30 Units divided in 6 sites
F	Cervical paraspinals†	20 Units divided in 4 sites
G	Trapezius†	30 Units divided in 6 sites

Total Dose: 155 Units divided in 31 sites

! Consider changing needles frequently to reduce patient discomfort‡



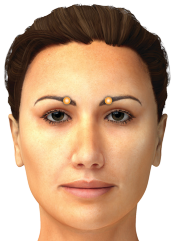
Before Use | Dullness at 2-3 Uses | Bluntness at 4-5 Uses

*Each intramuscular (IM) injection site = 0.1 mL = 5 Units of BOTOX®.
†Dose distributed bilaterally.
‡Adapted from Majcher K, Eichorn D, Waldner C, Johnston J, Clark C, Jelinski M. Assessing the sharpness of hypodermic needles after repeated use. *Can Vet J*. 2018;59(10):1112-1114.

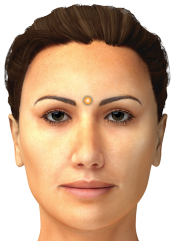
IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Human Albumin and Transmission of Viral Diseases
This product contains albumin, a derivative of human blood.

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

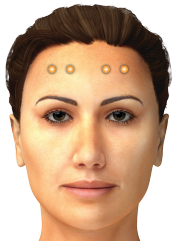
Summary of dose by area[23,‡,§]



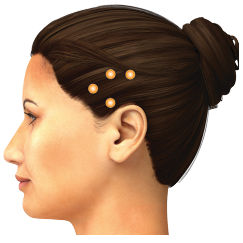
A. Corrugator
10 Units divided in 2 sites



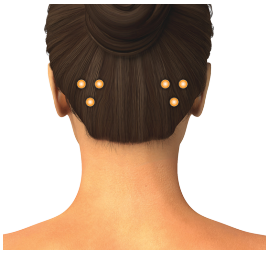
B. Procerus
5 Units in 1 site



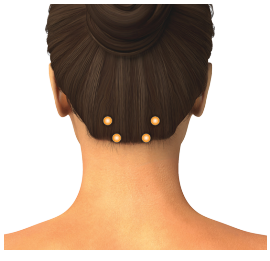
C. Frontalis
20 Units divided in 4 sites



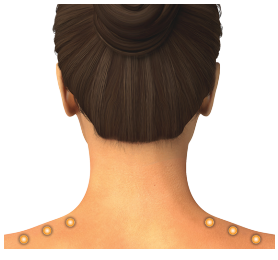
D. Temporalis
40 Units divided in 8 sites



E. Occipitalis
30 Units divided in 6 sites



F. Cervical paraspinals
20 Units divided in 4 sites



G. Trapezius
30 Units divided in 6 sites

The dosing and administration of BOTOX® is a detailed process. The information on this page contains highlights only and is not meant to be a substitute for appropriate training or review of full Prescribing Information.

‡Muscles and/or anatomical structures shown for anatomical reference only.

§The recommended dilution is 200 Units/4 mL or 100 Units/2 mL, with a final concentration of 5 Units per 0.1 mL (see Sections 2.1 and 2.2 of the full Prescribing Information for preparation and dilution techniques and additional dosing information).[22]

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Human Albumin and Transmission of Viral Diseases (continued)
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 the following pages.

Notes

Anterior injections*

Anatomy of the face and head

Frontalis

Originates from the epicranial aponeurosis, and attaches distally to the skin of the forehead and eyebrow[36]

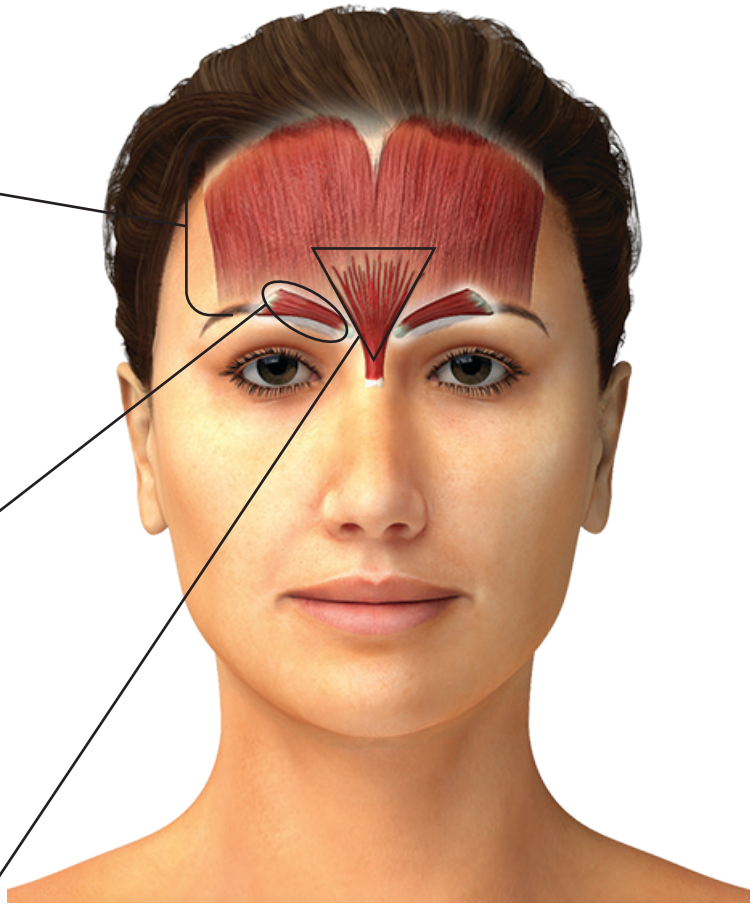
Corrugator

Sits deep to the frontalis in the region of the medial brow and attaches to the nasal-frontal bone medially and the skin of the eyebrows laterally. The muscles are shown in this visual to more clearly portray it[36]

Note: The two corrugator muscles are highlighted and shown superior to the frontalis to more clearly portray them for training purposes only.

Procerus

Originates from the aponeurotic fascia of the nose and inserts into the glabellar skin[36]



*Muscles and/or anatomical structures shown 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*.

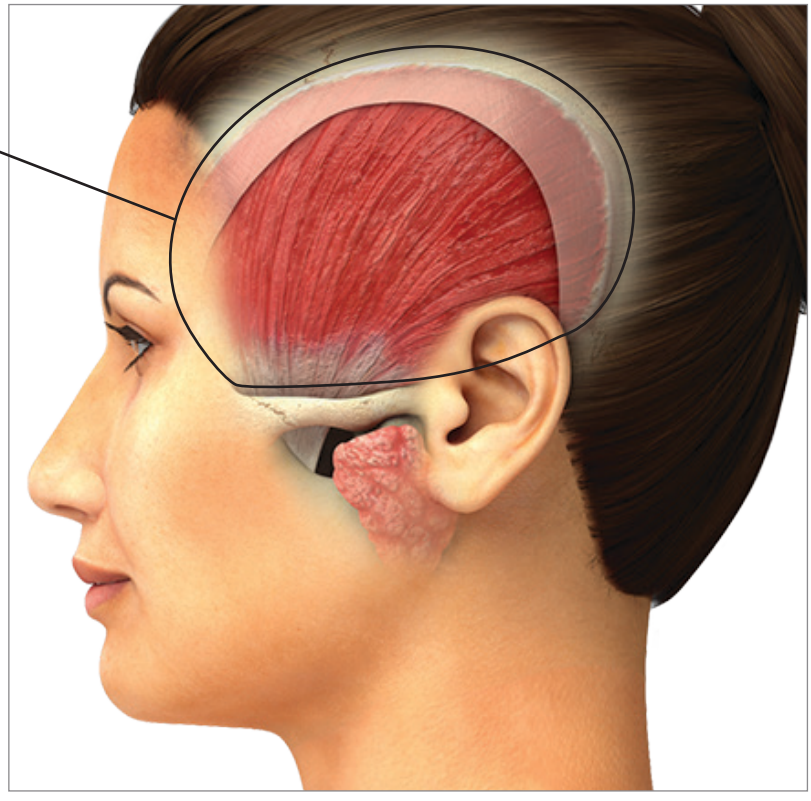
Chronic Migraine
The most frequently reported adverse reactions following injection of BOTOX for chronic migraine vs placebo include, respectively, neck pain (9% vs 3%); headache (5% vs 3%); eyelid ptosis (4% vs <1%); migraine (4% vs 3%); muscular weakness (4% vs <1%); musculoskeletal stiffness (4% vs 1%); bronchitis (3% vs 2%); injection-site pain (3% vs 2%); musculoskeletal pain (3% vs 1%); myalgia (3% vs 1%); facial paresis (2% vs 0%); hypertension (2% vs 1%); and muscle spasms (2% vs 1%).

Severe worsening of migraine requiring hospitalization occurred in approximately 1% of BOTOX treated patients in study 1 and study 2, usually within the first week after treatment, compared to 0.3% of placebo-treated patients.

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

Temporalis[36,37]

Originates from the temporal fossa and deep surface of the temporal fascia, and inserts onto the tip and medial surface of the coronoid process of the mandible[36,37]



Interrelationship between muscles[36]

- Corrugator muscle fibers and frontalis muscle fibers interdigitate in the region of the medial brow where the corrugator inserts into skin
- On the corrugator's medial aspect, it is deep to both the procerus muscle and the superficial, thinned-out frontalis muscle fibers
- Because of the close proximity of these muscles, pay close attention to the depth and angle of the needle. There can be a difference between the insertion point and where the medication is ultimately delivered

*Muscles and/or anatomical structures shown for anatomical reference only.

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

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

Anterior injections* (continued)

Functional anatomy

The **frontalis muscle** is a brow elevator, pulling the brow upward. Weakening of this muscle may result in brow ptosis.[36]

> Activating the frontalis creates transverse lines on the forehead **(Figure 9)**[36]

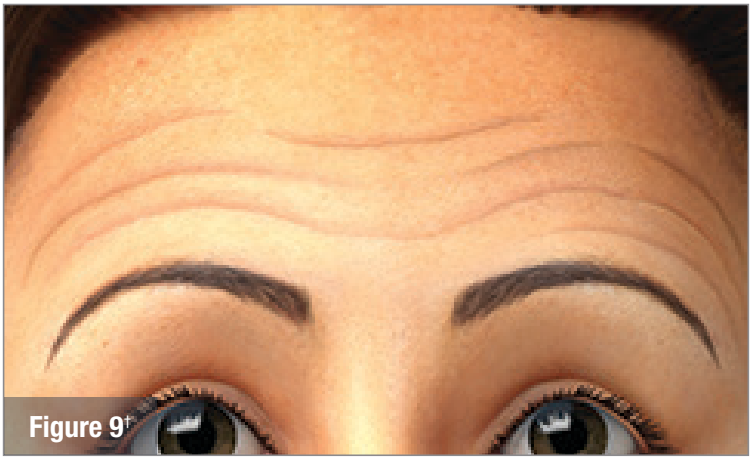


Figure 9†

The **corrugator muscles** act as a brow depressor, pulling the brow downward. Weakening of this muscle may elevate the brow.[36]

> Activating the corrugator muscles creates vertical lines between the brow **(Figure 10)**[36]

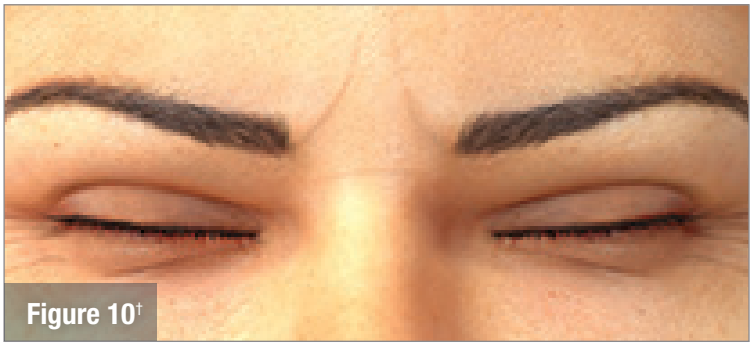


Figure 10†

*Muscles and/or anatomical structures shown for anatomical reference only.
†This is a hypothetical patient.

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 the following pages.

Functional anatomy (continued)

The **procerus muscle** draws down the medial aspect of the brow.[36]

> Activating the procerus creates a transverse ridge over the nose **(Figure 11)**[36]

Figure 11†

The **temporalis** is a masticatory muscle. Clenching the teeth activates the temporalis and can help localize the muscle **(Figure 12)**.[36]

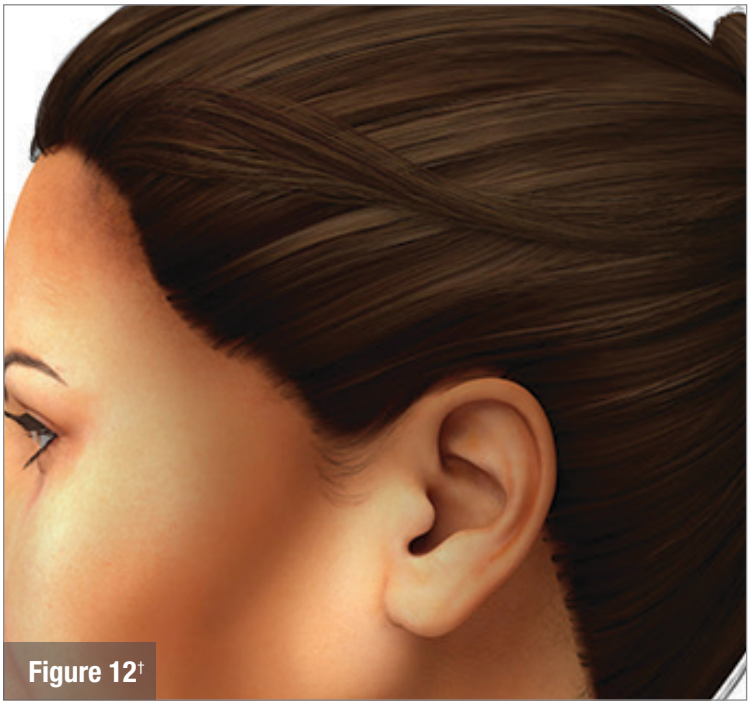


Figure 12†

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

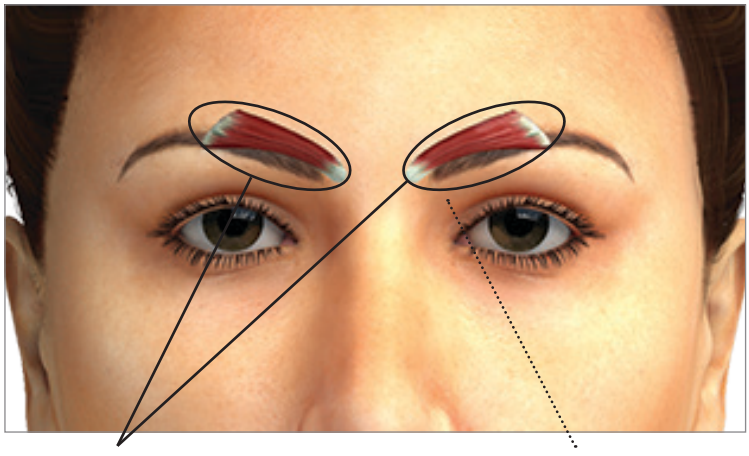
Please see accompanying full Prescribing Information, including Boxed Warning and Medication Guide, or visit https://www.rxabbvie.com/pdf/botox_pi.pdf

Standard **corrugator** PREEMPT* injection protocol†

Video does not show all of the injection sites per the PREEMPT Protocol.

Dose[23]

- 5 Units per site; 1 site per side
- Total of 10 Units divided in 2 sites in the corrugators

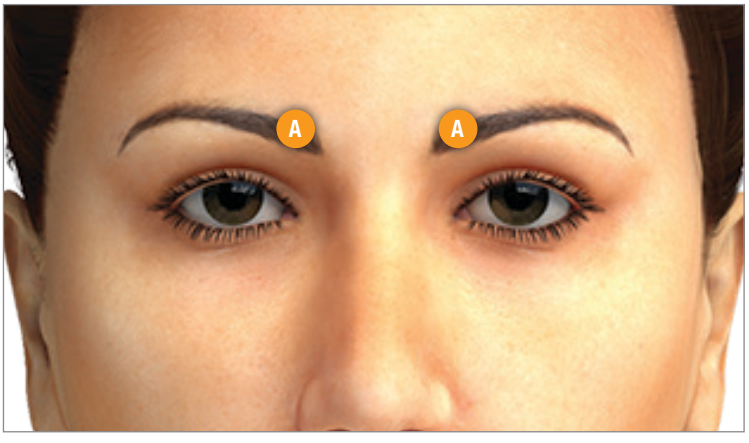


Corrugator muscle[36,†]

Medial inferior edge of the superior orbital rim[36,†]

Injection site[36]

A 1 injection site per side **(Figure 13)**. This may vary based on individual anatomy



Corrugator injection sites[23]

*__PREEMPT__ = **P**hase 3 **RE**search **E**valuating **M**igraine **P**rophylaxis **T**herapy.
†Muscles and/or anatomical structures shown for anatomical reference only.

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

WARNINGS AND PRECAUTIONS
Spread of Toxin Effect
See *Boxed Warning*.

No definitive serious adverse event reports of distant spread of toxin effect associated with BOTOX for chronic migraine at the labeled dose have been reported.

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

Figure 13

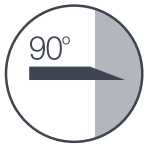
Additional injection considerations[36,37]

Muscle Localization

- Ask the patient to furrow the brow, which activates the corrugator and causes brow depression
- Palpate and pinch at the medial inferior edge of the superior orbital rim to localize **(Figure 13)**

Angle/Depth

- Inject at a 90° angle into the belly of the muscle, remaining superficial to the periosteum, to help ensure medication delivery into the corrugator and not into a nearby muscle **(Figure 13)**
- Shallow injection into the belly of the muscle, but remaining superficial to the periosteum



Insights

- Corrugator muscles are thin, so when injecting at a 90° angle, use caution not to inject too deep and hit the periosteum, which may trigger headache/migraine

Note: The considerations above cannot eliminate the risk of adverse events following BOTOX® injections.

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

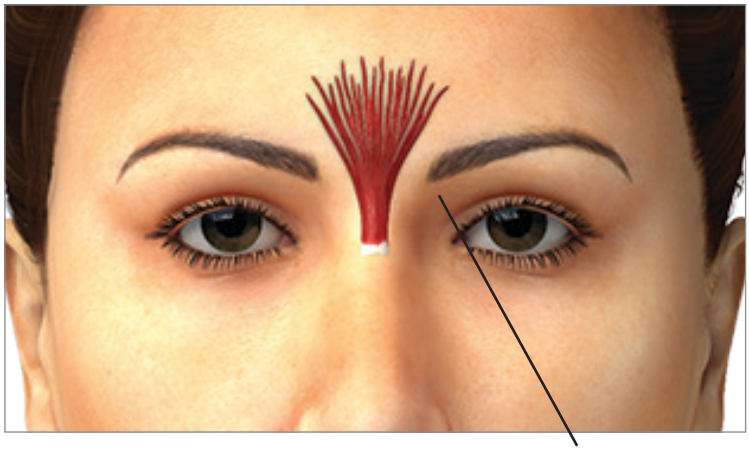
Please see additional Important Safety Information about BOTOX® on the following pages.

Standard **procerus** PREEMPT* injection protocol†

Video does not show all of the injection sites per the PREEMPT Protocol.

Dose[23]

- 5 Units in 1 site for the procerus

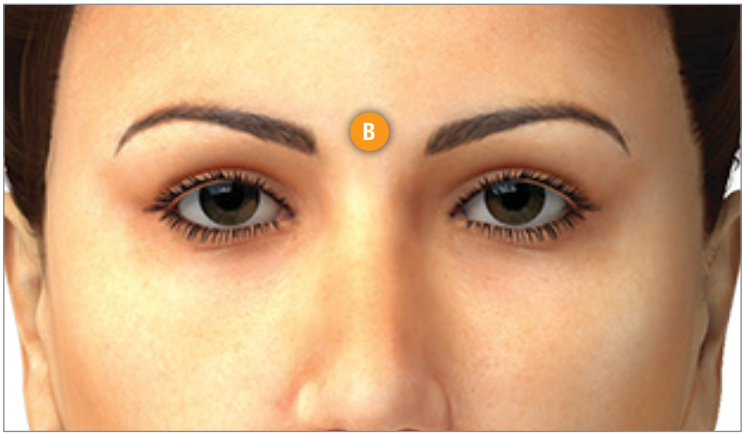


Procerus muscle[23,36,†]

Medial inferior edge of the superior orbital rim[23,36,†]

Injection site[23,36]

B 1 injection site that is approximately midway between the 2 corrugator injections **(Figure 14)**. This may vary based on individual anatomy



Procerus injection site[23]

*__PREEMPT__ = **P**hase 3 **RE**search **E**valuating **M**igraine **P**rophylaxis **T**herapy.
†Muscles and/or anatomical structures shown 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 the following pages.

Figure 14

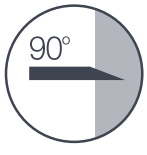
Additional injection considerations[36,37]

Muscle Localization

- Ask the patient to furrow the brow, and use the vertical and horizontal lines for orientation

Angle/Depth

- Inject at a 90° angle **(Figure 14)**
- Shallow injection remaining superficial to the periosteum



Insights

- Procerus muscle is thin, so when injecting at a 90° angle, use caution not to inject too deep and hit the periosteum, which may trigger headache/migraine
- Injecting too high in the brow area (in the lower frontalis instead of the procerus) can lead to ptosis

Note: The considerations above cannot eliminate the risk of adverse events following BOTOX® injections.

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.

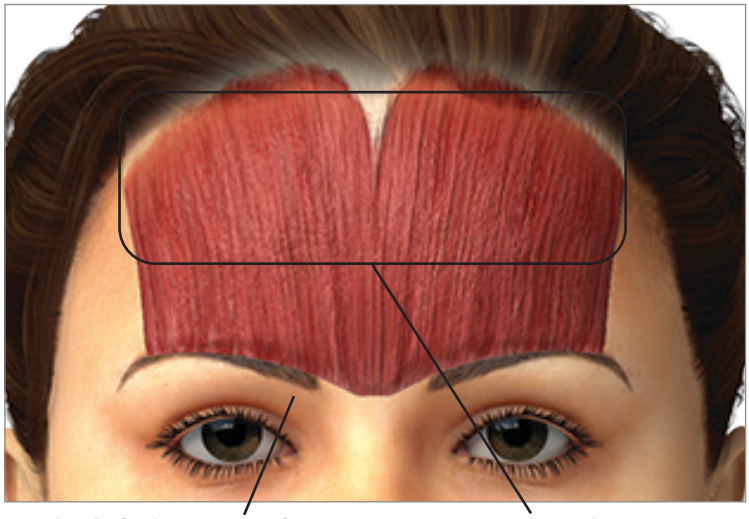
Please see additional Important Safety Information about BOTOX® on the following pages.

Standard **frontalis** PREEMPT* injection protocol†

Video does not show all of the injection sites per the PREEMPT Protocol.

Dose[23]

- 5 Units per site; 2 sites per side; a total of 10 Units on each side
- Total 20 Units divided in 4 sites for the frontalis



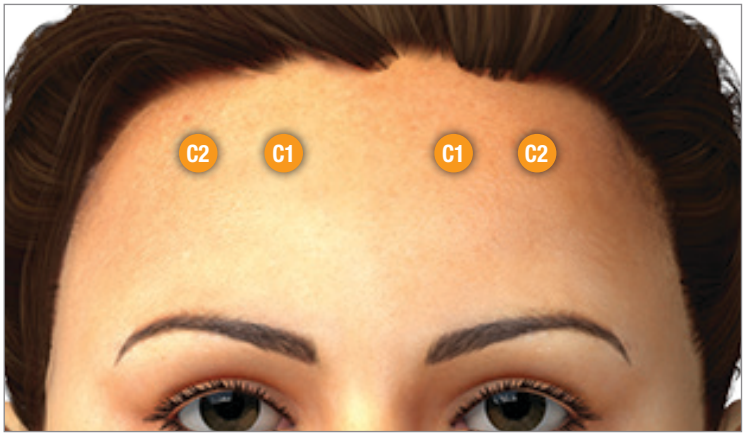
Medial inferior edge of the superior orbital rim[36,†]

Frontalis[36,†]

Medial injection site[36]

C1 The medial injection site is vertically in line with the medial inferior edge of the superior orbital rim and the first corrugator injection site

- All injection sites should be within the upper 1/3 of the forehead, at least 1–2 fingerbreadths (1.5–3 cm) superior to the corrugator injection site **(Figure 16)**. This may vary based on individual anatomy



Frontalis injection sites[23]

Lateral injection site[36]

C2 The lateral injection is parallel to the medial injection site and in line with the lateral limbus of the cornea, at least 1 fingerbreadth (1.5 cm) lateral to the medial injection site **(Figure 15)**. This may vary based on individual anatomy

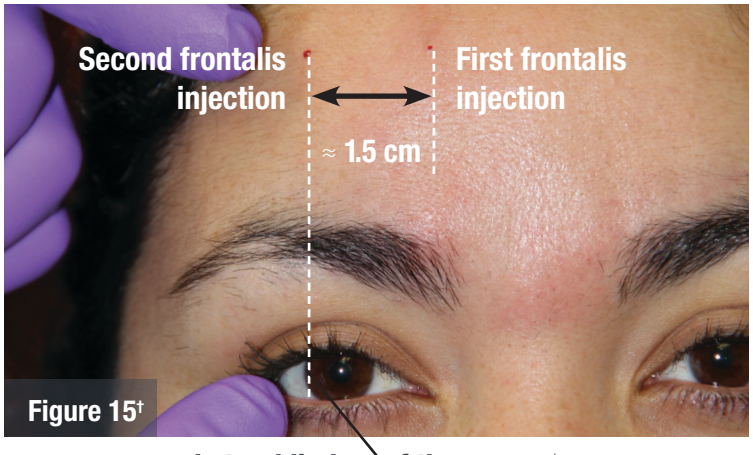


Figure 15†

Lateral limbus of the cornea†

*PREEMPT = Phase 3 REsearch Evaluating Migraine Prophylaxis Therapy.
†Muscles and/or anatomical structures shown for anatomical reference only.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Hypersensitivity Reactions (continued)
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 the following pages.

Figure 16

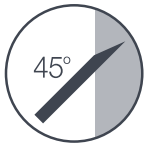
Additional injection considerations[36]

Muscle Localization

- Injections should be in the upper 1/3 of the forehead to avoid the lower frontalis
- Account for individual anatomy, as forehead sizes are different

45° Angle/Depth

- Inject at a 45° angle, away from the face **(Figure 16)** and angle the needle superiorly
- Shallow injections in the most superficial aspect of the muscle to avoid reaching the periosteum



Insights

- Consider that injection points are different than medication delivery points
- If patients are concerned about discomfort, consider using a topical anesthetic in this area

Note: The considerations above cannot eliminate the risk of adverse events following BOTOX® injections.

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*).

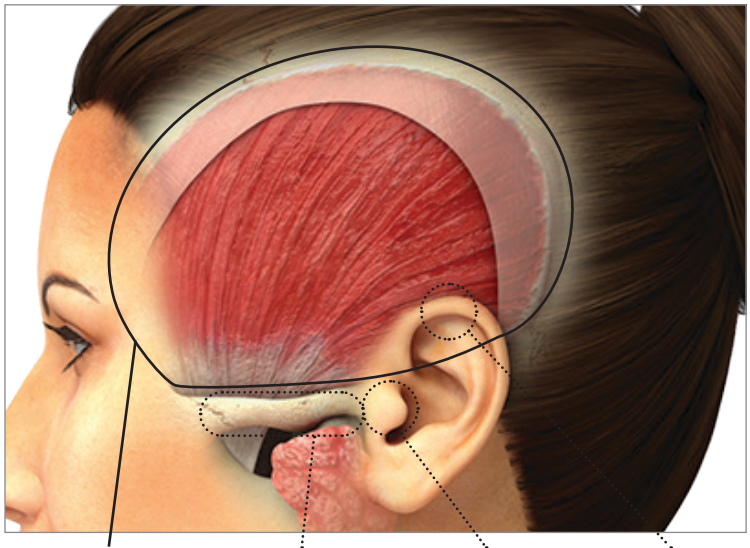
Please see additional Important Safety Information about BOTOX® on the following pages.

Standard **temporalis** PREEMPT* injection protocol†

Video does not show all of the injection sites per the PREEMPT Protocol.

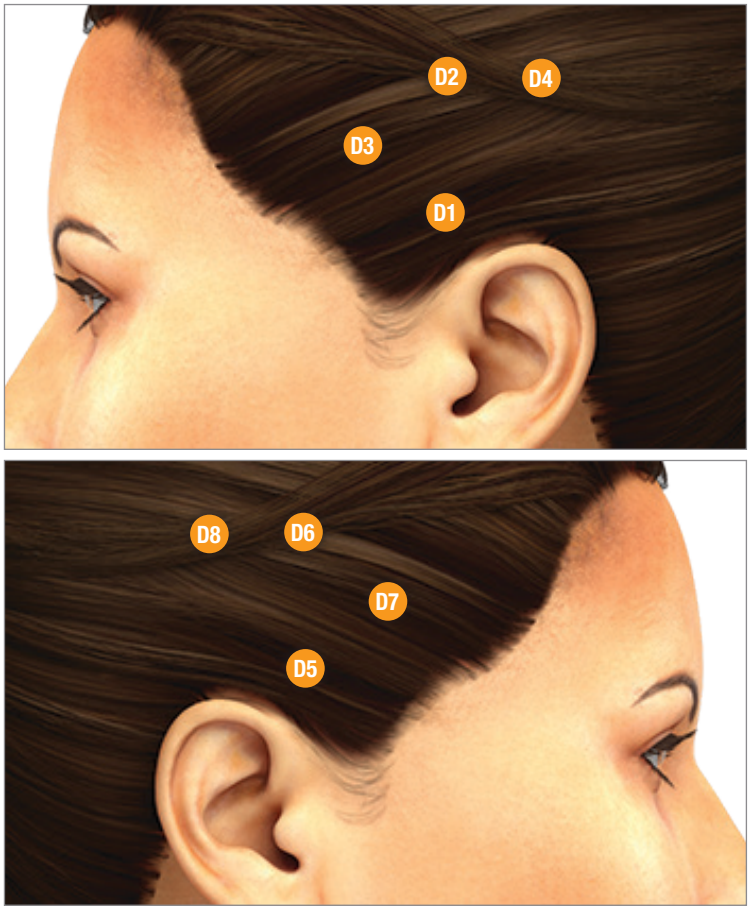
Dose[23]

- 5 units per site; 4 sites on the temporalis on the left side and 4 sites on the right side
- Total 40 Units divided in 8 sites: 4 sites on the temporalis on the left side and 4 sites on the right side



Injection sites[36]

- D1 Landmark the tragus of the ear
- D5 The first injection site is at least 2 fingerbreadths (3 cm) superior to the tragus of the ear
- D2 D6 The second injection site is 1 to 2 fingerbreadths (1.5–3 cm) superior to the first injection, still in line with the tragus of the ear
- D3 D7 The third injection is about 1 fingerbreadth (1.5 cm) anterior to the first 2 injection sites and halfway vertically between the first and second injection sites **(Figure 17)**, still within the hairline
- D1 D8 The fourth injection is about 1 fingerbreadth (1.5 cm) posterior to the second injection site and in line with the superior helix of the ear



Temporalis injection sites[23]

*PREEMPT = **P**hase 3 **RE**search **E**valuating **M**igraine **P**rophylaxis **T**herapy.
†Muscles and/or anatomical structures shown for anatomical reference only.

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

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

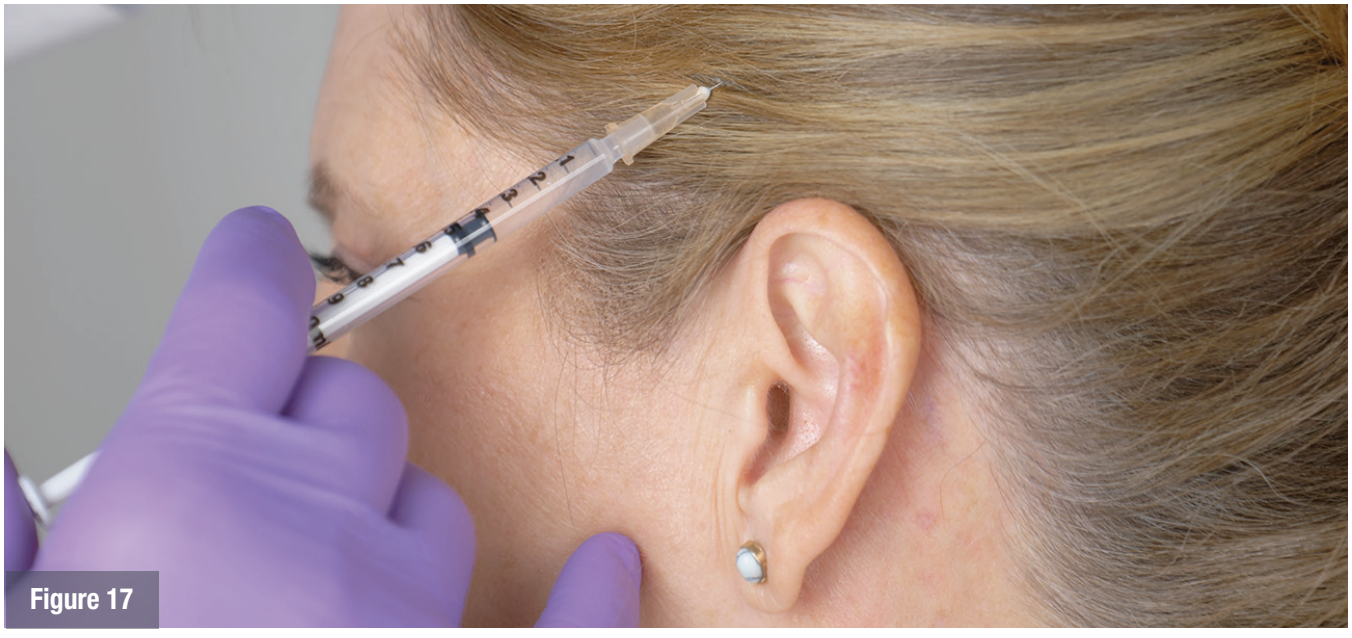


Figure 17

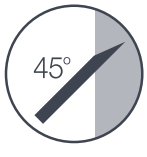
Additional injection considerations[36,37]

Muscle Localization

- The patient can clench their teeth to activate the temporalis to help localize the muscle

Angle/Depth

- Inject at a 45° angle, away from the face **(Figure 17)**
- Shallow injections in the most superficial aspect of the muscle



Insights

- The temporalis is covered by a thick fascia made up of fibrous bands. Make the patient aware that it is normal for them to hear a slight crunch/pop as the needle passes through this fascia
- Keep all injections within the hairline and angled posteriorly away from the face. Muscle atrophy in this area may cause an unwanted hourglass appearance
- Since this is a vascular area, aspirate the needle to ensure no blood return
- Being a vascular area, these injections may be prone to bleeding, so it's helpful to have gauze handy and apply pressure to control bleeding

Note: The considerations above cannot eliminate the risk of adverse events following BOTOX® injections.

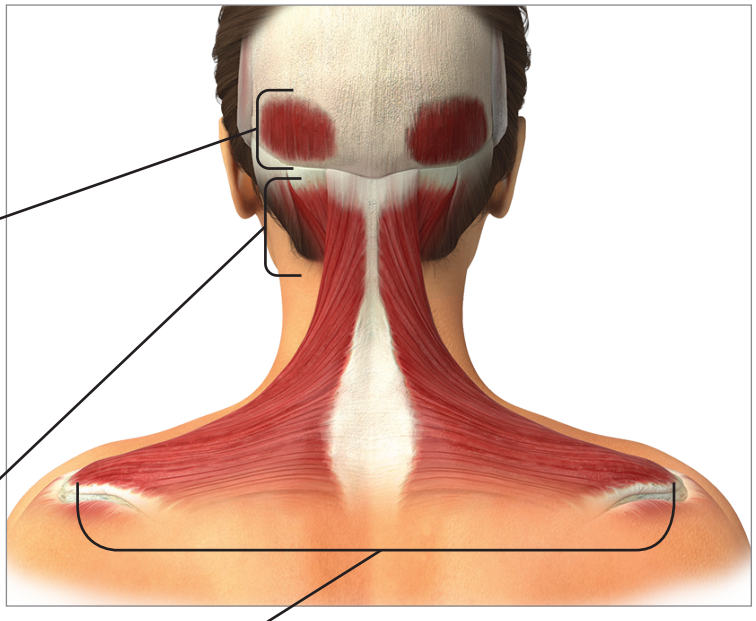
IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)
Dysphagia and Breathing Difficulties (continued)
Patients with preexisting swallowing or breathing difficulties may be more susceptible to these complications. In most cases, this is a consequence of weakening of muscles in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

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

Notes

Posterior injections*

Muscles of the neck and posterior head



Occipitalis

Originates at the highest nuchal line and inserts into the epicranial aponeurosis, which is attached to the frontalis[36,*]

Cervical paraspinal muscles

Should be considered a group (including the trapezius, splenius capitis, splenius cervicis, and semispinalis capitis) running deep alongside the cervical spine[36,*]

Trapezius

A flat, triangular muscle situated over the back of the neck and upper thorax[36,*]

*Muscles and/or anatomical structures shown for anatomical reference only.

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

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

Functional anatomy

Figure 18

- One function of the occipitalis is as an anchor for the frontalis[36]
- Cervical paraspinal muscles stabilize and allow for movement of the head and cervical spine **(Figure 18)**[36]
- In addition to the muscles that are deep to the trapezius, the trapezius muscles function to stabilize and bend the head and neck backward and laterally **(Figure 18)**[36]

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*.

Chronic Migraine
The most frequently reported adverse reactions following injection of BOTOX for chronic migraine vs placebo include, respectively, neck pain (9% vs 3%); headache (5% vs 3%); eyelid ptosis (4% vs <1%); migraine (4% vs 3%); muscular weakness (4% vs <1%); musculoskeletal stiffness (4% vs 1%); bronchitis (3% vs 2%); injection-site pain (3% vs 2%); musculoskeletal pain (3% vs 1%); myalgia (3% vs 1%); facial paresis (2% vs 0%); hypertension (2% vs 1%); and muscle spasms (2% vs 1%).

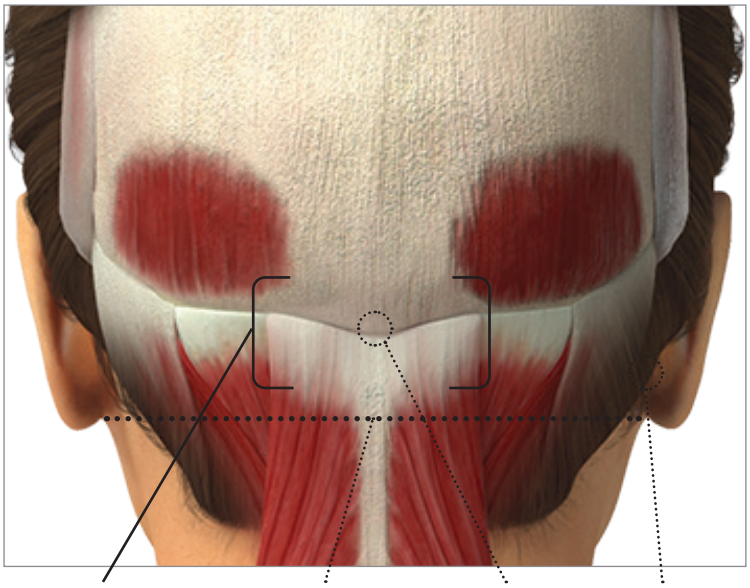
Please see additional Important Safety Information about BOTOX® on the following pages.

Standard **occipitalis** PREEMPT* injection protocol†

Video does not show all of the injection sites per the PREEMPT Protocol.

Dose[23]

- 5 Units per site, 3 sites per side; a total of 15 Units on each side
- Total 30 Units divided in 6 sites across both right and left sides of the occipitalis (3 on each side)



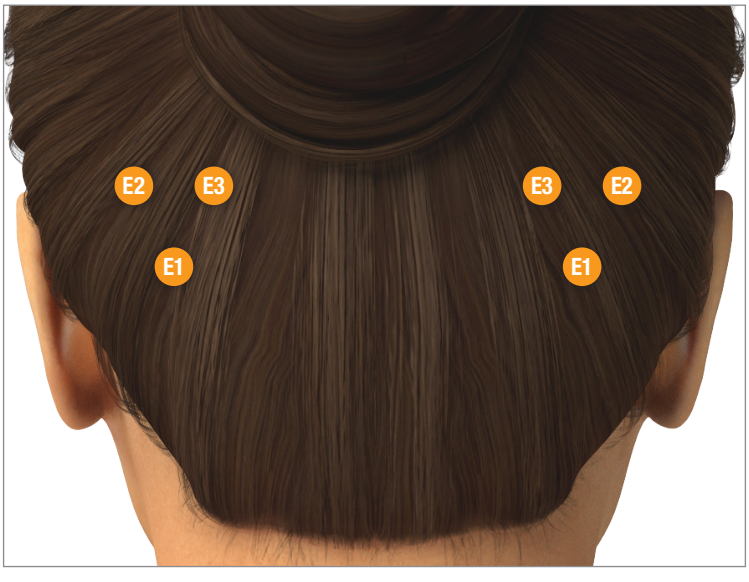
Injection sites[36]

E1 Locate two landmarks: the inion on the superior aspect of the occipital protuberance and the tip of the mastoid process behind the ear **(Figure 19)**. This may vary based on individual anatomy

- For the first injection site, find the midpoint between these two landmarks. Place the injection at this midpoint, staying just superior to the nuchal ridge **(Figure 19)**. This may vary based on individual anatomy

E2 The second injection site is 1 diagonal fingerbreadth superior and lateral from the first injection site, toward the helix of the ear (eg, at the 10 o'clock position for the left side; at the 2 o'clock position for the right side)

E3 The third injection site is 1 diagonal fingerbreadth, superior and medial from the first injection site (eg, at the 2 o'clock position for the left side; at the 10 o'clock position for the right side)



Occipitalis injection sites[23]

*PREEMPT = **P**hase 3 **RE**search **E**valuating **M**igraine **P**rophylaxis **T**herapy.
†Muscles and/or anatomical structures shown for anatomical reference only.

IMPORTANT SAFETY INFORMATION (continued)
ADVERSE REACTIONS
Chronic Migraine (continued)
Severe worsening of migraine requiring hospitalization occurred in approximately 1% of BOTOX treated patients in study 1 and study 2, usually within the first week after treatment, compared to 0.3% of placebo-treated patients.

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

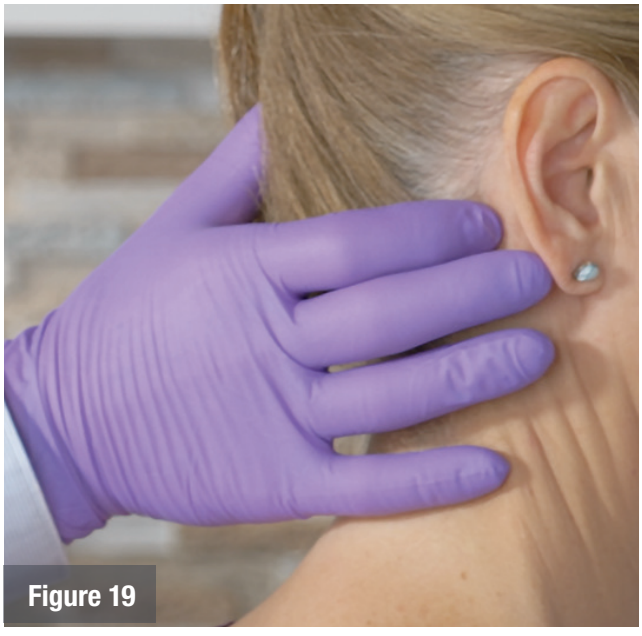


Figure 19

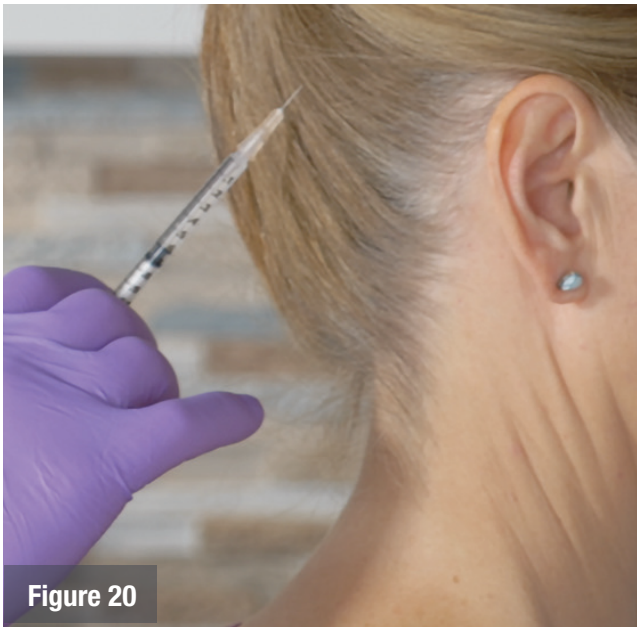


Figure 20

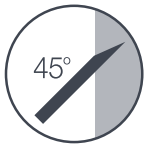
Additional injection considerations[36]

Muscle Localization

- Landmark the inion on the superior aspect of occipital protuberance. Also landmark the tip of the mastoid process behind the ear

45° Angle/Depth

- Inject at a 45° upward angle, away from the neck **(Figure 20)**
- Inject the most superficial aspect of the muscle, just upon penetration of the dermis **(Figure 20)**



Insights

- Angle the needle away from the neck and superior to the highest nuchal ridge. The diffusion of BOTOX® into the lower neck may result in neck weakness and pain

Note: The considerations above cannot eliminate the risk of adverse events following BOTOX® injections.

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.

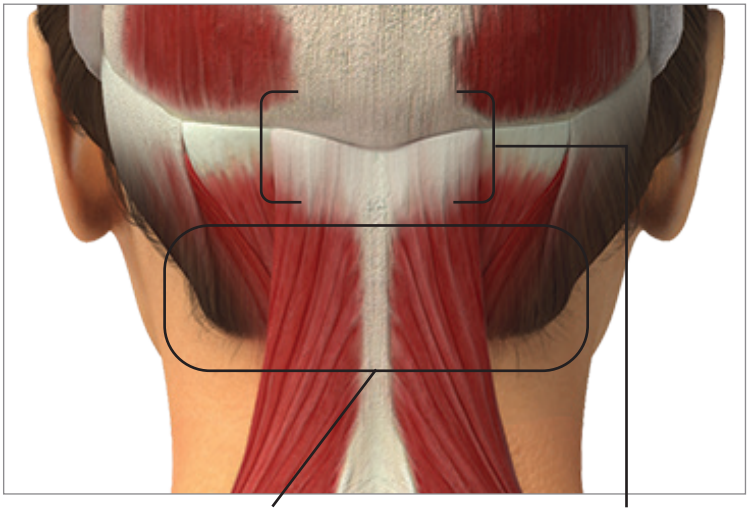
Please see additional Important Safety Information about BOTOX® on the following pages.

Standard **cervical paraspinal** PREEMPT* injection protocol†

Video does not show all of the injection sites per the PREEMPT Protocol.

Dose[23]

- 5 Units per site; 2 sites on the left side of the cervical paraspinal muscle group and 2 sites on the right side
- Total 20 Units divided in 4 sites across both the right and left sides of the cervical paraspinal muscle group



Cervical paraspinal muscle group[36,†]

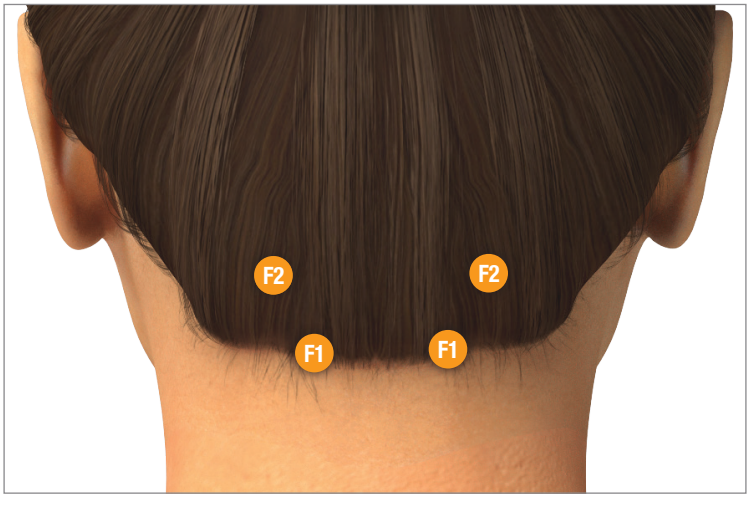
Occipital protuberance[36,†]

Injection sites[36]

F1 Landmark the lower border of the occipital protuberance

- For the first injection site, measure approximately 2 fingerbreadths (about 3 cm) inferior to the lower border of the occipital protuberance and about 1 cm lateral to the midline of the cervical spine **(Figure 21)**

F2 The second injection site is 1 diagonal fingerbreadth, superior and lateral from the first injection site, toward the helix of the ear. This may vary based on individual anatomy



Cervical paraspinal injection sites[23]

*__PREEMPT__ = **P**hase 3 **RE**search **E**valuating **M**igraine **P**rophylaxis **T**herapy.
†Muscles and/or anatomical structures shown 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 accompanying full Prescribing Information, including Boxed Warning and Medication Guide, or visit https://www.rxabbvie.com/pdf/botox_pi.pdf

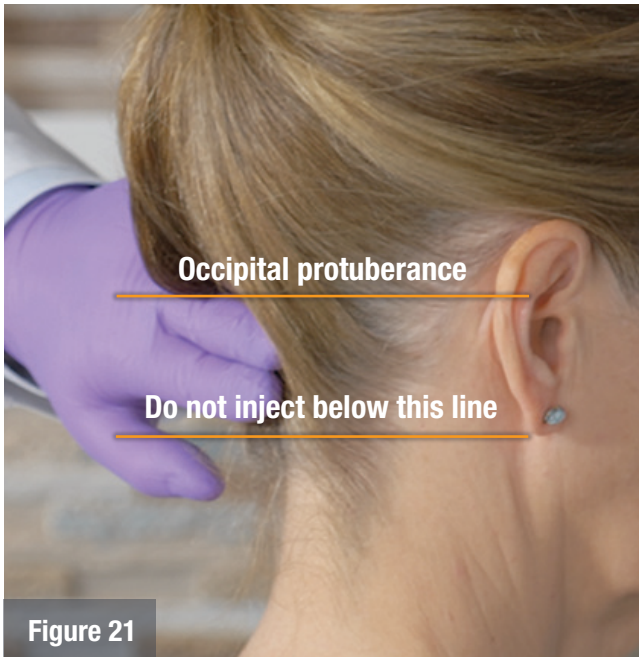


Figure 21

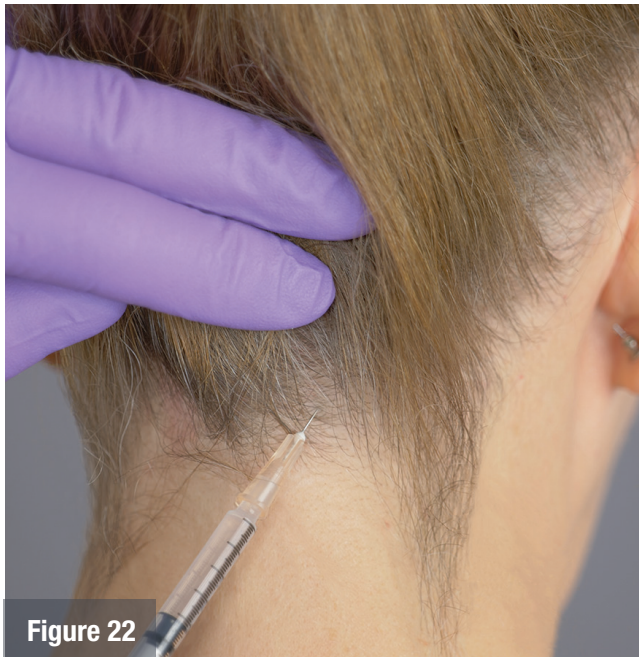


Figure 22

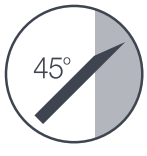
Additional injection considerations[36]

Muscle Localization

- Landmark the lower border of the occipital protuberance
- All cervical paraspinal injections should be placed approximately 2 fingerbreadths inferior to the lower border of the occipital protuberance, generally within the hairline
- The cervical paraspinal muscles can be palpated 1 cm lateral to the right and left of the cervical spine **(Figure 21)**

45° Angle/Depth

- Inject at a 45° upward angle, away from the neck
- Inject the most superficial aspect of the muscle, just through the fascia **(Figure 22)**



Insights

- Position the patient upright, with head in a neutral position to minimize injecting too deep. If the patient flexes their head down/forward, the posterior neck muscles stretch and thin, which may result in accidentally injecting too deep
- Angle the needle away from the neck. The diffusion of BOTOX® into the lower neck may result in neck weakness

Note: The considerations above cannot eliminate the risk of adverse events following BOTOX® 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.

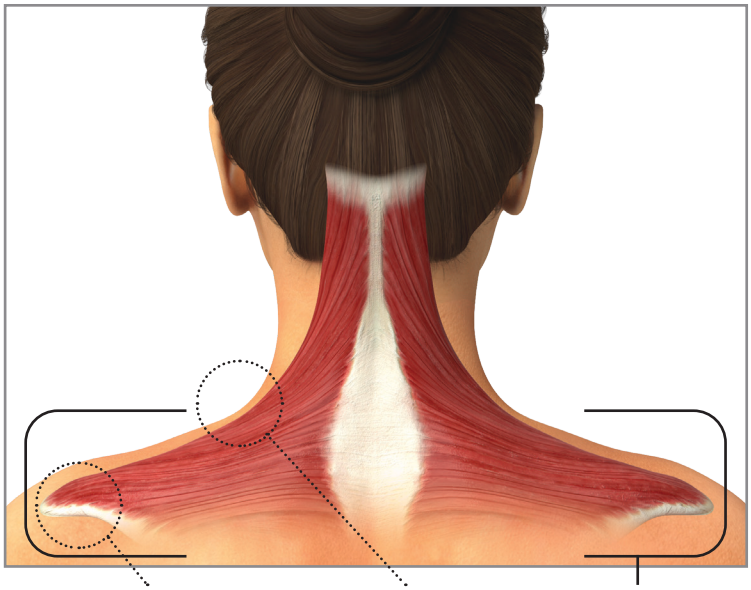
Please see additional Important Safety Information about BOTOX® on the following pages.

Standard **trapezius** PREEMPT* injection protocol†

Video does not show all of the injection sites per the PREEMPT Protocol.

Dose[23]

- 5 Units per site, 3 sites per side; a total of 15 Units on each side
- Total 30 Units divided across 6 sites in the trapezius muscle: 3 sites on the right side and 3 sites on the left side



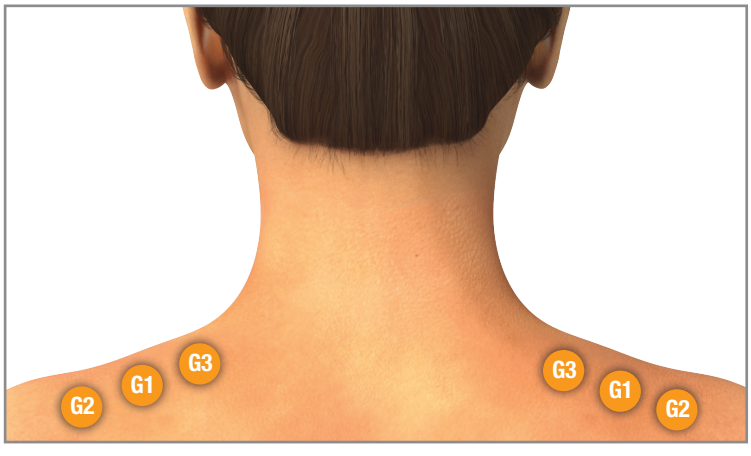
Injection sites[36]

G1 Landmark the inflection point of the neck (necklace line) and the acromioclavicular joint (AC joint)

- The first injection site is at the midpoint between those 2 landmarks (AC joint and inflection point of the neck)

G2 The second injection site is at the midpoint between the first injection site and the acromioclavicular joint **(Figure 23)**. This may vary based on individual anatomy

G3 The third injection site is at the midpoint between the first injection site and the inflection point of the neck



Trapezius injection sites[23]

*PREEMPT = **P**hase 3 **RE**search **E**valuating **M**igraine **P**rophylaxis **T**herapy.
†Muscles and/or anatomical structures shown for anatomical reference only.

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

No definitive serious adverse event reports of distant spread of toxin effect associated with BOTOX for chronic migraine at the labeled dose have been reported.

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

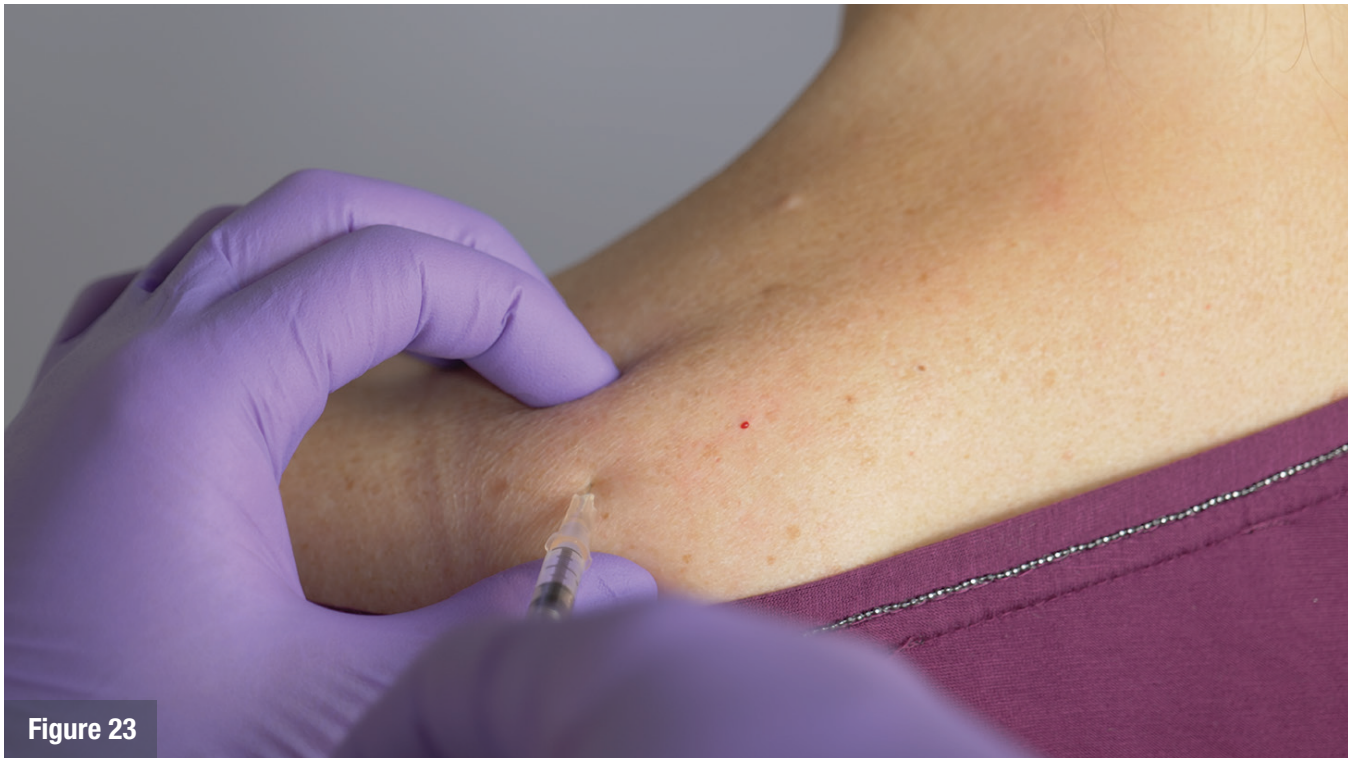


Figure 23

Additional injection considerations[36]

Muscle Localization

- Landmark the inflection point of the neck (necklace line) and the acromioclavicular joint

Angle/Depth

- Inject at a 0° angle (horizontal approach) **(Figure 23)**
- Inject the most superficial aspect of the muscle, in the supraclavicular portion of the muscle **(Figure 23)**

Insights

- Use a horizontal, 0° angle injection approach, supraclavicular and lateral to the neckline, to avoid injecting too deep or too high into the cervical spine
- Assess the patient for preexisting neck/shoulder weakness. Consider that patients with small frames may be predisposed to weakness in this area and set those expectations with the patient

Note: The considerations above cannot eliminate the risk of adverse events following BOTOX® injections.

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

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

Notes

Tips to help efficiently administer BOTOX® treatment for Chronic Migraine in the office

OFFICE STAFF AND PROCESSES

Assign staff to specific roles

- ☑ Roles include ordering BOTOX® and submitting insurance verifications, prior authorizations, and claims

Have a process to identify Chronic Migraine patients

- ☑ Ensure proper documentation is completed by the patient at intake: HIT-6*, MIDAS†, headache diary, etc

Evaluate eligible BOTOX® Chronic Migraine patients

- ☑ Check insurance requirements are met prior to BOTOX® treatment by ensuring you have patient's medication history, headache diary, screener, intake form, and/or ensure symptom assessment tools are readily available

Use a system to track and schedule recurring BOTOX® treatment

- ☑ Ensure patients receive treatment every 12 weeks
- ☑ Ensure staff books next treatment before the patient leaves the office

Consider involving additional office staff to help

- ☑ Include NPs/PAs for follow-ups, patient counseling, and injections, as appropriate
- ☑ Train nursing staff to reconstitute and prepare syringes for BOTOX® treatment

*HIT-6 : Headache Impact Test; a reliable, 6-item test measuring the impact headache has on pain, social functioning, role functioning, vitality, cognitive functioning, and psychological distress.

†MIDAS: The Migraine Disability Assessment.

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 the following pages.

Make the decision for BOTOX® today

Many of your patients with Chronic Migraine may already meet criteria for BOTOX® and may be ready to start BOTOX® today

Once diagnosed, Chronic Migraine patients often cycle through multiple medications[24]

Chronic Migraine patients have tried

≈4 preventive treatments on average[24,‡]

[‡]According to market research (N = 329).[24]

93% of payer lives **only require 2 or fewer preventives**[24,§]

American Academy of Neurology (AAN) guidelines state that BOTOX® has a Level A recommendation for effectiveness and should be offered to appropriate patients.[38,39]

The **American Headache Society** states that BOTOX® is a first-line preventive treatment option for Chronic Migraine.[40]

Nearly all insurance plans cover BOTOX® for Chronic Migraine[24]

≈100% of commercial and Medicare lives covered[24,‖]

If insurance does not provide full coverage, the BOTOX® Savings Program may be able to help eligible, commercially insured patients with any remaining costs, including procedure fees.[24,*,¶]

[§]Based on 2024 data covering 314,820,598 medical lives.[24]
[‖]Not a guarantee of coverage or partial or full payment. Check each patient's coverage with applicable insurer. Formulary coverage does not imply safety or efficacy.
[¶]Restrictions may vary by state.

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 the following pages.

BOTOX TODAY™ savings and support for your patients and office staff

BOTOX TODAY®

Savings

Features **$0 BOTOX® treatments for eligible patients**;* personalized dashboard for claims and reimbursement management, How-To videos, and more

- In a survey, **2 out of 3** Chronic Migraine patients **say they would try** BOTOX® if there were **no associated out-of-pocket costs**†

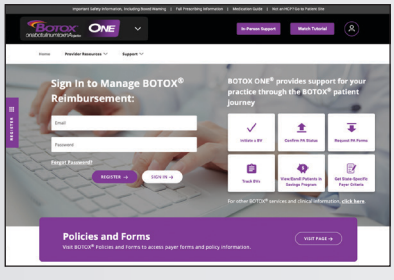
  †According to market research (n = 140).[24]

- **≈85%** of eligible, commercially insured Chronic Migraine patients **paid nothing out of pocket** after using the **BOTOX® Savings Program**[24]

BOTOX® SAVINGS PROGRAM

BOTOXSavingsProgram.com

*By participating in the BOTOX® Savings Program, you acknowledge and agree to the full Terms & Conditions set out at BOTOXSavingsProgram.com/TermsandConditions. Patients enrolled in Medicare, Medicaid, TRICARE, or any other government-reimbursed healthcare program are not eligible. Other restrictions and maximum limits apply.



BOTOXOneGo.com

Support

Get assistance including:

- Insurance verification
- Prior authorization
- Denied/underpaid claims
- Relevant billing codes for BOTOX®

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 the following pages.

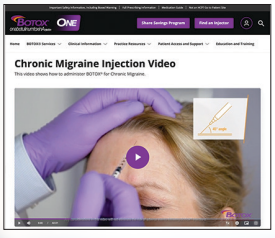
Resources available to help patients, clinicians, and office staff

BOTOX® onabotulinumtoxinA injection ONE

BOTOXOne.com

Resources

Injection videos and more



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

Patient education

- Brochures are available for both current and prospective patients to help them understand what to expect with BOTOX® treatment (also available in Spanish)

Peer-to-Peer training

- Both live and virtual training programs are available

Ask your Account Specialist or visit BOTOXOne.com to learn more.

Samples

Appropriate new Chronic Migraine patients **could receive same-day samples** to evaluate the efficacy and safety of BOTOX®

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

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

BOTOX® onabotulinumtoxinA injection

PROVEN

PROVEN prevention in Chronic Migraine with significant headache day reductions. **8 to 9 fewer headache days per month** from baseline at week 24 (vs 6 to 7 with placebo)[23,24]

PRECISE

PREEMPT* Protocol — the only locally administered procedure delivered with purposeful fixed-site, fixed-dose injections into 7 head and neck muscle areas[23,35]

PREDICTABLE

BOTOX® is PREDICTABLE with **a legacy of ~15 years in Chronic Migraine**[24,†]

Find more helpful information on the Chronic Migraine Anatomy app.

Customer Service:
1-800-44-BOTOX (1-800-442-6869)

AbbVie Medical Information Line:
1-800-678-1605

Ask your Account Specialist or visit BOTOXOne.com to learn more.

*__PREEMPT__ = __P__hase 3 __RE__search __E__valuating __M__igraine __P__rophylaxis __T__herapy.
†Since FDA approval in October 2010.

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 inside.

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

References: 1. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition. *Cephalalgia.* 2018;38(1):1-211. 2. Burch R, Rizzoli P, Loder E. The prevalence and impact of migraine and severe headache in the United States: figures and trends from government health studies. *Headache.* 2018;58(4):496-505. 3. Dodick DW, Loder EW, Manack Adams A, et al. Assessing barriers to Chronic Migraine consultation, diagnosis, and treatment: results from the Chronic Migraine Epidemiology and Outcomes (CaMEO) study. *Headache.* 2016;56(5):821-834. 4. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet.* 2017;390(10100):1211-1259. 5. Global burden of disease 2004. Part 3. Disease incidence, prevalence and disability. World Health Organization. March 2004. Accessed January 29, 2025. http://www.who.int/publications/i/item/9789241563710. 6. Ailani J, Burch RC, Robbins MS; Board of Directors of the American Headache Society. The American Headache Society consensus statement: update on integrating new migraine treatments into clinical practice. *Headache.* 2021;61(7):1021-1039. 7. Aurora SK, Brin MF. Chronic migraine: an update on physiology, imaging, and the mechanism of action of two available pharmacologic therapies. *Headache.* 2017;57(1):109-125. 8. Lipton RB, Varon SF, Grosberg B, et al. OnabotulinumtoxinA improves quality of life and reduces impact of chronic migraine. *Neurology.* 2011;77(15):1465-1472. 9. The timeline of a migraine attack. American Migraine Foundation. Published January 18, 2018. Accessed January 29, 2025. https://americanmigrainefoundation.org/understanding-migraine/timeline-migraine-attack. 10. Blumenfeld AM, Varon SF, Wilcox TK, et al. Disability, HRQoL and resource use among chronic and episodic migraineurs: results from the International Burden of Migraine Study (IBMS). *Cephalalgia.* 2011;31(3):301-315. 11. Buse DC, Manack A, Serrano D, Turkel C, Lipton RB. Sociodemographic and comorbidity profiles of chronic migraine and episodic migraine sufferers. *J Neurol Neurosurg Psychiatry.* 2010;81(4):428-432. 12. Bigal ME, Lipton RB. Concepts and mechanisms of migraine chronification. *Headache.* 2008;48(1):7-15. 13. Buse DC, Greisman JD, Baigi K, Lipton RB. Migraine progression: a systematic review. *Headache.* 2019;59(3):306-338. 14. Ashina S, Serrano D, Lipton RB, et al. Depression and risk of transformation of episodic to chronic migraine. *J Headache Pain.* 2012;13(8):615-624. 15. Schwedt TJ, Chong CD, Wu T, Gaw N, Fu Y, Li J. Accurate classification of chronic migraine via brain magnetic resonance imaging. *Headache.* 2015;55(6):762-777. 16. Blau JN. Migraine: theories of pathogenesis. *Lancet.* 1992;339(8803):1202-1207. 17. Kelman L. The postdrome of the acute migraine attack. *Cephalalgia.* 2006;26(2):214-220. 18. Diamond ML. The role of concomitant headache types and non-headache co-morbidities in the underdiagnosis of migraine. *Neurology.* 2002;58(9):S3-S9. 19. Drossman DA. 2012 David Sun lecture: Helping your patient by helping yourself—how to improve the patient-physician relationship by optimizing communication skills. *Am J Gastroenterol.* 2013;108(4):521-528. 20. Dodick DW. Chronic daily headache. *N Engl J Med.* 2006;354(2):158-165. 21. Silberstein SD; US Headache Consortium. Practice parameter: evidence-based guidelines for migraine headache (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology.* 2000;55(6):754-762. 22. Buse DC, Andrasik F. Behavioral medicine for migraine. *Neurol Clin.* 2009;27(2):445-465. 23. BOTOX® Prescribing Information, November 2023. 24. Data on file, AbbVie. 25. Dodick DW, Silberstein SD, Lipton RB, DeGryse RE, Adams AM, Diener HC. Early onset of effect of onabotulinumtoxinA for chronic migraine treatment: analysis of PREEMPT data. *Cephalalgia.* 2019;39(8):945-956. 26. Diener HC, Dodick DW, Lipton RB, et al. Benefits beyond headache days with onabotulinumtoxinA treatment: a pooled PREEMPT analysis. *Pain Ther.* 2020;9:683-694. 27. Dodick DW, Silberstein S, Saper J, et al. The impact of topiramate on health-related quality of life indicators in chronic migraine. *Headache.* 2007;47:1398-1408. 28. Shibata M, Nakamura T, Ozeki A, Ueda K, Nichols RM. Migraine-Specific Quality-of-Life Questionnaire (MSQ) version 2.1 score improvement in Japanese patients with episodic migraine by galcanezumab treatment: Japan phase 2 study. *J Pain Res.* 2020;13:3531-3538. 29. Speck RM, Shaloub H, Wyrwich KW, et al. Psychometric validation of the Role Function Restrictive Domain of the Migraine Specific Quality-of-Life Questionnaire version 2.1 electronic patient-reported outcome in patients with episodic and chronic migraine. *Headache.* 2019;59:756-774. 30. Bagley CL, Rendas-Baum R, Maglinte GA, et al. Validating Migraine-Specific Quality of Life Questionnaire v2.1 in episodic and chronic migraine. *Headache.* 2012;52:409-421. 31. Blumenfeld AM, Stark RJ, Freeman MC, Orejudos A, Manack Adams A. Long-term study of the efficacy and safety of onabotulinumtoxinA for the prevention of chronic migraine: COMPEL study. *J Headache Pain.* 2018;19(1):1-12. 32. Winner PK, Blumenfeld AM, Eross EJ, et al. Long-term safety and tolerability of onabotulinumtoxinA treatment in patients with chronic migraine: results of the COMPEL study. *Drug Saf.* 2019;42(8):1013-1024. 33. Blumenfeld AM, Stark RJ, Freeman MC, Orejudos A, Manack Adams A. Long-term study of the efficacy and safety of onabotulinumtoxinA for the prevention of chronic migraine: COMPEL study. *J Headache Pain.* 2018;19(1):1-12. 34. Schwedt TJ, Lee J, Knievel K, et al. Real-world persistence and costs among patients with chronic migraine treated with onabotulinumtoxinA or calcitonin gene-related peptide monoclonal antibodies. *J Manag Care Spec Pharm.* 2023;29(10):1119-1128. 35. Blumenfeld A, Silberstein SD, Dodick DW, Aurora SK, Turkel CC, Binder WJ. Method of injection of onabotulinumtoxinA for chronic migraine: a safe, well-tolerated, and effective treatment paradigm based on the PREEMPT clinical program. *Headache.* 2010;50:1406-1418. 36. Blumenfeld AM, Silberstein SD, Dodick DW, Aurora SK, Brin MF, Binder WJ. Insights into the functional anatomy behind the PREEMPT injection paradigm: guidance on achieving optimal outcomes. *Headache.* 2017;57(5):766-777. 37. Standring S, ed. *Gray's Anatomy: The Anatomical Basis of Clinical Practice.* 42th ed. Churchill Livingstone; 2016. 38. Simpson DM, Hallet M, Ashman EJ, et al. Practice guideline update summary: botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache. *Neurology.* 2016;86(19):1818-1826. 39. Gronseth GS, Cox J, Gloss D, et al; on behalf of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *2017 Edition Clinical Practice Guideline Process Manual.* The American Academy of Neurology. Accessed January 29, 2025. https://www.aan.com/siteassets/home-page/policy-and-guidelines/guidelines/about-guidelines/17guidelineprocman_pg.pdf. 40. Charles AC, Digre KB, Goadsby PJ, Robbins MS, Hershey A; American Headache Society. Calcitonin gene-related peptide-targeting therapies are a first-line option for the prevention of migraine: an American Headache Society position statement update. *Headache.* 2024;64(4):333-341.

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