



## Botulinum Neurotoxin for Treating Blepharospasm, Cervical Dystonia, Adult Spasticity, and Headache

This information sheet is provided to help you understand the evidence for using botulinum neurotoxin (BoNT) to treat four neurologic disorders: blepharospasm, cervical dystonia, spasticity in adults, and chronic and episodic migraine. This sheet is a service of the American Academy of Neurology (AAN).

The AAN is the world's largest association of neurologists and neuroscience professionals. Neurologists are doctors who identify and treat diseases of the brain and nervous system. The AAN is dedicated to promoting the highest quality patient-centered neurologic care.

Experts from the AAN carefully reviewed the available scientific studies on using BoNT for treating these four neurologic disorders. The following information\* is based on evidence from those studies. The information summarizes the main findings of the 2016 AAN guideline update on BoNT use for treating these disorders. This guideline update was published in *Neurology*® online on April 18, 2016. It appears in the May 10, 2016, *Neurology* print issue.

The guideline updates parts of three 2008 AAN guidelines on BoNT use in neurologic disorders:

- *"Botulinum Neurotoxin for the Treatment of Movement Disorders"*
- *"Botulinum Neurotoxin for the Treatment of Spasticity"*
- *"Botulinum Neurotoxin in the Treatment of Autonomic Disorders and Pain"*

To read the full 2008 guidelines or the 2016 guideline update, visit [AAN.com/guidelines](http://AAN.com/guidelines).

**Drug Warning:** The US Food and Drug Administration (FDA) has issued a warning for use of BoNT products. For more information, visit [fda.gov](http://fda.gov).

### What is BoNT? How does it work?

BoNT is a drug often used to treat certain neurologic disorders. The drug is a toxin made by a specific type of bacteria. This toxin can cause a condition called botulism. Scientists use safe amounts of the toxin to make the drug. The drug works as a nerve blocker, which stops nerves from communicating with muscles or transmitting pain information. However, there may be other ways the drug works in the body. Doctors inject BoNT into the targeted muscles. This helps stop excessive contracting (tightening) of the muscles.

The US Food and Drug Administration (FDA) has approved four forms (formulations) of BoNT for treating certain neurologic disorders. The following table shows the forms and their approved uses.

**Table: BoNT Forms and FDA-approved Uses**

BoNT Form	Brand Name (Manufacturer)	FDA-approved Use <sup>†</sup>
OnabotulinumtoxinA (onaBoNT-A)	Botox (Allergan, Inc., Irvine, CA)	Blepharospasm, cervical dystonia, upper limb spasticity, lower limb spasticity, chronic migraine
AbobotulinumtoxinA (aboBoNT-A)	Dysport (Ipsen Ltd, Paris, France)	Cervical dystonia, upper limb spasticity
IncobotulinumtoxinA (incoBoNT-A)	Xeomin (Merz Pharmaceuticals, Frankfurt, Germany)	Blepharospasm, cervical dystonia, upper limb spasticity
RimabotulinumtoxinB (rimaBoNT-B)	Myobloc, Neurobloc (US WorldMeds/Solstice Neurosciences, Louisville, KY)	Cervical dystonia

<sup>†</sup>FDA-approved uses for the conditions discussed here. BoNT is also approved for other uses.

## Why does the 2016 guideline update cover just four disorders?

The 2008 guidelines looked at the evidence for BoNT use in these types of neurologic disorders:

- Movement disorders
- Spasticity in children and adults—spasticity occurs in several neurologic disorders
- Autonomic disorders—disorders that affect the automatic processes of the body, such as sweating
- Pain disorders

For the 2016 guideline update, the experts looked at all studies published on this topic since the 2008 guideline publication. These newer studies changed what the experts concluded about the evidence for four neurologic disorders:

- Blepharospasm
- Cervical dystonia
- Spasticity in adults
- Chronic and episodic migraine

The other disorders examined in the 2008 guidelines were not updated. This is because there were not many newer studies at the time the guideline update was initiated that would lead to changes in the conclusions about the evidence. The 2008 guideline recommendations for these other disorders are considered current until reviewed and updated.

## What does the research say about BoNT in these four disorders?

BoNT is generally safe and effective for treating these disorders. In each condition, the evidence level for the different forms may vary. It is important for patients and their families to talk with their doctors about which BoNT form is right for their condition.

### **Blepharospasm**

Blepharospasm is a type of dystonia. Dystonias are movement disorders that cause uncontrollable muscle spasms. In blepharospasm, the muscles around the eyes spasm, causing the eyelids to close uncontrollably. The spasms can interfere with vision. The cause of this disorder is not fully understood. However, experts think that nerves in the brain send faulty messages to the muscles around the eyes.

There is moderate evidence\* that onaBoNT-A and incoBoNT-A can help treat blepharospasm. Weak evidence\* shows aboBoNT-A may be helpful. Doctors commonly use these three BoNT forms to treat blepharospasm.

### **Cervical Dystonia**

Cervical dystonia is a brain disorder that affects the neck muscles. These muscles move uncontrollably or spasm, which can be painful. The spasms also cause abnormal head and neck movements or positions. The person may have sustained movements or jerky movements, or both. The posture of the head and neck may be abnormal. The uncontrollable movements can spread to the shoulders. The cause of cervical dystonia is not yet known.

Strong evidence\* shows that aboBoNT-A and rimaBoNT-B can help treat cervical dystonia. There is moderate evidence\* that onaBoNT-A and incoBoNT-A can be helpful.

The FDA has approved all BoNT forms for treating cervical dystonia. Doctors commonly use BoNT for treating this disorder.

### **Spasticity in Adults**

Spasticity is muscle tightness that interferes with movement. The affected muscles contract or tighten. This tightening gets worse the faster the muscles are pulled or stretched. The affected muscles develop too much tone (tension or resistance). As a result, people with spasticity cannot voluntarily tighten or relax their muscles. They often cannot move in a coordinated and effective way. Spasticity has many causes, including stroke, head or spinal cord trauma, and multiple sclerosis.

In the studies examined here, there is evidence that BoNT has an effect on muscle tone. It can help the ability to position limbs and to clean and wash oneself. It can also reduce pain. However, it is not clear if BoNT can help people actively use their limbs.

In upper limb spasticity, strong evidence\* shows that aboBoNT-A, incoBoNT-A, and onaBoNT-A can help reduce excess muscle tone. There is moderate evidence\* that rimaBoNT-B can be helpful. In lower limb spasticity, strong evidence\* shows that aboBoNT-A and onaBoNT-A can help reduce muscle tone. There is not enough evidence\* to show if incoBoNT-A or rimaBoNT-B can be helpful.

A 2010 AAN guideline looks at the evidence for BoNT in spasticity in children. To read the findings of that guideline, visit [AAN.com/guidelines](http://AAN.com/guidelines).

## Chronic and Episodic Migraine

Migraine is a subset of headache disorders. It involves recurring headaches. Each headache may last from four hours to two days. Throbbing head pain is a primary symptom. Other symptoms may include nausea (upset stomach), vomiting, and extreme sensitivity to light or sound. Most people with migraine have attacks that happen repeatedly. In some people, the headaches can be triggered by certain foods, drinks, or odors. Stress and release from stress may also trigger migraine attacks.

In chronic migraine, attacks happen 15 days or more monthly for three months or longer. At least eight of those attacks include other migraine symptoms. The attacks last four hours or longer. In episodic migraine, attacks happen less often than in chronic migraine.

In chronic migraine, there is evidence that onabotulinumtoxin A (onabotA) can help reduce how often headaches happen. This evidence is based on studies that compared a botulinum toxin (BoNT) injection to a placebo injection. A placebo is a harmless substance used for comparison with an actual therapy. In these studies, the placebo was an inactive form of the drug.

The evidence in these studies is rated as strong\* because the studies are well designed. However, the studies show that the drug has only a small impact on how often headaches happen. In the four weeks after BoNT treatment, people had about 15 percent fewer days of headache compared with placebo.

There is moderate evidence\* that onabotA can lessen the impact of headache on the person's quality of life.

There is strong evidence\* that onabotA does **not** help treat episodic migraine.

## How can I know the best BoNT dose to use?

The best BoNT dose for each disorder is not yet known. In studies of BoNT, certain doses are used for treating various disorders. However, sometimes doctors decide to modify these doses. They base these decisions on their clinical experience with the drug or the needs of an individual patient. More research is needed on this important topic.

## This guideline was endorsed by the American Association of Neuromuscular & Electrodiagnostic Medicine and by the American Society of Plastic Surgeons.

\*After the experts review all of the published research studies, they describe the strength of the evidence supporting each recommendation:

*Strong evidence* = more than one high-quality scientific study

*Moderate evidence* = at least one high-quality scientific study or two or more studies of a lesser quality

*Weak evidence* = the studies, while supportive, are weak in design or strength of the findings

*Not enough evidence* = either different studies have come to conflicting results or there are no studies of reasonable quality

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