LEADING WITH EXPERIENCE: EFFICACY

“Getting some mobility back, gave me momentum to do what I love”

PrBOTOX® (onabotulinumtoxinA) is indicated[1]:

- In the management of focal spasticity, including the treatment of upper limb spasticity associated with stroke in adults
- For the symptomatic treatment of lower limb spasticity associated with stroke in adults

Allergan
an AbbVie company

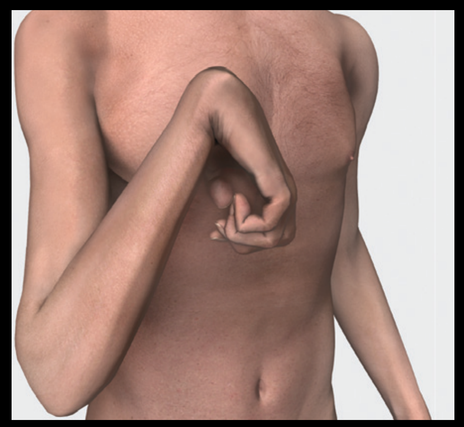
BOTOX®
onabotulinumtoxinA

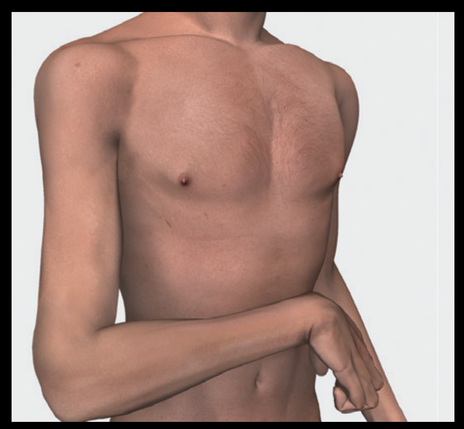
BOTOX®

EFFICACY YOU CAN RELY ON

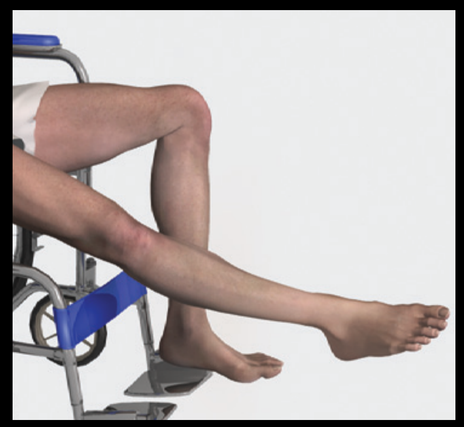
Demonstrated efficacy in:

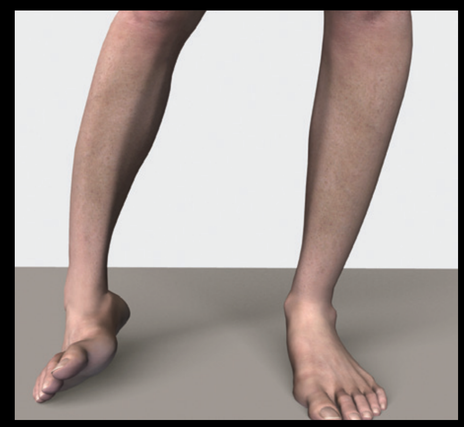
Upper limb post-stroke spasticity

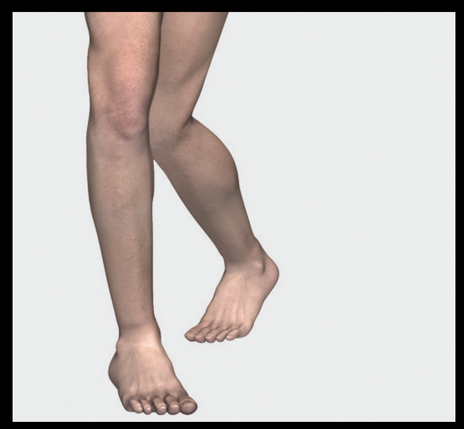


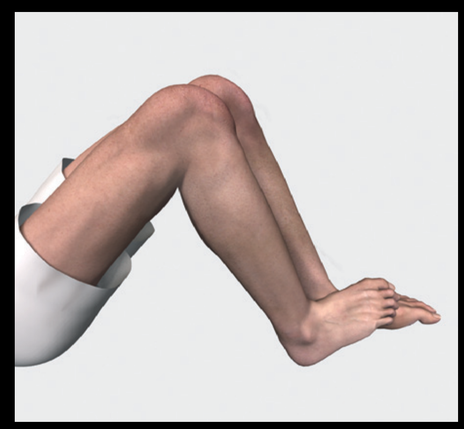


Lower limb post-stroke spasticity









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BOTOX® REDUCED MUSCLE TONE, IMPROVED QUALITY OF LIFE AND DEMONSTRATED GREATER FUNCTIONAL GOAL ACHIEVEMENT[1,2]*

CHANGES IN MEAN SCORES ON THE ASHWORTH SCALE AT WEEK 12 FOR THE FOLLOWING THERAPEUTIC TARGETS†:

WRIST FLEXOR

-1.07 with BOTOX® **VS** **-0.31** with placebo (p<0.001)

FINGER FLEXOR

-0.78 with BOTOX® **VS** **-0.12** with placebo (p<0.001)

THUMB FLEXOR

-0.92 with BOTOX® **VS** **-0.31** with placebo (p<0.001)

CHANGES IN MEAN DAS SCORES ON PRINCIPAL THERAPEUTIC TARGET AT WEEK 12:

-0.88 with BOTOX® **VS** **-0.46** with placebo (p=0.002)‡

AS EARLY AS 6 WEEKS:

62% of BOTOX®-treated patients showed improvement in the principal treatment target **VS** **27%** of placebo-treated patients (p<0.001)

62% of patients with wrist and finger spasticity reported improvements toward functional goals at Week 6 (n=62, p<0.001 vs placebo)

Footnotes & References

BOTOX® REDUCED MUSCLE TONE, IMPROVED QUALITY OF LIFE AND DEMONSTRATED GREATER FUNCTIONAL GOAL ACHIEVEMENT[1,2*]

CHANGES IN MEAN SCORES ON THE ASHWORTH SCALE AT WEEK 12 FOR THE FOLLOWING THERAPEUTIC TARGETS[†]:

WRIST FLEXOR

-1.07 with BOTOX® **VS** **-0.31** with placebo

($p<0.001$)

FINGER FLEXOR

CHANGES IN MEAN DAS SCORES ON PRINCIPAL THERAPEUTIC TARGET AT WEEK 12:

-0.88 with BOTOX® **VS** **-0.46** with placebo ($p=0.002$)[‡]

AS EARLY AS 6 WEEKS:

62% **VS** **27%**

CLOSE

* Results from a 3-month, double-blind, placebo-controlled study in which patients with upper limb spasticity post-stroke (n=126) were treated with 200 U to 240 U of BOTOX® into the wrist, finger and thumb flexor muscles. (Brashear *et al*., Intramuscular injection of botulinum toxin for the treatment of wrist and finger spasticity after a stroke; 2002)

† Efficacy was measured using the Ashworth scale – a 5-point scale ranging from 0 (no increase in muscle tone) to 4 (rigid flexion). (Brashear *et al*., Intramuscular injection of botulinum toxin for the treatment of wrist and finger spasticity after a stroke; 2002)

‡ Efficacy was measured using the Disability Assessment Scale (DAS) – a 4-point scale ranging from 0 (no disability) to 3 (severe disability). (Brashear *et al.*, Intramuscular injection of botulinum toxin for the treatment of wrist and finger spasticity after a stroke; 2002)

REFERENCES: 1. BOTOX® Product Monograph, Allergan Inc. October 16, 2018. **2.** Brashear A, Gordon MF, Elovic E, *et al.* Intramuscular injection of botulinum toxin for the treatment of wrist and finger spasticity after a stroke. *N Engl J Med* 2002;347:395–400.

Footnotes & References

BOTOX® REDUCED MUSCLE TONE, IMPROVED QUALITY OF LIFE AND DEMONSTRATED GREATER FUNCTIONAL GOAL ACHIEVEMENT[1,2*]

CHANGE FROM BASELINE IN ANKLE PLANTAR FLEXORS IN MAS SCORE (AVERAGE SCORE AT WEEKS 4 AND 6):

-0.81
with BOTOX®

VS

-0.61
with placebo ($p<0.01$)[†]

AS EARLY AS 6 WEEKS:

53%
of BOTOX®-treated patients achieved ≥1 grade decrease in MAS score

VS

39.3%
of placebo-treated patients ($p\leq0.04$)[†]

Additional treatment into the toe flexors significantly improved ankle tone vs placebo
Change from baseline in ankle plantar flexors in MAS score (average score at Weeks 4 and 6):

-0.98
with BOTOX®

VS

-0.52
with placebo ($p<0.002$)[3‡]

SECONDARY ENDPOINT

Mean CGI scores
(average score at Weeks 4 and 6):

0.86
achieved in BOTOX®-treated patients

VS

0.65
in placebo-treated patients ($p<0.012$)[§]

BOTOX® HELPED SIGNIFICANTLY MORE PATIENTS ACHIEVE THEIR FUNCTIONAL GOALS

>50%
of patients reported significant treatment benefits at Week 16 ($n=28$, $p\leq0.05$ vs placebo)[4]

Footnotes & References

BOTOX® REDUCED MUSCLE TONE, IMPROVED QUALITY OF LIFE AND DEMONSTRATED GREATER FUNCTIONAL GOAL ACHIEVEMENT[1,2*]

CHANGE FROM BASELINE IN ANKLE PLANTAR FLEXORS IN MAS SCORE (AVERAGE SCORE AT WEEKS 4 AND 6):

-0.81
with BOTOX®

VS

-0.61
with placebo ($p<0.01$)†

SECONDARY ENDPOINT

Mean CGI scores
(average score at Weeks 4 and 6):

0.86
achieved in BOTOX®-treated patients

CLOSE

* Results from a randomized, multicentre, double-blind, placebo-controlled study including 468 post-stroke patients (233 BOTOX® and 235 placebo) with ankle spasticity. Patients received 300 to 400 units of BOTOX®. (Wein *et al.*, OnabotulinumtoxinA for the treatment of poststroke distal lower limb spasticity: A randomized trial; 2018)

† Efficacy was measured using the Modified Ashworth Scale (MAS) – a 5-point nominal scale using subjective clinical assessments of tone ranging from 0 (no increases in tone) to 4 (limb rigid in flexion or extension [abduction/adduction]). Patients were followed for 12 weeks. (Wein *et al*., OnabotulinumtoxinA for the treatment of poststroke distal lower limb spasticity: A randomized trial; 2018)

‡ Results from a multicentre, randomized, double-blind, phase 3 placebo-controlled trial in which patients with post-stroke lower limb spasticity (n=468) were randomized to receive BOTOX® (300 U, mandatory ankle plantar flexors; ≤100 U into optional lower-limb muscles) or placebo (n=235). (Esquenazi, *et al.*, Optimal muscle selection for OnabotulinumtoxinA injections in poststroke lower-limb spasticity: A randomized trial; 2019)

§ The Clinical Global Impression (CGI) employs a 9-point scale from -4 (very marked worsening) to +4 (very marked improvement). (BOTOX® Product Monograph; 2018)

REFERENCES: 1. BOTOX® Product Monograph, Allergan Inc. October 16, 2018. **2.** Wein T, Esquenazi A, Jost WH, *et al.* OnabotulinumtoxinA for the treatment of poststroke distal lower limb spasticity: A randomized trial. *PM R* 2018;10:693–703. **3.** Esquenazi A, Wein TH, Ward AB, *et al.* Optimal muscle selection for OnabotulinumtoxinA injections in poststroke lower-limb spasticity: A randomized trial. *Am J Phys Med Rehabil* 2019;98:360–368. **4.** Data on file. Allergan.

Footnotes & References

Clinical use:

Studies specifically designed to determine the dose in elderly patients have not been performed. Dosages for the elderly are as for other adults. Initial dosing should begin at the lowest recommended dose for the specific indication.

The safety and effectiveness of BOTOX® in the management of focal spasticity, including the treatment of upper and lower limb spasticity associated with stroke has not been investigated in children and adolescents under 18 years of age.

Contraindications:

- Patients who are hypersensitive to any botulinum toxin type A or to any ingredient in the formulation or component of the container
- The presence of infection at the proposed injection site(s)

Most serious warnings and precautions:

Not interchangeable: The term "Allergan unit" upon which dosing is based is a specific measurement of toxin activity that is unique to Allergan's formulation of botulinum toxin A. Therefore, the "Allergan units" used to describe BOTOX® activity are different from those used to describe that of other botulinum toxin preparations and the units representing BOTOX® activity are not interchangeable with other products.

Appropriate qualifications and experience: BOTOX® should only be given by physicians with the appropriate qualifications and experience in the treatment and the use of required equipment.

Follow the recommended dosage and frequency of administration for BOTOX®.

Distant spread of toxin effect: 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 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 occur in adults, particularly in those patients who have underlying conditions that would predispose them to these symptoms.

Other warnings and precautions:

- Serious adverse events including fatal outcomes have been reported in patients who had received BOTOX® injected directly into salivary glands, the oro-lingual-pharyngeal region, esophagus and stomach; some patients had pre-existing dysphagia or significant debility
- Pneumothorax associated with injection procedure has been reported following administration near the thorax; caution is warranted when injecting in proximity to the lung, particularly the apices
- Caution should be used when BOTOX® is used in the presence of inflammation at the proposed injection site(s) or when excessive weakness or atrophy is present in the target muscle
- Muscle weakness remote to the site of injection and other serious adverse effects (e.g. dysphagia, aspiration pneumonia) have been rarely reported in both pediatric and adult patients, in some cases associated with a fatal outcome
- Patients with a history of underlying neurological disorders, dysphagia and/or aspiration should be treated with extreme caution. The botulinum toxin product should be used under specialist supervision in these patients and only if the benefit is considered to outweigh the risk
- Patients or caregivers should be advised to seek immediate medical care if swallowing, speech or respiratory disorders arise
- Cardiovascular events: There have been reports following administration of botulinum toxin of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. The exact relationship with BOTOX® is unknown
- Immune: Formation of neutralizing antibodies to botulinum toxin A may reduce the effectiveness of BOTOX® treatment by inactivating the biological activity of the toxin
- Anaphylactic reactions: As with all biologic products, an anaphylactic reaction may occur, necessary precautions should be taken and epinephrine should be available
- Neurologic: Extreme caution should be exercised with administering BOTOX® to individuals with peripheral motor neuropathic disorders or neuromuscular junction disorders. These patients may be at increased risk of clinically significant systemic effects including severe dysphagia and respiratory compromise from typical doses of BOTOX®, in some cases requiring placement of a gastric feeding tube. When exposed to very high doses, patients with neurologic disorders (e.g., pediatric cerebral palsy or adult spasticity) may also be at increased risk of clinically significant systemic effects
- New onset or recurrent seizures have been reported, typically in patients who are predisposed to experiencing these events
- Skin: As is expected for any injection procedure, localized pain, inflammation, paresthesia, hypoaesthesia, tenderness, swelling/edema, erythema, localized infection, bleeding and/or bruising have been associated with the injection
- Special populations: BOTOX® should not be used during pregnancy unless clearly necessary. Caution should be exercised when BOTOX® is administered to a nursing woman

For more information:

Please consult the Product Monograph at: https://pdf.hres.ca/dpd_pm/00047832.PDF for important information relating to adverse reactions, interactions and dosing information which have not been discussed in this piece.

The Product Monograph is also available by calling: 1-800-668-6424.

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