

# Botulinum Neurotoxins and Non-Medical Switching



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**Imagine living with the debilitating pain of chronic migraine, the annoyance of excessive perspiration, or the embarrassment of involuntary neck twisting and jerking. Patients who experience these conditions may benefit from treatment with a biologic.**

Derived from living organisms or cells, biologics are innovative therapies that physicians typically infuse or inject at their office or a medical facility. One group of biologics that treats conditions caused by overactive muscle movement or hyperactive nerves is called “botulinum neurotoxin.”

Targeted and often life-changing, biologics can also be expensive. This has led some health plans to change their coverage rules to drive stable patients from one botulinum neurotoxin to another that's less expensive for the insurer. The tactic, known as non-medical switching, is problematic for several reasons.

# Understanding Botulinum Neurotoxins

Botulinum neurotoxins are targeted medicines, injected directly into the muscle or skin. They relax overactive muscles or glands, allowing patients to manage their condition.

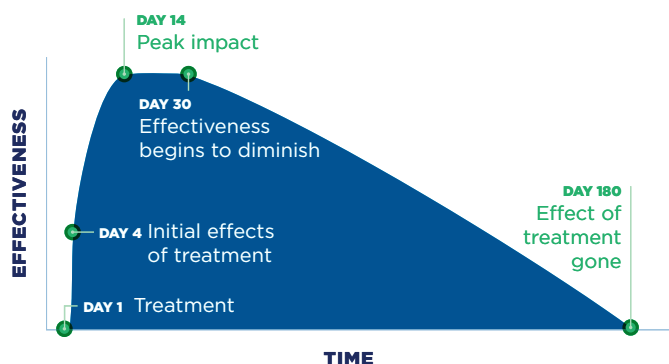
The medications take effect gradually. A botulinum neurotoxin typically takes three to five days before a patient begins to feel its effect, and peak impact typically occurs about two weeks after treatment. But relief is temporary.

Depending upon the specific medication and dosing, they can be effective for as many as six months. However, the effects are typically helpful for about three months and then repeat treatment is needed.

In the United States, patients and physicians have a choice of four botulinum neurotoxins, depending upon condition. Each botulinum neurotoxin is distinct, and each received independent approval from the Food and Drug Administration.

While a few botulinum neurotoxins are approved to treat the same conditions, they are not interchangeable. The products may vary in dose, efficacy, duration of effect and immunogenicity for patients. There is no accepted conversion between products. In fact, the FDA requires a “non-interchangeability” clause in the label of all four available botulinum neurotoxins. It specifies the botulinum neurotoxins can be neither “compared nor converted into units of any other botulinum toxin products.”<sup>1</sup> So switching requires physicians to restart the process of determining the optimal dose for each patient.





## ARC OF TREATMENT RELIEF



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## BOTULINUM NEUROTOXINS APPROVED FOR USE IN THE UNITED STATES

NAME*	DOSING	FDA APPROVED INDICATIONS
OnabotulinumtoxinA	 Measured by <b>TENS</b> of units	Overactive bladder Urinary incontinence Chronic migraine Spasticity in adults Cervical dystonia Axillary hyperhidrosis Blepharospasm Strabismus
RimabotulinumtoxinB	 Measured by <b>THOUSANDS</b> of units	Cervical dystonia
AbobotulinumtoxinA	 Measured by <b>HUNDREDS</b> of units	Cervical dystonia Glabellar lines Upper limb spasticity in adults Lower limb spasticity in pediatrics
IncobotulinumtoxinA	 Measured by <b>TENS</b> of units	Cervical dystonia Blepharospasm Glabellar lines

*\*Listed in order of FDA approval*

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## Non-Medical Switching

The biochemical materials and complex manufacturing process used to make botulinum neurotoxins mean they, like most biologics, are costlier than conventional chemically synthesized drugs. Therefore, despite the fact that botulinum neurotoxins are not interchangeable, they have become targets of health plans' strategy to cut costs through non-medical switching.

Non-medical switching occurs when insurance companies compel stable patients to change to an insurer-preferred medication. In some cases, insurers or their pharmacy benefit managers negotiate with manufacturers to secure rebates or step discounts on the cost of the medications. The botulinum neurotoxin with the highest rebate becomes the insurer's preferred option. Insurers then take multiple steps in attempt to force patients to that particular medication.

This can happen in several different ways. Some insurers cut a medication from their formulary, meaning they opt not to cover it at all.

This is an attempt to force patients to switch to the insurer-preferred botulinum neurotoxin.

Or, insurers can place certain botulinum neurotoxins on a higher tier in their formulary of approved drugs. That is, health plans designate only one botulinum neurotoxin as "preferred" and place the others on a higher tier. The higher the tier, the higher the out-of-pocket cost for patients.

Formulary changes like these force patients to make a difficult choice. Patients can either pay out of pocket to keep using the botulinum neurotoxin prescribed by their physician, or they can disrupt their course of care by switching to the insurer-preferred product.



# Challenges Caused by Non-Medical Switching

For insurance companies, non-medical switching comes down to cost savings. For patients and physicians, however, the tactic can present several problems.



## Physician-Patient Relationship Breach

Through non-medical switching, insurance companies disrupt the care plan patients and physicians established together. Non-medical switching undermines the physicians' medical expertise and can create a rift in the physician-patient relationship.



## Interrupted Course of Care

When insurers require established patients to switch botulinum neurotoxins, they are forcing them from an effective treatment regimen. A switch often requires the physician to administer a different dose of the new product and then adjust the injections over months to identify an ideal dose and pattern of injection for the new product. Patients and physicians must also monitor for newly developing side effects that were not occurring with the established medication and dose. These are all unnecessary steps, especially when considering that the patient and physician could simply continue using the medication they have already established as safe and effective.



## Underdosing

Non-medical switching introduces the risk of underdosing, which can affect quality of life by causing the patient to miss out on the intended benefit and suffer inadequate pain control. This is especially problematic for those with chronic migraine, cervical dystonia or spasticity.



## Excessive Dosing

Excessive dosing can also lead to complications. For example, for patients receiving treatment in their neck for cervical dystonia, effects of switching medications can include excessive neck weakness. In extreme cases, patients can experience difficulty swallowing or choking.



## Opportunity for Errors

Non-medical switching also challenges physicians. Just as an artist specializes in one medium or a marathon runner wears a certain brand of shoes, so too do physicians become more comfortable with their preferred botulinum neurotoxin. Switching between products forces physicians to recalculate the patient's medication dose, thus creating the opportunity for medical errors.



## Potential Declining Response to Treatment

Patient response to treatment could decline because of changing products. It is possible for patients to become immune to one or more types of botulinum toxin. When this occurs, the patient may no longer receive any benefit from their treatment. For this reason, some physicians are concerned about the potential effect of multiple switches on immunogenicity.



## Potentially Higher Health Care Expenditures

Research suggests that non-medical switching can lead to higher non-drug costs due to hospitalizations, lab work and additional physician visits. Analysis of commercial claims data found patients who experienced multiple medication changes saw "higher average non-drug costs downstream,"<sup>2</sup> thus demonstrating lower medication cost does not necessarily translate to reduced expenses.



## Conclusion

Innovative biologics like botulinum neurotoxins have revolutionized patient care. Collectively, they are remarkably safe and effective for treating a wide range of conditions.

Patients and their physicians have come to rely on botulinum neurotoxins as their choice for relief from symptoms that are often painful, annoying and, in some cases, embarrassing. Effectively treating these and other symptoms with botulinum neurotoxins allows patients to fully live their lives, care for their families and contribute to their communities.

While a few of the products available in the United States are approved to treat the same conditions, each botulinum neurotoxin is unique. Non-medical switching not only disregards differences in dosing but it also undermines physicians' ability to exercise their best medical judgment. The tactic can also disrupt patient care, unnecessarily interrupting an established and effective treatment plan.



## References

1. Brin, M F, James, C, and Maltman, Jo. "Botulinum toxin type A products are not interchangeable: a review of the evidence." Dove Press, 2014, October 6, DOI: <https://doi.org/10.2147/BTT.S65603>
2. Institute for Patient Access. "Cost-motivated treatment changes & non-medical switching." August 2017. Available from: [https://instituteforpatientaccess.org/wp-content/uploads/2018/05/IfPA\\_Non-Medical-Switching-Commercial-Claims-Analysis\\_Aug-2017.pdf](https://instituteforpatientaccess.org/wp-content/uploads/2018/05/IfPA_Non-Medical-Switching-Commercial-Claims-Analysis_Aug-2017.pdf)

### ABOUT THE AUTHORS

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