BOTOX® onabotulinumtoxinA injection

CHRONIC MIGRAINE

BOTOX® for Chronic Migraine?

is it time to get started?

BOTOX® prevents headaches in adults with Chronic Migraine: 15 or more headache days a month, each lasting 4 hours or more. BOTOX® is not approved for 14 or fewer headache days a month.

BOTOX® prevents, on average, 8 to 9 headache days and migraine/probable migraine days a month (vs 6 to 7 for placebo).

It's time to think differently about how you treat your Chronic Migraine.

It's time to talk to your doctor about BOTOX® and ask if samples are available.†

in a survey,

92%

of current BOTOX® users wish they'd talked to their doctor and started treatment sooner!*

and

97%

of current BOTOX® users plan to keep using it!*

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.

text SAVE to 27747‡

you may pay

$0

BOTOXChronicMigraine.com

*2020 BOTOX® Chronic Migraine Patient Market Research BOTOX® Current Users (n=71).
†Only a doctor can determine if BOTOX® is right for you. Sample availability may vary by provider or location.

‡See Privacy & Terms: http://bit.ly/2RvxiWr. Message & data rates may apply. Message frequency may vary. Text HELP for help or STOP to end.

Indication

BOTOX® is a prescription medicine that is injected to prevent headaches in adults with chronic migraine who have 15 or more days each month with headache lasting 4 or more hours each day in people 18 years or older.

It is not known whether BOTOX® is safe and effective to prevent headaches in patients with migraine who have 14 or fewer headache days each month (episodic migraine).

IMPORTANT SAFETY INFORMATION

BOTOX® may cause serious side effects that can be life threatening. Get medical help right away if you have any of these problems any time (hours to weeks) after injection of BOTOX®:

- **Problems swallowing, speaking, or breathing,** due to weakening of associated muscles, can be severe and result in loss of life. You are at the highest risk if these problems are pre-existing before injection. Swallowing problems may last for several months
- **Spread of toxin effects.** The effect of botulinum toxin may affect areas away from the injection site and cause serious symptoms including: loss of strength and all-over muscle weakness, double vision, blurred vision and drooping eyelids, hoarseness or change or loss of voice, trouble saying words clearly, loss of bladder control, trouble breathing, and trouble swallowing

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

Allergan
an AbbVie company

Summary of Information about BOTOX® (onabotulinumtoxinA)

What is the most important information I should know about BOTOX®?

BOTOX® may cause serious side effects that can be life threatening. Call your doctor or get medical help right away if you have any of these problems any time (hours to weeks) after injection of BOTOX®:

- **Problems swallowing, speaking, or breathing,** due to weakening of associated muscles, can be severe and result in loss of life. You are at the highest risk if these problems are pre-existing before injection. Swallowing problems may last for several months
- **Spread of toxin effects.** The effect of botulinum toxin may affect areas away from the injection site and cause serious symptoms including: loss of strength and all-over muscle weakness, double vision, blurred vision and drooping eyelids, hoarseness or change or loss of voice, trouble saying words clearly, loss of bladder control, trouble breathing, and trouble swallowing

There has not been a confirmed serious case of spread of toxin effect away from the injection site when BOTOX® has been used at the recommended dose to treat Chronic Migraine.

BOTOX® may cause loss of strength or general muscle weakness, vision problems, or dizziness within hours to weeks of taking BOTOX®. **If this happens, do not drive a car, operate machinery, or do other dangerous activities.**

BOTOX® dosing units are not the same as, or comparable to, any other botulinum toxin product.

What is BOTOX®?

BOTOX® is prescription medicine a medical professional injects into muscles to prevent headaches in adults with chronic migraine who have 15 or more days each month with headache lasting 4 or more hours each day in people 18 years and older.

It is not known whether BOTOX® is safe or effective to prevent headaches in people with migraine who have 14 or fewer headache days each month (episodic migraine).

Who should not receive BOTOX®?

Do not receive BOTOX® if you are: allergic to any of the ingredients in BOTOX® such as botulinum toxin type A and human serum albumin; had an allergic reaction to another botulinum toxin product such as Myobloc® (rimabotulinumtoxinB), Dysport® (abobotulinumtoxinA), or Xeomin® (incobotulinumtoxinA); or have a skin infection at the planned injection site.

What should I tell my doctor before treatment?

Tell your doctor about all your muscle or nerve conditions, such as amyotrophic lateral sclerosis (Lou Gehrig's disease), myasthenia gravis, or Lambert-Eaton syndrome, as you may be at increased risk of serious side effects.

Tell your doctor if you have or have had breathing problems such as asthma or emphysema; swallowing problems; bleeding issues; plan to or have had surgery; have forehead muscle weakness such as trouble raising your eyebrows; drooping eyelids; or any changes to your face.

Tell your doctor if you are pregnant, plan to become pregnant, are breastfeeding or plan to breast feed. It is not known if BOTOX® (onabotulinumtoxinA) can harm your unborn baby or if BOTOX® passes into breast milk.

What Are Common Side Effects?

The most common side effects include neck pain; headache; migraine; slight or partial facial paralysis; drooping eyebrows; eyelid drooping; bronchitis; musculoskeletal stiffness; muscular weakness; pain in 1 or more muscles, ligaments, tendons, or bones; muscle spasms; injection site pain; and high blood pressure. Other side effects have been reported including allergic reactions e.g. itching, rash, red itchy welts, wheezing, asthma symptoms, or dizziness or feeling faint.

These are not all of the possible side effects. Call your doctor for medical advice if you experience any side effects after treatment with BOTOX®.

What Should I Tell My Doctor About Medicines and Vitamins I Take?

Using BOTOX® with certain other medicines may cause serious side effects. **Do not start any new medicines until you have told your doctor that you have received BOTOX® in the past.** Tell your doctor if you have received an injection with another botulinum toxin product in the last 4 months, such as Myobloc®, Dysport®, or Xeomin®. Be sure your doctor knows which product you received.

Tell your doctor about all prescription and over-the-counter medicines, vitamins and herbal supplements you take; recent antibiotic injections; anticholinergics; muscle relaxants; allergy or cold medicine; sleep medicine; aspirin-like products; and blood thinners. **Ask your doctor if you are not sure whether your medicine is listed above.**

To Learn More

If you would like more information, talk to your doctor and/or go to BotoxChronicMigraine.com for full Product Information.

You may report side effects to the FDA at www.fda.gov/medwatch or call 1-800-FDA-1088.

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Dysport® is a registered trademark of Ipsen Biopharm Limited Company.

Xeomin® is a registered trademark of Merz Pharma GmbH & Co KGaA

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Optimal Pharmacologic Treatment of Acute Migraine Headache

Matching medication to headache intensity

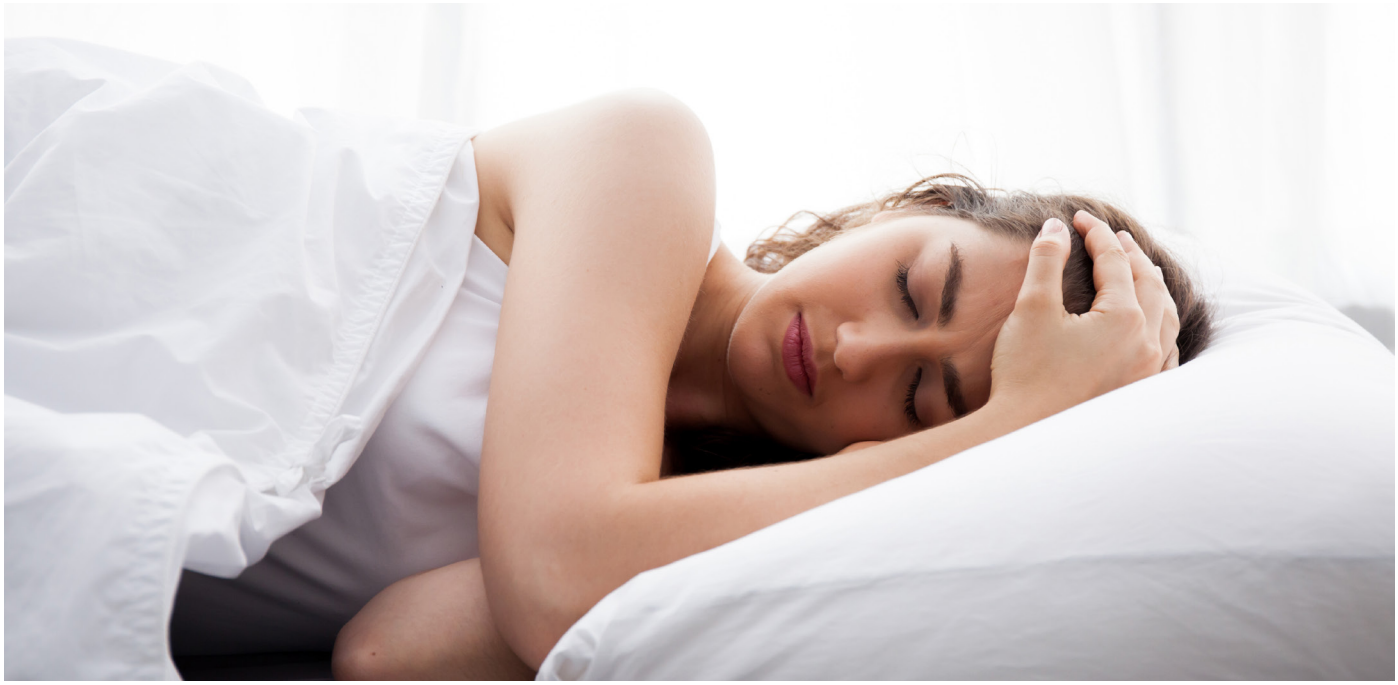
As most migraineurs know well from personal experience, not all migraine episodes are created equal.

For those 20 to 25% of the migraine population who at least occasionally have migrainous aura, an episode of migraine may involve only aura and no headache whatsoever. Or perhaps only aura and prominent *postdrome*, that final phase of a migraine episode which, for those who have had the experience, closely resembles a hangover.

We often tell our patients that migraine is the "Baskin Robbins of headache", as the headache of migraine comes in a wide variety of flavors that range from the "classic" severe and pounding half a head headache to much lower intensity and all over the head pain that is identical to the discomfort described by individuals with tension-type headache. And everything in between.

If migraine episodes are so varied in their symptomatology and their clinical course, it only makes sense that most migraineurs will require more than one medication to treat those various types of headache effectively. Injectable sumatriptan may be a magnificent self-administered therapy for "rescue" from your most severe migraine headaches, but it makes little sense to inject sumatriptan for a migraine headache that is in its early stages and involves headache of much milder intensity.

So what is the best strategy? In your arsenal of weapons for acute migraine treatment have a medication which is capable of terminating a migraine episode when the headache is still in the early stages of development and mild in intensity. If you are tolerant of nonsteroidal anti-inflammatory drugs (NSAIDs), then try an adequate dose of, say, naproxen sodium or ibuprofen, and consider washing down your oral medication with a caffeinated beverage. If NSAIDs play havoc with your gastrointestinal track, try an adequate



> **...match the medication chosen to the level of headache intensity**

dose of acetaminophen instead. In any event, save the limited supply of your favorite oral triptan, rimigepant (*Nurtec*), ubrogepant (*Ubrelvy*) or lasmiditan (*Reyvow*) for headaches that are more biologically and clinically advanced.

Any of those last mentioned medications is appropriate for "headache on the rise... meaning a headache that has progressed despite your first line therapy (e.g., naproxen sodium and caffeine) or is escalating so rapidly in intensity that it may be best to skip your early/mild migraine headache therapy and go to the next step. If your medication of choice for headache "on the rise" is a triptan, there is wide clinical experience and some limited research data to suggest that combining the triptan with an NSAID (either ibuprofen or naproxen sodium) may be more effective than either medication taking alone. In other words, try a "cocktail" approach: administer a migraine-appropriate dose of the NSAID along with the NSAID and wash them down with your favorite caffeinated beverage. Whether the same "cocktail" approach to using such newer therapies as *Nurtec*, *Ubrelvy* or *Reyvow* is unknown.

If you wake up in the morning and your migraine headache has already reached the stage of being moderate to severe in intensity, orally administrated administered medication may be too slow to catch up with the biologic process generating the migraine and thus incapable of putting your headache "back in the box". The same holds true for headaches that have advanced from a mild to moderate level of intensity to becoming moderate to severe despite levels 1 or 2 of oral therapy. Now you need *speed*, and orally administered medication is not going to give you that rapidity of action. Even after all these years, injectable sumatriptan remains the most effective therapy for "rescue" from migraine headache of moderate to severe intensity. If for whatever reason you find injectable sumatriptan to be less than ideal, very nice alternatives for "rescue" include intranasal zolmitriptan and a relatively new link arrival featured in this issue as a "migraine treatment of the month, intranasal DHE (*Trudhesa*).

In short, from your arsenal of weapons for acute migraine treatment match the medication chosen to the level of headache intensity. Have something on hand for early/mild headache, something for "headache on the rise" and something for "rescue". Don't use a BB gun to treat severe migraine headache, and, alternatively, don't use a guided missile to treat the first inkling of acute migraine headache.

Two commonly asked questions:

If I'm taking a medication for migraine prevention, is it all right for me to continue to use my usual medication for any acute headaches I may have?

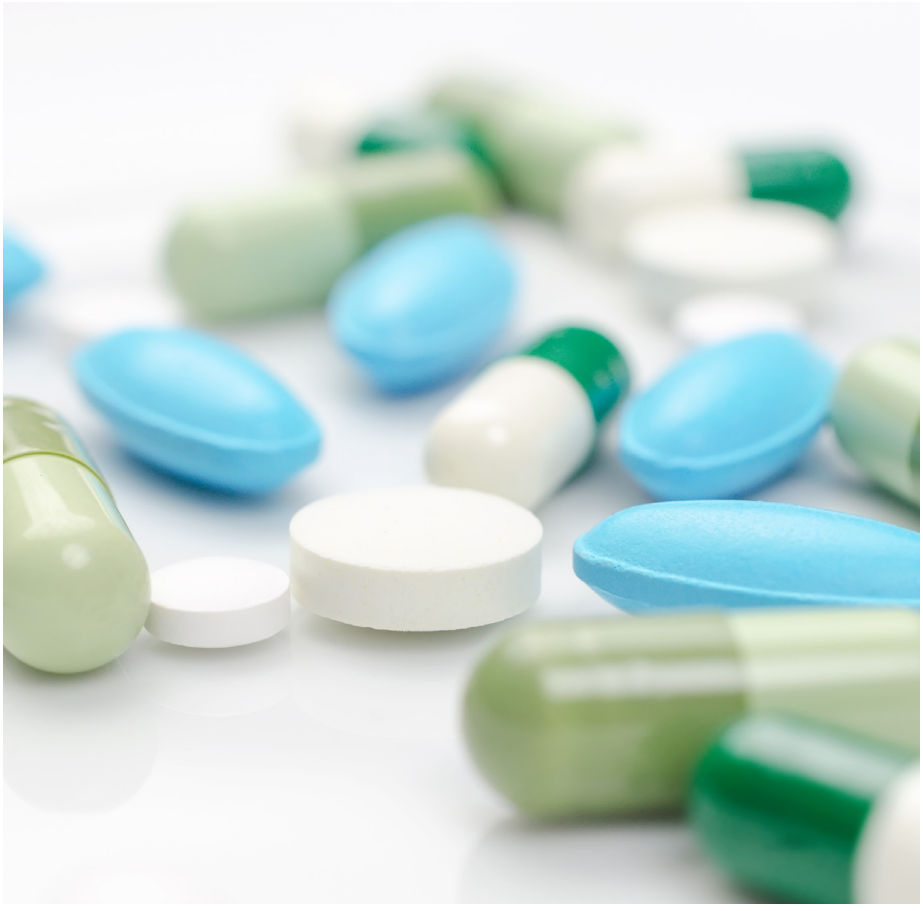
Absolutely! If your migraine burden has increased to the point that a course of prevention therapy for stabilization is indicated, rapidly and effectively treating any acute "breakthrough" headaches that

occur will play a key supporting role in reducing the hypersensitivity of the nervous system's biologic circuitry that is generating your headaches. Prolonged episodes of severe migraine headache will work against the prevention medication's effort to desensitize that circuitry, and snuffing out an acute migraine headache early, soon after it ignites, will assist the prevention medication in the desensitization effort. Rarely is a prevention medication so effective that it entirely eliminates migraine episodes. Expect "breakthrough" headaches, and treat them aggressively.

But I'm having headaches almost every day. If I use medication to treat every one of those headaches, won't I start having rebound headaches? Treat acute migraine episodes aggressively but don't overuse acute medication? How can I manage to do both?

An excellent question. Medication overuse headache (commonly referred to as "rebound" headache) occurs when a migraineur uses a given medication or class of medications intended for acute migraine treatment so frequently that the overuse itself begins to generate headache that adds to the existing migraine burden. This often happens subtly, without any dramatic escalation of headache but instead with a gradual overall increase in headache burden (see Doctor on Call in this issue for the important distinction between medication overuse headache (MOH) and "rebound" due to early headache recurrence following a temporarily effective acute treatment response).

Ironically, it is the triptans, the first true "designer drugs" for migraine, that appear to have the highest potential for producing MOH and to do so more rapidly than other medications commonly used for acute migraine. Persistent use of a triptan preparation more than 9 days a month is sufficient to cause MOH and thus to amplify the burden imposed by migraine itself. A sneakier culprit is plain old acetaminophen (in such OTC preparations as Tylenol and Excedrin), easily obtainable and, in the short run, often quite helpful in controlling acute headache. taken more than 15 month days a month persistently, however, just as with the triptans, acetaminophen can produce MOH.



"Don't use a BB gun to treat severe migraine headache

So that's the bad news. Especially in the first few weeks following initiation of treatment with a prevention therapy, and especially if you are having headache more days than not, it's difficult not to overuse whatever medication you have been prescribed for acute headache treatment. Two pieces of good news: first, the newer medications for migraine prevention tend to work rapidly for those patients destined to respond, with a positive treatment effect evident as early as the first week, and as the prevention medication desensitizes the migraine circuitry and correspondingly reduces headache burden, the need for acute migraine treatment will progressively decrease; second, even if you are stuck in the swamp of medication overuse headache at the time you begin one of these newer prevention medications, there is compelling evidence that these medications will be just as effective as they would be if MOH was not present. An important caveat to the second point is that not all classes of acute migraine medication are created equal, and there is some evidence to indicate that overuse of opiates/opioids (egs, hydrocodone, oxycodone) or barbiturates (butalbital in particular) may reduce the effectiveness of even the newer prevention medications.