

CHRONIC MIGRAINE

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.[†]

BOTOX[®] for Chronic Migra<u>ine?</u>

is it time to get started?



in a survey, 92% of current BOTOX® users

wish they'd talked to their doctor and started treatment sooner!*

97% of current BOTOX[®] users plan to keep using it!*

and



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



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 $BOTOX^{\otimes}$ 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 \textsc{BOTOX}^{\otimes} on the adjacent page.



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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Myobloc[®] is a registered trademark of Solstice Neurosciences, Inc.

Dysport[®] is a registered trademark of Ipsen Biopharm Limited Company. Xeomin[®] is a registered trademark of Merz Pharma GmbH & Co KGaA



Status Migrainosus: What Do You Do When the Migraine Won't Stop?



t was only 3 days ago when you started developing that familiar pain above your right eyebrow, but it seems more like a month. Telling yourself that maybe this time the pain spontaneously would fade away, for the first few hours you tried to ignore it...but from years of bitter experience you knew better than that. Once this particular ball gets rolling, it's all downhill.

Blend together, say, the onset of your period, a stressful day at work and an annoying dust-up with your partner, and... *voila*! There you have the perfect recipe for an episode of migraine. That faint piercing discomfort is going to settle itself down behind your eye in its favorite location, put up its feet and then merrily turn up the volume. In parallel with the increasing and inescapable pain, a retreat to total darkness will escalate from luxury to necessity. There must be absolute silence. And just the thought of food will bring on the dry heaves.

Meet friends for a drink after work? *Hah!* Prepare dinner? *Forget it!* A romantic makeup with that partner? *There...is...NO...way.*

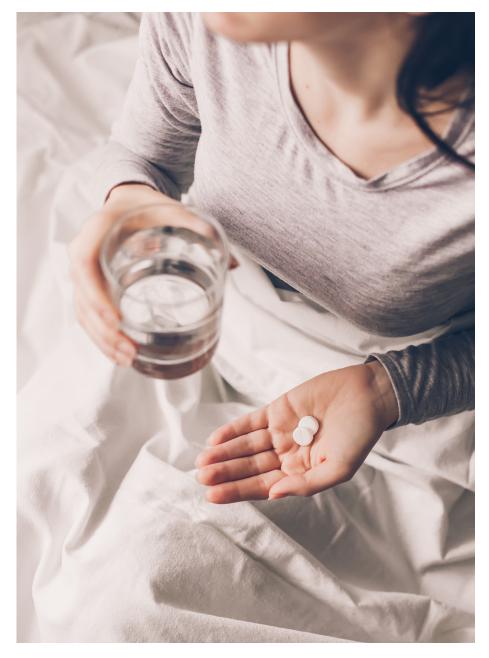
Sound familiar? Most migraineurs have experienced precisely this or something similar, and for many it becomes an all too frequent intrusion that drains away quality of life. Thankfully, in most cases the individual migraine episode is self-limited and, as if grown exhausted by the effort of imposing such dreadful symptoms, ceases spontaneously. Or with sleep. Or, oddly enough, with vomiting. Or with administration of an effective medication.

Not uncommonly, however, a migraine episode will just keep on rolling, and no amount of bedrest, cold compresses, relaxation techniques or medication administered seems to make any real difference. When the individual migraine episode extends to exceed 72 hours in duration, it is referred to as *status migrainosus*.

Aside from the misery you experience from the prolonged headache and

associated symptoms, what is the downside of status migrainosus? We know that a major risk factor for the "transformation" of *episodic* migraine into *chronic* migraine is increasing frequency of migraine episodes. Put simply, if what we term "migraine" represents a genetically hypersensitized biologic circuit within the nervous system that clinically expresses that hypersensitivity by generating migraine symptoms, then the more migraine episodes one experiences, the more active that circuit becomes. If the migraine circuit becomes sufficiently sensitized, the afflicted individual is always on the brink of having a migraine or is acutely symptomatic. That person now has "chronic migraine".

It logically follows that experiencing prolonged episodes of migraine – ie, status migrainosus – accelerates the development of chronic migraine or reinforces chronic migraine once it has developed. Even worse, status migrainosus may <u>directly</u> cause chronic migraine. How long can status migrainosus last? By definition, at least 3 days, but in some unfortunate cases it may *never* stop. What begins as a simple migraine episode persists indefinitely, and



the result is constant headache that may fluctuate in intensity but never entirely remit. For *years*.

While this is a relatively rare occurrence, the risk of status migrainosus directly evolving into chronic migraine underscores the importance of intervening early to terminate the acute migraine episode. "Treat early/treat hard" is the mainstay of <u>all</u> acute migraine treatment. If an attack of acute migraine reflects acute sensitization of an inherently sensitive biologic circuit, then the longer the attack persists (and the more acutely sensitized the circuit becomes), then the more difficult it will be to stop the momentum of that biologic boulder that has picked up speed as it rolls down the hill. Three aspirin and a caffeinated soda taken early for migraine headache can be more effective than intravenous narcotics administered in the emergency room 24 hours later, after the headache has become severe. There is evidence that the most potent self-administered medication for rescue from severe migraine headache, injectable sumatriptan, may lose its effectiveness if treatment is delayed until after the migraine circuit has reached a certain level of acute sensitization.

But what if you do everything right treat early with an adequate dose of an appropriate medication; use a more potent therapy when the headache persists and increases despite early treatment – and the migraine attack stubbornly refuses to back off? What can you do then? The unvarnished truth is: not a whole lot. If you have developed status migrainousus, if your headache is persistent and severe despite optimal selfadministered therapy, you well may require provider-administered therapy to end the attack successfully. Occasionally status migrainosus will respond to a short course of high-dose oral steroid (eg, prednisone 60 mg daily for several days), but often treatment with intravenous medications and hydration will be required. And intravenous therapy typically means an emergency room, an urgent care center or, if you are lucky enough to have one available to you, a "headache rescue room" (more on this later).



The ER is not a great option for obtaining treatment of acute migraine headache. Waits can be long, lights bright and the

The ER is not a great option for obtaining treatment of acute migraine headache. environment noisily chaotic. The providers are unlikely to know you personally, and they may have developed a certain cynicism in regards to patients seeking medication for pain. Even if they are sympathetic to your situation they may be distracted by the critically ill patients in the adjacent exam rooms. Urgent care centers generally are less busy and more convenient than ERs, but they also tend to lack much in the way of therapeutic options.

Whether it's an ER or an urgent care center, you are more likely to experience a positive outcome if you come bearing a treatment plan recommended by your usual headache provider. A note from that provider serves as evidence that someone has made the effort to establish that you have migraine, and the treatment plan the provider recommends will help guide management, avoid delays and maximize the likelihood of a good treatment outcome. One of my patients knows from experience that for her most severe migraine episodes a combination of intravenous hydration, magnesium and a steroid invariably relieves her pain and prevents early headache recurrence. With my note in hand testifying to this, she is received much more positively by a busy ER staff than a similar patient who is unknown and lacking any formal medical records from the treating physician.

Now, what was that about a "headache rescue room"? Some physician offices and clinics that sub-specialize in headache medicine provide their patients with the option of coming in on an urgent/ as needed basis for intravenous infusion therapy when they call to report they are experiencing a severe migraine headache that has resisted self-administered therapy. The "rescue room" may vary from something as simple as a regular exam or procedure room temporarily used to treat the patient with acute migraine to a more elaborate facility involving physically separate space intended exclusively for that purpose. More important than the physical details of the facility utilized is the availability to patients of an attractive alternative to seeking care at an ER or simply suffering in silence at home. In our own "headache rescue room" located within the George Washington University headache clinic patients can be evaluated rapidly by providers who know them and treated with evidence-based intravenous protocols customized to their particular needs and previous experience. The cost involved is a fraction of that associated with an ER visit, and in prospective studies we have found high rates of favorable clinical outcome and patient satisfaction. For more on this topic, see the "Rescue Room" article that follows.

The best treatment for status migrainosus, "the migraine attack that refuses to stop", is to prevent it from developing in the first place by treating the attack early. If the headache persists and worsens despite early treatment, use a self-administered "rescue" medication. If all else fails, seek care at an ER or urgent care center, but do so armed with information provided by your usual headache provider. If you are lucky enough to have access to a "headache rescue room", use it.