



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.



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

Migraine's "Supply: Demand" Problem...and How to Fix it

A public health bottleneck



Very few chronic medical disorders exert more of a negative impact on the public health than does migraine. The World Health Organization ranks migraine second globally on the list of the chronic medical disorders that produce disability and reduce quality of life. For the young female population, migraine is first on that list.

How can this be? Migraine rarely kills or inflicts permanent neurologic, cardiovascular or other systemic injury. After all, it's "just a headache", right?

Wrong. First of all, migraine is often much more than "just a headache", and even

when headache alone is considered, thousands of days of productive living are lost to American citizens each year because of functionally incapacitating migraine headache. If you spend a "migraine day" closeted in a darkened room, unable to function and miserable with pain, nausea and other common accompanying symptoms, for that day you might as well be dead. Each and every day, as many Americans are transiently "dead" with migraine as perished in the entire Vietnam conflict.

Two major factors account for migraine's tremendous impact on public health. First, migraine is astoundingly prevalent.

Approximately 12% of the American population, almost 40 million citizens, have active migraine, and 1 in 50 have [chronic migraine](#) (a variant of the disorder that is associated with a lower quality of life and higher level of healthcare resource utilization than the more common episodic form). With this high prevalence, adding together the emotional, social and economic costs of migraine associated with each individual case yields total sums that are jaw-droppingly high.

Second, despite the tremendous advances made in our understanding of migraine's biology, the emergence of so many new treatments that are effective in managing the disorder, and the efforts that have been made to heighten awareness of migraine in the general population and the community of healthcare providers (HCPs), many millions of migraineurs remain undiagnosed, misdiagnosed, untreated or treated inadequately. Sequential research studies addressing the issue found that the number of American migraineurs seeking and receiving medical care for their headache disorder has not increased substantially.

Of the roughly 40 million Americans with active migraine, how many would benefit from seeing a HCP? This is not a number easily calculated, but data from meticulously conducted epidemiologic research suggest that over 38% percent of migraineurs - about 15 million individuals - currently have a migraine burden sufficient to justify a course of headache prevention therapy; of that subgroup, only about 13% are receiving such therapy. As regards chronic migraine, the common variant of migraine which exerts a disproportionately negative effect on the public health,

results from the CaMEO Study indicated that <5% percent have been evaluated for their headache disorder by an HCP, have received an accurate diagnosis and have been appropriately treated.

Even with our increased knowledge of what causes migraine and the consequent introduction of exciting new “designer drugs” for migraine’s for treatment, many who would benefit from those therapies never see an HCP or do not experience a positive result from their medical evaluation. Granted, not every migraineur requires assistance from an HCP; those who experience a handful of non- incapacitating migraine

“**...we still are making only a modest dent in the public health burden imposed by migraine.**”

episodes annually and whose headaches respond consistently and well to aspirin, acetaminophen or Excedrin typically do not require medical attention. On the other hand, *all* migraineurs with high frequency episodic migraine (9 to 14 headache days per month) or chronic migraine (15 or more days per month) typically do deserve evaluation by an informed HCP, as do most migraineurs with mid-frequency



episodic migraine (4 to 8 headache days per month) or any migraineur who is experiencing functionally incapacitating migraine episodes on a monthly or near monthly basis.

In summary, despite the dramatic increase in migraine awareness and the tremendous improvement in migraine therapeutics that has occurred over the past 30 years, we still are making only a modest dent in the public health burden imposed by migraine.

Why? The potential answers are legion, but difficult to ignore is the medical community’s enduring disinclination to regard migraine as being a medical disorder worthy of attention. This “just a headache” attitude is pervasive amongst HCPs engaged both in medical training and clinical practice. Migraine remains the most common neurologic disorder prompting an individual to seek medical attention and ranks first amongst the

disorders encountered by neurologists working in clinics. Despite this, and even quite recently, I have served as a member of the neurology faculty in medical schools where the curriculum for students and even for neurology residents contained no required formal clinical rotation focused on headache. Too often, headache - and migraine in particular - remains an afterthought within the realm of medical education.

Not surprising then that there exist relatively few physicians with the training, experience and inclination required to manage migraine effectively. Confronting that relative handful of physicians is an enormous population of migraineurs. The result: a staggeringly huge and persisting problem of inadequate supply (physicians) vs overwhelming demand (migraineurs in need of care). It’s like trying to find a nice but inexpensive apartment near Central Park: precious few exist, and the market for such a rarity is vast.

Well-intentioned efforts to increase public awareness of migraine - this magazine serving as an obvious example - will only add fuel to the supply:demand fire. As more and more migraineurs seek medical attention from a static pool of subspecialists, accessibility to care becomes yet more of a problem. At one university medical center where I worked for some years, the wait time for a new patient appointment hovered around one year. This is ridiculous. Especially for chronic migraine, a disorder which appears to become increasingly resistant to effective treatment if such treatment is delayed, imposing a one year waiting period for those migraineurs motivated to seek attention obviously works against therapeutic success and the patient's best interests.

So how can migraine's supply:demand problem be fixed? Even if the existing pool of physicians who specialize in headache worked 24/7, the effect on the supply:demand problem would be negligible. We could increase that pool by training more students and residents to become competent in the practice of headache medicine and, more specifically, by increasing the number of existing post-residency headache fellowship programs. While many would argue that these efforts are likely to bear much fruit, there exists a stubborn resistance to change within the culture of American medical training. Also an obstacle is the fact that economic self interest is drawing medical school graduates to higher-earning specialties such as orthopedic surgery, plastic surgery, cardiology, ophthalmology and gastroenterology rather than neurology... let alone neurology with a subspecialty focus on headache. That's great for those of us who break a bone, require cataract extraction or desire better skin and cosmetic enhancement, but it does nothing to help those 40 million American migraineurs.

The development of telemedicine accelerated dramatically following the onset of the COVID pandemic, and with its strong emphasis on verbal communication telemedicine lends

itself especially well to the practice of headache medicine. Unfortunately, in addressing the supply:demand problem associated with migraine, telemedicine is something of a double-edged sword. While it may be that more patients can be seen more efficiently via telemedicine, any increase in efficiency tends to be balanced by improved access and a corresponding increase in patient volume. Without question, telemedicine has made an invaluable contribution to the practice of headache medicine, but expanding provider access to migraineurs who otherwise might not seek medical attention will not solve the supply:demand problem.

More promising is the prospect of increasing the supply side (ie, the number of providers) by the recruitment of "physician extenders". It seems clear from simple observation that "advanced practice providers" (APPs: nurse practitioners and physician assistants) can be trained to serve as highly effective headache subspecialists. While regulations regarding the degree of supervision required vary widely from state to state, there currently are a number

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of nurse practitioners who manage clinical/clinical research programs in headache at a high level of competence and do so working independent or largely independent of any supervising physician. This has occurred in the absence of any formal, standardized training programs devoted to APPs seeking particular expertise in the



field of headache medicine, and if such programs were established the resulting increase in the number of headache subspecialists available could go a long ways towards helping to resolve headache's supply:demand problem.

Even more intriguing is the prospect of using artificial intelligence (AI) to augment HCP-associated headache management. In a [previous issue](#) of this magazine we described how one electronic algorithm under development at Stanford and UCLA may be effective in both headache diagnosis and in offering patients assistance with migraine management. With continued development such

algorithms could evolve into "smart programs" that learn from experience. As with a human provider, feedback data resulting from implementation of algorithm-generated diagnoses and management plans could be expected progressively to improve the reliability and effectiveness of the program.

Finally, education of patients intended to increase active participation in their own migraine care could relieve much of the management burden currently born by HCPs. As one example, six years ago this magazine was conceived to serve just that purpose: to provide patients with a greater understanding

of migraine and its treatment than they could expect to receive and absorb during the course of a clinic visit. The Table illustrates how this magazine can be put to use to enhance provider:patient communication, improve compliance, increase patient satisfaction and produce a more positive clinical outcome.

Yes, supply:demand is a problem in headache medicine, but there exist these and other creative solutions which can serve to mitigate that problem. Rather than simply moan about existing and impending physician shortages, it's time to get creative. **IV**

Table

Incorporating Migraineur Magazine into the Clinical Management of Patients

Ms.,
It was a pleasure seeing you in clinic today.

The first attachment will take you to the website for ***Migraineur***, our healthcare magazine for individuals with migraine, and the webpage will provide you with open access to all of our issues. I would suggest you start with "Migraine 101" in the Fall 2017 issue for an overview of migraine and its treatment. The feature article for the Spring 2018 issue is on the topic of chronic migraine. The feature article for the Summer 2018 issue concerns medications for migraine prevention. The Spring 2019 issue has a "treatment tip of the month" on the topic of matching acute therapy to the intensity of the acute headache (an issue we discussed that is relevant to your management strategy). PDFs of those issues are attached.

Your diagnosis:

- Chronic daily headache/chronic migraine

Your treatment strategy:

For migraine prevention >

- Qulipta (atogepant) 60 mg daily

For treatment of acute migraine >

- Early/mild intensity headache: naproxen sodium with caffeine
- Headache that is "on the rise" from mild to becoming moderate or severe in intensity: naproxen sodium/caffeine and oral sumatriptan 100 mg
- Your most severe headaches: injectable sumatriptan 4 mg

If you encounter problems or have questions, I can be reached most easily through our patient portal, MyChart. The main number for our clinic is (XXX) XXX-XXXX.

John/Jane Doe, MD