migraineurmagazine.com

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Migraineur

For those who strive to live well despite migraine

PREEMPTIVE THERAPY FOR ACUTE MIGRAINE HEADACHE:

Treatment during the “prodrome”

MIGRAINE PREVENTION THERAPY:

How long is “long enough”?

BOTOX® onabotulinumtoxinA injection

CHRONIC MIGRAINE

BOTOX® for 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).

does it work?

what about cost?

Questions about BOTOX®? It's time to ask your doctor.

INDICATION

BOTOX® (onabotulinumtoxinA) is a prescription medicine that is injected into muscles and used 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 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 preexisting 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; 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 receiving BOTOX. **If this happens, do not drive a car, operate machinery, or do other dangerous activities.**

Do not receive BOTOX if you are allergic to any of the ingredients in BOTOX (see Medication Guide for ingredients); had an allergic reaction to any other botulinum toxin product such as Myobloc® (rimabotulinumtoxinB), Dysport® (abobotulinumtoxinA), or Xeomin® (incobotulinumtoxinA); have a skin infection at the planned injection site.

The dose of BOTOX is not the same as, or comparable to, another botulinum toxin product.

Serious and/or immediate allergic reactions have been reported, including itching; rash; red, itchy welts; wheezing; asthma symptoms; dizziness; or feeling faint. Get medical help right away if you experience symptoms; further injection of BOTOX should be discontinued.

in a survey,

97%

of current BOTOX® users say they plan to keep using it!*(n=71)

and

92%

of current BOTOX® users said they wish they'd talked to a doctor and started sooner!*(n=71)

BOTOX® prevents headaches in adults with Chronic Migraine before they even start.

It's about 10 minutes of treatment once every 3 months.†

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

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.

you may pay

$0

text SAVE to 27747‡

BOTOX® onabotulinumtoxinA injection

CHRONIC MIGRAINE

BOTOXChronicMigraine.com

*2020 BOTOX® Chronic Migraine Patient Market Research BOTOX® Current Users. †BOTOX® injections are given by your doctor. ‡See Privacy & Terms: http://bit.ly/2RvxiWr. Message & data rates may apply. Message frequency may vary. Text HELP for help or STOP to end.

IMPORTANT SAFETY INFORMATION (continued)

Tell your doctor about all your muscle or nerve conditions, such as ALS or Lou Gehrig's disease, myasthenia gravis, or Lambert-Eaton syndrome, as you may be at increased risk of serious side effects, including difficulty swallowing and difficulty breathing from typical doses of BOTOX.

Tell your doctor about all your medical conditions, including if you have or have had bleeding problems; have plans to have surgery; had surgery on your face; have weakness of forehead muscles, trouble raising your eyebrows, drooping eyelids, and any other abnormal facial change; are pregnant or plan to become pregnant (it is not known if BOTOX can harm your unborn baby); are breastfeeding or plan to (it is not known if BOTOX passes into breast milk).

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. 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 received any other botulinum toxin product in the last 4 months; have received injections of botulinum toxin such as Myobloc®, Dysport®, or Xeomin® in the past (tell your doctor exactly which product you received); have recently received an antibiotic by injection; take muscle relaxants; take an allergy or cold medicine; take a sleep medicine; take aspirin-like products or blood thinners.

Other side effects of BOTOX include dry mouth; discomfort or pain at the injection site; tiredness; headache; neck pain; eye problems such as double vision, blurred vision, decreased eyesight, drooping eyelids, swelling of your eyelids, and dry eyes; drooping eyebrows; and upper respiratory tract infection.

For more information, refer to the Medication Guide or talk with your doctor.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see accompanying Summary of Information about BOTOX®.

If you are having difficulty paying for your medicine, AbbVie may be able to help. Visit AbbVie.com/myAbbVieAssist to learn more.

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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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Migraineur

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Special Features

In Every Issue

Editor's Note

Dr. Rothrock is director of neurology advanced practice provider training and professor of neurology at Inova Health and the University of Virginia School of Medicine. He has served as editor of ***Migraineur*** *since the magazine's inception in 2016.*

In 2016, when we first conceived of publishing an "educational, but entertaining" magazine for the 12% of the general population who cope with migraine, our focus was on producing a conventional print magazine and simultaneously to begin developing an electronic version of that magazine which progressively would expand our readership and eventually come to dwarf its print twin in accessibility and readership.

For the first 3+ years of ***Migraineur's*** existence this strategy worked quite well. A pharmaceutical company, Supernus, sponsored production of the magazine, purchased many tens of thousands of copies and mailed those copies to their representatives to provide to the doctors they called upon… who in turn distributed the magazine to their headache patients. It was the essence of a "direct to consumer" distribution model. While we also published an electronic version on the ***Migraineur*** website, the print version was the large rock we tossed into the pool of water, with the electronic version representing the early ripples that eventually would reach the farthest shore.

And then came Covid. Traditional clinic-based in-person care of patients drastically declined, and along with it so did the direct interactions between the representatives of pharmaceutical companies and medical providers. The one-source sponsorship of the magazine we had enjoyed during those early years abruptly ceased.

To contend with this new set of circumstances we pivoted quickly to shift our focus to the electronic version of the magazine and our website. To fund continued production of the magazine we were left with no immediate option but to solicit advertisers to replace the sponsorship that had vanished in lockstep with the pandemic.

And so it has remained for the ensuing 4 years. We have taken pains to maintain a clear distinction between the magazine's content and the promotional material provided by our advertisers, publishing only unbiased articles that are meticulously peer-reviewed by physician headache experts who have no financial ties to the magazine. The boundary between promotional advertising and educational content is strictly maintained.

That said, the stark fact remains that within this brave new world of electronic medical publishing, advertisers favor educational resources which reach a wide audience, yield a high volume of "click- throughs" and downloads and, particularly in the case of ***Migraineur***, maintain a large volume of electronic subscribers. While with our shift of focus to electronic publishing the number of those who read our magazine has increased immensely, with our readership now extending to be international in scope, the magazine's financial viability is intimately linked to to its electronic subscribership. Regular and frequent use of our website and magazine by many thousands of non-subscribers ultimately may raise the standard of care for migraine, but this does little to enhance that viability.

If you enjoy this magazine – if you have found it to be helpful in understanding and managing your headache disorder (and hopefully entertaining as well) – please go a step beyond simply recommending the magazine to others and encourage them to become electronic subscribers. If you are not currently a subscriber…join up!

To subscribe is both easy and free. On the magazine's webpage at migraineurmagazine.com is a "subscribe" option. Click on that option, and it will take no more than 15 seconds for you to become an electronic subscriber. You subsequently will receive emails advising you when a new issue of the magazine is published and providing a direct link to that issue. You also will receive notifications of and links to any blogs posted on our website which will provide access to important new information involving migraine that may arise during the intervals between publication of our quarterly issues, as well as news of interesting conferences, symposia, and other educational initiatives intended for those with migraine or related headache disorders.

Migraineur has come a long way in its 7 years of existence, and the magazine is now considered by many to be the premier educational resource for those seeking to learn more about their headache disorder. Help us continue to help you by subscribing.

John F. Rothrock

John F. Rothrock, MD, Editor in Chief
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QULIPTA™ (atogepant) tablets CAN HELP PREVENT MIGRAINE ATTACKS

Migraine attacks? You can't always avoid triggers, like changes in the weather. QULIPTA™ gets right to work to prevent migraine attacks and keeps them away over time.

In a 3-month study, QULIPTA significantly reduced monthly migraine days.

Ask your healthcare provider about QULIPTA.

WHAT IS QULIPTA?

QULIPTA (atogepant) is a prescription medicine used for the preventive treatment of episodic migraine in adults.

IMPORTANT SAFETY INFORMATION

Before taking QULIPTA, tell your healthcare provider about all your medical conditions, including if you:

- Have kidney problems or are on dialysis
- Have liver problems
- Are pregnant or plan to become pregnant. It is not known if QULIPTA will harm your unborn baby
- Are breastfeeding or plan to breastfeed. It is not known if QULIPTA passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby while taking QULIPTA

Please see Brief Summary of the full Patient Information on the next page.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. QULIPTA may affect the way other medicines work, and other medicines may affect how QULIPTA works. Your healthcare provider may need to change the dose of QULIPTA when taken with certain other medicines.

The most common side effects of QULIPTA are nausea, constipation, and fatigue. These are not all the possible side effects of QULIPTA.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

If you are having difficulty paying for your medicine, AbbVie may be able to help. Visit AbbVie.com/myAbbVieAssist to learn more.

abbvie

QULIPTA™ (atogepant) tablets, for oral use

PROFESSIONAL BRIEF SUMMARY
CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE

QULIPTA is indicated for the preventive treatment of episodic migraine in adults.

CONTRAINDICATIONS

None.

DOSAGE AND ADMINISTRATION

Recommended Dosage

The recommended dosage of QULIPTA is 10 mg, 30 mg, or 60 mg taken orally once daily with or without food.

Dosage Modifications

Dosing modifications for concomitant use of specific drugs and for patients with renal impairment are provided in Table 1.

Table 1: Dosage Modifications for Drug Interactions and for Specific Populations

Dosage Modifications	Recommended Once Daily Dosage
Concomitant Drug *[see Drug Interactions]*	
Strong CYP3A4 Inhibitors	10 mg
Strong and Moderate CYP3A4 Inducers	30 mg or 60 mg
OATP Inhibitors	10 mg or 30 mg
Renal Impairment *[see Use in Specific Populations]*	
Severe Renal Impairment and End-Stage Renal Disease (CLcr <30 mL/min)	10 mg

ADVERSE REACTIONS

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of QULIPTA was evaluated in 1958 patients with migraine who received at least one dose of QULIPTA. Of these, 839 patients were exposed to QULIPTA once daily for at least 6 months, and 487 patients were exposed for 12 months.

In the 12-week, placebo-controlled clinical studies (Study 1 and Study 2), 314 patients received at least one dose of QULIPTA 10 mg once daily, 411 patients received at least one dose of QULIPTA 30 mg once daily, 417 patients received at least one dose of QULIPTA 60 mg once daily, and 408 patients received placebo. Approximately 88% were female, 80% were White, 17% were Black, and 12% were of Hispanic or Latino ethnicity. The mean age at study entry was 41 years (range 18 to 74 years).

The most common adverse reactions (incidence at least 4% and greater than placebo) are nausea, constipation, and fatigue.

Table 2 summarizes the adverse reactions that occurred during Study 1 and Study 2.

Table 2: Adverse Reactions Occurring with an Incidence of At Least 2% for QULIPTA and Greater than Placebo in Studies 1 and 2

	Placebo (N= 408) %	QULIPTA 10 mg (N=314) %	QULIPTA 30 mg (N=411) %	QULIPTA 60 mg (N=417) %
Nausea	3	5	6	9
Constipation	1	6	6	6
Fatigue/Somnolence	3	4	4	6
Decreased Appetite	<1	2	1	2

The adverse reactions that most commonly led to discontinuation in Studies 1 and 2 were constipation (0.5%), nausea (0.5%), and fatigue/somnolence (0.5%).

Liver Enzyme Elevations

In Study 1 and Study 2, the rate of transaminase elevations over 3 times the upper limit of normal was similar between patients treated with QULIPTA (1.0%) and those treated with placebo (1.8%). However, there were cases with transaminase elevations over 3 times the upper limit of normal that were temporally associated with QULIPTA treatment; these were asymptomatic, and resolved within 8 weeks of discontinuation. There were no cases of severe liver injury or jaundice.

Decreases in Body Weight

In Studies 1 and 2, the proportion of patients with a weight decrease of at least 7% at any point was 2.8% for placebo, 3.8% for QULIPTA 10 mg, 3.2% for QULIPTA 30 mg, and 4.9% for QULIPTA 60 mg.

DRUG INTERACTIONS

CYP3A4 Inhibitors

Coadministration of QULIPTA with itraconazole, a strong CYP3A4 inhibitor, resulted in a significant increase in exposure of atogepant in healthy subjects. The recommended dosage of QULIPTA with concomitant use of strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin) is 10 mg once daily. No dosage adjustment of QULIPTA is needed with concomitant use of moderate or weak CYP3A4 inhibitors.

CYP3A4 Inducers

Coadministration of QULIPTA with steady state rifampin, a strong CYP3A4 inducer, resulted in a significant decrease in exposure of atogepant in healthy subjects. Concomitant administration of QULIPTA with moderate inducers of CYP3A4 can also result in decreased exposure of atogepant. The recommended dosage of QULIPTA with concomitant use of strong or moderate CYP3A4 inducers (e.g., rifampin, carbamazepine, phenytoin, St. John's wort, efavirenz, etravirine) is 30 mg or 60 mg once daily. No dosage adjustment of QULIPTA is needed with concomitant use of weak CYP3A4 inducers.

OATP Inhibitors

Coadministration of QULIPTA with single dose rifampin, an OATP inhibitor, resulted in a significant increase in exposure of atogepant in healthy subjects. The recommended dosage of QULIPTA with concomitant use of OATP inhibitors (e.g., cyclosporine) is 10 mg or 30 mg once daily.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no adequate data on the developmental risk associated with the use of QULIPTA in pregnant women. In animal studies, oral administration of atogepant during the period of organogenesis (rats and rabbits) or throughout pregnancy and lactation (rats) resulted in adverse developmental effects (decreased fetal and offspring body weight in rats; increased incidence of fetal structural variations in rabbits) at exposures greater than those used clinically *[see* Data*]*.

In the U.S. general population, the estimated background risk of major birth defects and miscarriages in clinically recognized pregnancies is 2-4% and 15-20%, respectively. The estimated rate of major birth defects (2.2%-2.9%) and miscarriage (17%) among deliveries to women with migraine are similar to rates reported in women without migraine.

Clinical Considerations

Disease-Associated Maternal and/or Embryo/Fetal Risk

Published data have suggested that women with migraine may be at increased risk of preeclampsia and gestational hypertension during pregnancy.

Data

Animal Data

Oral administration of atogepant (0, 5, 15, 125, or 750 mg/kg/day) to pregnant rats during the period of organogenesis resulted in decreases in fetal body weight and in skeletal ossification at the two highest doses tested (125 and 750 mg/kg), which were not associated with maternal toxicity. At the no-effect dose (15 mg/kg/day) for adverse effects on embryofetal development, plasma exposure (AUC) was approximately 4 times that in humans at the maximum recommended human dose (MRHD) of 60 mg/day.

Oral administration of atogepant (0, 30, 90, or 130 mg/kg/day) to pregnant rabbits during the period of organogenesis resulted in an increase in fetal visceral and skeletal variations at the highest dose tested (130 mg/kg/day), which was associated with minimal maternal toxicity. At the no-effect dose (90 mg/kg/day) for adverse effects on embryofetal development, plasma exposure (AUC) was approximately 3 times that in humans at the MRHD.

Oral administration of atogepant (0, 15, 45, or 125 mg/kg/day) to rats throughout gestation and lactation resulted in decreased pup body weight at the highest dose tested (125 mg/kg/day), which persisted into adulthood. At the no-effect dose (45 mg/kg/day) for adverse effects on pre- and postnatal development, plasma exposure (AUC) was approximately 5 times that in humans at the MRHD.

Lactation

There are no data on the presence of atogepant in human milk, the effects of atogepant on the breastfed infant, or the effects of atogepant on milk production. In lactating rats, oral dosing with atogepant resulted in levels of atogepant in milk approximately 2-fold higher than that in maternal plasma. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for QULIPTA and any potential adverse effects on the breastfed infant from QULIPTA or from the underlying maternal condition.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

Population pharmacokinetic modeling suggests no clinically significant pharmacokinetic differences between elderly and younger subjects. Clinical studies of QULIPTA did not include sufficient numbers of patients aged 65 years and over to determine whether they respond differently from younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Renal Impairment

The renal route of elimination plays a minor role in the clearance of atogepant. In patients with severe renal impairment (CLcr 15-29 mL/min), and in patients with end-stage renal disease (ESRD) (CLcr <15 mL/min), the recommended dosage of QULIPTA is 10 mg once daily. For patients with ESRD undergoing intermittent dialysis, QULIPTA should preferably be taken after dialysis. No dose adjustment is recommended for patients with mild or moderate renal impairment.

Hepatic Impairment

No dose adjustment of QULIPTA is recommended for patients with mild or moderate hepatic impairment. Avoid use of QULIPTA in patients with severe hepatic impairment *[see Adverse Reactions]*.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity

Atogepant was administered orally to mice (0, 5, 20, or 75 mg/kg/day in males; 0, 5, 30, 160 mg/kg/day in females) and rats (0, 10, 20, or 100 mg/kg in males; 0, 25, 65, or 200 mg/kg in females) for up to 2 years. There was no evidence of drug-related tumors in either species. Plasma exposures at the highest doses tested in mice and rats were approximately 8 and 20-35 times, respectively, that in humans at the maximum recommended human dose (MRHD) of 60 mg/day.

Mutagenicity

Atogepant was negative in in vitro (Ames, chromosomal aberration test in Chinese Hamster Ovary cells) and in vivo (rat bone marrow micronucleus) assays.

Impairment of Fertility

Oral administration of atogepant (0, 5, 20, or 125 mg/kg/day) to male and female rats prior to and during mating and continuing in females to Gestation Day 7 resulted in no adverse effects on fertility or reproductive performance. Plasma exposures (AUC) at the highest dose tested are approximately 15 times that in humans at the MRHD.

PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Drug Interactions

Inform patients that QULIPTA may interact with certain other drugs, and that dosage modifications of QULIPTA may be recommended when used with some other drugs. Advise patients to report to their healthcare provider the use of any other prescription medications, over-the-counter medications, herbal products, or grapefruit juice *[see Drug Interactions]*.

Manufactured by:
Forest Laboratories Ireland Ltd.
Dublin, Ireland

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US-QULI-210010 **MASTER**

US-QLP-220043

abbvie

Preemptive Therapy for Acute Migraine Headache

Treatment during the "prodrome"

As was discussed in a previous issue, a compleat migraine episode, one that produces all the courses from soup to nuts, includes 4 phases: a prodrome, aura, headache phase and a postdrome.

Not all migraineurs are "blessed" with this complete meal. Only about 25% will ever experience aura symptoms, and very few of those 25% will have aura with each and every migraine episode. In an individual migraineur, episodes may vary such that only a portion of the various phases are experienced in a given episode. For example, aura can occur independent of any temporally associated headache but may be followed by a postdrome. The migraineur may experience his or her typical prodromal symptoms even in the absence of aura or postdrome and with little or no headache. For those of us who have migraine – and especially for those with chronic migraine - these "prodromal days" are days when we describe ourselves as "feeling migrainous". Even absent much in the way of headache, one is out of sorts, cognitively a bit foggy, fatigued or afflicted with one of other many vague but unpleasant prodromal symptoms.

In other words, any permutation of the 4 phases may occur, and to complicate matters further the phases may not necessarily occur neatly, one after the other in the order described (eg, aura may persist into and even beyond the headache phase). As we have emphasized many times in this magazine, migraine is the "Baskin Robbins" of headache; migraine episodes come in many different flavors, and it is much more common for migraine episodes to be symptomatically diverse than to be stereotyped.

In our clinic we often advise patients that acute migraine headache is a symptom best treated early, as it is first developing. For that 25% of migraineurs who at times have aura, if their aura symptoms invariably are followed by headache of moderate to severe intensity we will recommend trying certain medications during the aura phase, *before* the headache develops. What about treating even earlier? Say, during the prodromal phase?

Whereas only 25% of migraineurs ever experience aura, over 2/3rds of migraineurs report having symptoms

typical of prodrome prior to the headache phase. Those symptoms are legion, and their diversity ranges from something as specific as repetitive yawning, heightened sensitivity to light or urinary frequency to "I can't explain it precisely, but I just *know* I'm going to get a headache." What causes these prodromal symptoms? From where in the nervous system do they arise? And, as many migraineurs find the prodrome to be as distressing as the headache that follows, how can we treat prodrome?

All good questions and, at this point no good answers. Many believe that prodromal and postdromal symptoms may arise from the hypothalamus, a small chunk of gray matter within the brain that serves as the chronobiologic clock of the body, regulating everything from body temperature to sex drive. Hard to prove. Not surprisingly, without a clear understanding of prodrome's biologic circuitry we lack any evidence-based therapy for treating the prodromal symptoms.

In PRODROME, an interesting study recently conducted, migraineurs who consistently experienced prodromal symptoms followed by headache were randomized to taking either ubrogepant (*Ubrelvy*) or placebo during the prodromal phase. Those research subjects who took Ubrelvy were significantly less likely to experience a moderate to severe headache immediately subsequent to their prodromes. Although the medication was administered before any migraine headache had developed, it lingered long enough in the brain to short-circuit the electrochemical pathway that otherwise would have generated a headache.

While the results of this study do not provide any support for Ubrelvy as a treatment for the prodrome itself, it does reinforce the long-held notion that treatment administered early in the course of a migraine episode is more likely to be effective for preventing or reducing headache than treatment administered at a later point. Two aspirin and a cup of coffee taken early can be far more effective than an intravenous narcotic administered late.

UBRELVY QUICKLY STOPS MIGRAINE IN ITS TRACKS

In clinical studies, most people had pain relief and some even had pain freedom within 2 hours.

THE ANYTIME, ANYWHERE MIGRAINE MEDICINE™

ASK YOUR HEALTHCARE PROVIDER ABOUT UBRELVY

What is UBRELVY® (ubrogepant)?
UBRELVY is a prescription medicine used for the acute treatment of migraine attacks with or without aura in adults. UBRELVY is not used to prevent migraine headaches.

IMPORTANT SAFETY INFORMATION

Who should not take UBRELVY?
Do not take UBRELVY if you are taking medicines known as strong CYP3A4 inhibitors, such as ketoconazole, clarithromycin, itraconazole.

What should I tell my healthcare provider before taking UBRELVY?
Tell your healthcare provider about all your medical conditions, including if you:
- Have liver problems
- Have kidney problems
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Your healthcare provider can tell you if it is safe to take UBRELVY with other medicines.

What are the most common side effects of UBRELVY?
The most common side effects are nausea (4%) and tiredness (3%). These are not all of the possible side effects of UBRELVY.

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Migraine Prevention Therapy

How long is "long enough"?

You've had migraine for years, but until recently it was never really that much of a problem. A bad headache every six months or so since since college years…at times bad enough to demand bed rest in a dark room. But not really all *that* often or *that* much of a problem.

Then you went and had a baby, and as breast-feeding was winding down you began to experience not just more frequent versions of your same old migraine episodes but also a near-daily headache that often builds to become almost as bad as your "usual migraines".

You go to see your doctor, and he tells you that you need to start a medication for migraine prevention. *How long will I need to take it?* you ask. *As long as it takes,* he answers. When you get home from the appointment you do what you can to find out about this prevention medication and learn that it can cause weight loss (*sounds good*), some kind of weird tingling, kidney stones (*ugh*), and (*really ugh*) problems thinking and speaking. *What the hell?* you think.

But you start the medication, put up with some side effects and hang in there. After a year has passed you tell your doctor at a follow-up appointment that you have been essentially headache-free for months. *Can I stop the medication?* you ask.

A very, very good question. Many headache subspecialists who are expert clinicians will tell you what boils down to "*Don't kick a sleeping dog*", with the implication seeming to be that you should remain on this medication…forever. Your husband is just happy that you're not having headaches (and thinner). God knows, the pharmaceutical company that owns the medication obviously has no incentive to encourage you to stop therapy. What should you do?

As a migraineur myself, as a clinical neuroscientist who has, along with many others, assisted in the clinical development of every almost every new therapy for migraine since injectable sumatriptan in the late 1980s and, ultimately, as a Very Bad Patient who would prefer not to take *any* medication on a long-term basis, a portion of my research understandably has been devoted to answering the question: when it comes to migraine prevention therapy, how long is long enough?

As my colleagues and I were developing divalproex sodium (Depakote) for migraine prevention many years ago, my team and I conducted a study to see what would happen if after 2 months of migraine

eradication we tried discontinuing Depakote. The results were not so good. A majority of the patients who had responded so well to Depakote almost immediately relapsed to frequent migraine and required a restart of prevention therapy.

On the other hand, Dr. Robert Kaniecki, a respected colleague of mine possessed of both clinical expertise and excellent common sense, carefully looked at how his migraine patients fared after 1 year of successful treatment with one of the older prophylactic medications and found that most were able to stop their prevention medication without experiencing any consequent worsening of their migraine burdens.

My research team and I subsequently studied onabotulinumtoxinA (BotoxA) in an investigation entitled "Can Botox be Stopped?" and found that when patients reached a certain point of stable clinical improvement, the vast majority were able to stop treatment and continued to do well for up to 5 years of follow-up.

...relatively few patients with migraine require chronic "forever" prevention therapy.

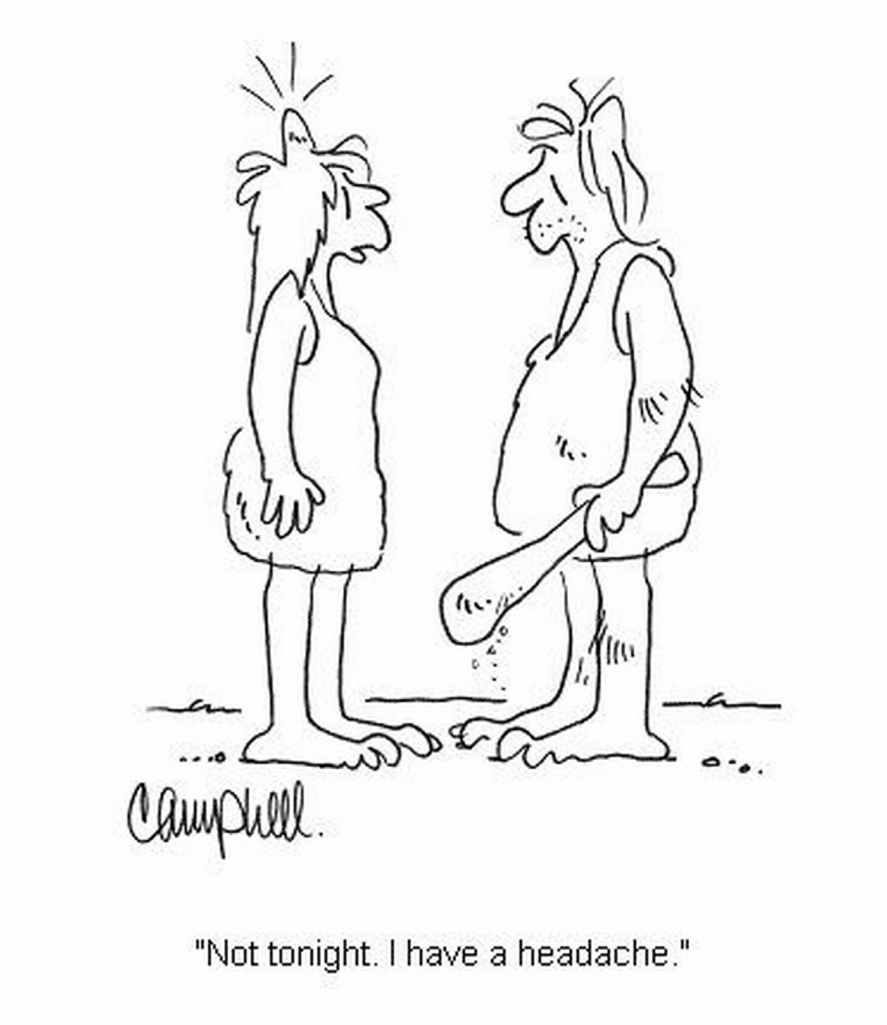
So what can we glean from this and other relevant research?

- There appear to be relatively few patients with migraine who require chronic "forever" prevention therapy.
- While it's entirely possible that the optimal duration of prevention therapy varies from migraineur to migraineur and from therapy to therapy, in general it appears that at least 6 months of migraine stabilization (and perhaps as much as 1 year) may be required before the prevention therapy being used can be stopped without a significant likelihood of rapid relapse.
- There conceivably may exist some prevention therapies that cannot be stopped without incurring a high risk of early relapse.
- There conceivably may exist some prevention therapies that will be effective for an extended time but then lose their effectiveness or, even worse, begin to promote headache.

Even without treatment, migraine is a variable beast, activating and deactivating on its own and without any obvious external provocation. Coupling this with the unproven but definitely hypothetical possibility that continuing a prevention treatment indefinitely might eventually come to be detrimental, be persistent in asking your physician, "How long do I need to be on this medication?"

Migraine Myth of the Month

Females with migraine have little interest in sex



However the notion initially arose and for whatever conflation of reasons, misogynistic or otherwise, there persists in America a prevailing cultural trope that females are prone to using headache as an excuse to avoid engaging in sexual intercourse. Given that migraineurs are disproportionally female and that as many as 28 million American females have active migraine, it should not be surprising that this cliché has been extended to imply that it is females with migraine who most commonly employ the "headache excuse" and, yet a step further, that female migraineurs are inherently deficient in libido. While clichés often have at least some basis in fact, there are data suggesting the truth may be otherwise.

Research in this area recently conducted by this magazine's editor and his colleagues involved 150 heterosexual and sexually active female migraine patients between the ages of 25 and 45 who were being evaluated at a university-based headache clinic, an equal number of sexually active females without migraine matched for age, race/ethnicity, socioeconomic status, marital status and highest educational level attained and a smaller group (67) of similarly matched females who had a history of migraine but were not actively under medical care for their headache disorders.

All of the research subjects anonymously completed the Female Sexual Function Index (FSFI), a validated survey commonly used in clinical care and research involving females with sexual dysfunction. This 19-item survey relates to the previous 4 weeks and includes 6 domains: sexual desire, arousal, lubrication, orgasm, satisfaction and pain. The highest attainable score is 36, and a score of 28 or less is considered to be indicative of sexual dysfunction.

We found that females with migraine scored significantly higher on the Index than the matched control group of migraine-free females. Mean FSFI scores for all three groups - females with migraine recruited from our headache clinic population, females without migraine and females with migraine from the general population - were above the level considered indicative of sexual dysfunction…but, again, female migraineurs scored higher in terms of sexual function and performance.

Your editor presented these findings at the annual scientific meeting of the American Headache Society held in Austin, Texas in June of this year. I introduced the topic by pointing out that this research was conducted at a particularly unusual time in American culture, when even the concept of gender - let alone what constitutes "libido" or "sex drive" - has become so obscured that a Supreme Court Justice nominee (now a justice) could/would not provide a direct answer to the question: "Can you provide a definition for the word

'woman'?" Her reply: "I'm not a biologist". [Disclaimer: me neither-while I did take some biology courses in college, I majored in history before going on to medical school]

So, what *is* a woman? I asked rhetorically. I advised the audience that in a study presented at the 57th annual meeting of the Association for Computational Linguistics involving a computer-assisted analysis of 3.5 million books published in the non-medical literature between 1900 and 2008, the most common adjectives used to describe a woman were "beautiful" and "sexy", while the most common applied to men were "righteous" "rational" and "brave". I then quoted Oscar Wilde's observation: "Men can be analyzed, but women…merely adored."

This well-intentioned, meant-to-be-amusing but perhaps ill-advised introduction and my subsequent description of our research met with a decidedly mixed reaction. These issues of gender, sex drive and sexual function and performance lie like mines buried in the volatile DMZ that separates the two Koreas, and one treads that ground at one's peril. Clearly there was a sizable segment of the audience in attendance who found my references to the Association for Computational Linguistics presentation and my Oscar Wilde quote to be offensive rather than amusing, and they didn't care much for my research either.

"… female migraineurs scored higher in terms of sexual function and performance.

Ah, that research. Nothing in my previous experience as a clinical neuroscientist investigating various aspects of stroke or headache had prepared me to present the results of a study where the variables examined included "arousal", "orgasmic frequency" and - perhaps most difficult for me to proclaim solemnly from the lectern - "lubrication… you know, *wetness*".

Locally, nationally and internationally, I've given hundreds of presentations and lectures to many diverse audiences over the past few decades, and typically I've enjoyed the verbal jousting which can accompany those presentations to which some audience members take exception. But something (or someone-perhaps me?) has changed. In this particular case, the hostile vibe arising from the audience like a bad odor – especially from the younger female physician scientists in attendance - compelled me to rush through my presentation, answer very briefly the questions posed by the session's moderator and then beat a hasty retreat to enjoy the pleasures of Austin with my wife. [Postscript: precisely the same presentation subsequently was received enthusiastically at the European Academy of Neurology annual meeting in Budapest.]

Although presenting our study results in Austin was a rather uncomfortable experience, I found the research itself to be profoundly interesting, and I'm pleased we were able to offer evidence that this cultural trope of "females with migraine are hyposexual" may be a mythic misperception propagated by cultural momentum. But the results do raise an interesting question: if our findings are accurate, why might females with migraine possess a higher libido and engage in heterosexual intercourse more frequently than their compatriots without migraine?

Before considering that question, it should be stated that this characteristic appears to apply to male migraineurs as well. In 2006, colleagues of mine now at Wake Forest University published the results

of a study which demonstrated male migraineurs to have a higher level of sexual desire than males free of migraine. Multiple studies have indicated that migraineurs of both genders may use sex – and orgasm specifically – as a means to treat acute migraine headache.

As for the "why?" question, no simple answer springs to mind, but it does recall a previous issue in which we posed to the readership the question: with evolution and natural selection at play, why has this disorder we name "migraine" endured in human society for at least 3,000 years? What possible evolutionary advantage could migraine convey that would prevent it from having been genetically eliminated long ago? At the time I hypothesized that with their biologically hypersensitive brains migraineurs may be especially attuned to changes in the external environment and that perhaps every tribe of 20 or so has needed a migraineur or two to predict when the weather was about to change or to anticipate how the beasts sought by the hunter-gatherers as a food source were reacting to human proximity and other factors.

My pragmatic wife's answer was simpler and perhaps more scientifically sound: because natural selection ultimately is intended to optimize reproduction, the primary goal of any species, and because nothing about migraine should significantly hinder reproductive capacity, there simply has not existed any compelling reason for the genetic permutations that produce migraine to be snuffed out with the passage of time.

She may be right, but these new data suggest an intriguing alternative answer that had not occurred to either of us. If migraine does convey an increase in libido and, with this, increased heterosexual activity favoring an increase in progeny, then migraine is advantageous to the species. If true, is it possible that over the centuries to come we will witness a progressive increase in the proportion of migraineurs within the general population?

Hard to know, but as a migraineur myself I welcome any data which suggest that having migraine enhances sexual performance.

JFR

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Tell your HCP about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Nurtec ODT may cause serious side effects including allergic reactions, including trouble breathing and rash. This can happen days after you take Nurtec ODT. Call your HCP or get emergency help right away if you have swelling of the face, mouth, tongue, or throat or trouble breathing. This occurred in less than 1% of patients treated with Nurtec ODT.

The most common side effects of Nurtec ODT were nausea (2.7%) and stomach pain/indigestion (2.4%). These are not the only possible side effects of Nurtec ODT. Tell your HCP if you have any side effects.

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Nurtec ODT orally disintegrating tablets is a prescription medicine that is used to treat migraine in adults. It is for the acute treatment of migraine attacks with or without aura and the preventive treatment of episodic migraine. It is not known if Nurtec ODT is safe and effective in children.

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Before you take NURTEC ODT, tell your healthcare provider about all of your medical conditions, including if you:

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- are breastfeeding or plan to breastfeed. Very small amounts of NURTEC ODT pass into your breast milk. Talk with your healthcare provider about the best way to feed your baby if you take NURTEC ODT.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How should I take NURTEC ODT?

- Take NURTEC ODT exactly how your healthcare provider tells you to.
- For the acute treatment of migraine attacks when they occur, NURTEC ODT can be taken 1 time each day as needed. You should not take more than 1 tablet in 24 hours.
  - It is not known if it is safe to take more than 18 doses of NURTEC ODT in 30 days.
- For the preventive treatment of episodic migraine, take NURTEC ODT 1 time every other day.

What are the possible side effects of NURTEC ODT?

NURTEC ODT may cause serious side effects including:

- **Allergic reactions.** Allergic reactions, including trouble breathing and rash, can happen after you take NURTEC ODT. This can happen days after you take NURTEC ODT. Call your healthcare provider or get emergency help right away if you have any of the following symptoms, which may be part of an allergic reaction:
  - Swelling of the face, mouth, tongue, or throat
  - Trouble breathing

The most common side effect of NURTEC ODT in acute treatment of migraine attacks with or without aura is:

- nausea

The most common side effects of NURTEC ODT in preventive treatment of episodic migraine are:

- nausea
- stomach pain
- indigestion

These are not the only possible side effects of NURTEC ODT. Call your doctor for medical advice about side effects.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

This information is not comprehensive. To learn more, talk to your healthcare provider and visit nurtec.com to obtain the full Prescribing Information. You can also call Pfizer Inc. at 1-833-4NURTEC for more information.

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Migraine Tip of the Month

Ask, and ye shall receive

After the more complex management recommendations we have made in this "Tip of the Month" section over the years this tip may seem pretty simple. But here it goes…

If you have questions about your headache diagnosis and management, by all means ask your relevant medical provider for answers.

Having provided care to many thousands of headache patients for a number of decades, I can assure you that consequent to a number of factors the volume in our headache clinics has progressively increased. With no additional time falling out of the sky to accommodate that increased volume, our clinics have become a veritable horse race.

Patient education is key to optimal management of migraine and other primary headache disorders, and attempting to jam adequate patient education into an all too short clinic visit is a near impossibility. This is one of the major reasons we first developed ***Migraineur***, anticipating that we could use this magazine to improve patient education and avoid answering the same (very appropriate) questions over and over (egs, what is involved with receiving Botox for suppression of chronic migraine? what are the most common potential side effects of these medications you are prescribing for me? what therapeutic response should I be hoping for?).

We refer each of our clinic patients to those specific articles in ***Migraineur*** that are most relevant to their specific needs. To assist in this we are in the process of developing what amounts to a "migraine Wikipedia", and our first attempt at creating an encyclopedia of migraine can be found on the magazine's website (migraineurmagazine.com) and accessed by clicking "Issues/Selected Topics" on the webpage.

What can happen if we the providers fail to advise patients that the triptan prescribed for acute headache may cause chest pressure or neck squeezing, annoying but ultimately benign side effects? I can assure you from bittersweet experience that with alarming frequency a patient using a triptan and experiencing these symptoms will present to the emergency room on Saturday evening understandably concerned that he or she is experiencing a heart attack or anaphylactic reaction. Many diagnostic tests unnecessarily are performed, and the patient often is hospitalized. Tens of thousands of dollars later it becomes clear that this time, effort and money were spent to evaluate an entirely benign and commonly occurring side effect of the medication. A little education… and none of this would have occurred.

So don't be shy about asking your questions. There truly are no dumb questions when it comes to headache diagnosis and management. If you think you need a brain MRI scan, ask your provider why none has been ordered. If you are starting a new medication for migraine prevention or acute migraine treatment, ask your provider what are the most common side effects that may occur and what should you be looking for in terms of therapeutic benefit.

Ask! You have nothing to lose but your migraine burden.

Migraine Treatment of the Month

Topiramate

Examined through the lens of the historical development of therapies for migraine, topiramate is a particularly interesting drug. Like virtually all medications prescribed for migraine prior to the advent of sumatriptan in the early 1990s, topiramate was first intended as a treatment for another medical disorder (in its case, epilepsy) and subsequently – some would say serendipitously – found to be effective for migraine. Topiramate bridges the gap between old-timers for migraine prevention such as amitriptyline (Elavil) and propranolol (Inderal) that were developed for the treatment of depression and high blood pressure, respectively, and then found to be useful for migraine and "designer drugs" such as the anti-CGRP monoclonal antibodies and the "gepants" that were developed specifically for migraine.

In what sense was topiramate a "bridge" therapy? The emergence of topiramate as a potential therapy for migraine prevention coincided with a new understanding that migraine is a disorder characterized by brain "hypersensitivity" and that medications which suppress that hypersensitivity can reduce migraine burden as well as, say, prevent seizures. Or stabilize bipolar disorder. Or inhibit compulsive behavior.

The topiramate "immediate release" (IR) formulation (initially marketed as *Topamax*) received FDA approval for the treatment of epilepsy in 1996, and eventually enough research data accumulated to support the FDA extending the drug's indication to include migraine prevention. From the outset it was clear to all of us engaged in the clinical development of topiramate for migraine that this medication represented a major step forward in migraine therapeutics. Also clear from the outset was that the drug would be difficult for many migraineurs to tolerate.

Almost 20 years have passed since topiramate received its FDA approval for use in migraine prevention, and during those years such therapies as

onabotulinumtoxinA (BotoxA) and, more recently, the anti-CGRP drugs have emerged as attractive alternatives. Unlike many of the older medications that never have been compared to the newer kids on the block for their safety, tolerability and effectiveness, topiramate is practically unique in the amount of effort that has gone into evaluating its effectiveness relative to its competitors.

The multicenter FORWARD study examined topiramate versus BotoxA for their clinical utility in treating chronic migraine. While the two therapies were more or less equally effective in treating chronic migraine for those research subjects who completed the treatment phase, a much higher percentage of patients randomized to topiramate found the drug difficult or impossible to tolerate; the discontinuation rate in that group was far greater than it was in the group randomized to receive BotoxA. In a subsequent study again involving patients with chronic migraine, erenumab (*Aimovig*) was similarly much easier than topiramate for the research patients to tolerate, and the effectiveness of Aimovig in reducing migraine burden was significantly higher.

“There is no... compelling reason for a provider to prescribe topiramate for migraine prevention.

Even starting with a low-dose and sequentially increasing to a target therapeutic dose of 50 mg twice daily, topiramate produces a strange intermittent “tingling” over various parts of the body in as many as 1/3rd of patients. While this side effect is benign and typically transient, of more concern are the potential side effects of impaired concentration, impaired memory and word-finding difficulties/decreased verbal fluency. The extended release/administered once-daily formulation of topiramate is less likely to produce cognitive side effects, but it is typically difficult to prescribe consequent to its higher cost and the corresponding disinclination of insurers to authorize its use.

So why does topiramate IR remain near or even at the top of prevention therapies for migraine prescribed by medical providers? The most obvious answer: the drug is generic and consequently far cheaper than either BotoxA or the new “designer drugs” such as the anti-CGRP monoclonal antibodies and the gepants. In the interest of protecting the financial bottom line, insurers consequently prefer that providers prescribe topiramate IR and often require that a patient try and fail the drug before something more tolerable and at least as effective may be prescribed. There is really no other compelling reason for a provider to prescribe topiramate for migraine prevention.

This “dance with the devil” involving providers and insurers has been described elsewhere in this magazine, but suffice it to say that for virtually all migraineurs whose migraine burdens are such that a course of prevention therapy is required, there are better alternatives than topiramate.

Doctor on Call

Amelia, a 25-year-old administrative assistant who lives in Philadelphia writes:

Dear Doctor,

I am really steamed! For the past two months I've been having a miserable time with my migraine, and when I send my doctor messages through the portal we are supposed to use as part of the electronic healthcare system to let him know that I'm having a severe headache or to ask questions about treatment, I typically receive a very brief and unhelpful response.

My chronic problem with his lack of responsiveness hit an all-time high last week when I sent him a message letting him know that I'd had a migraine attack severe enough to put me down for two days and cause me to miss work. In my message I asked him to provide me with a medical excuse for my having been absent from work, along with suggested accommodations for how my workplace environment could be rearranged to minimize my chance of having an acute migraine while on the job (different lighting, breaks to lie down, teleworking when needed, etc.). My supervisor at work is very demanding, and I needed that letter within 24 hours. His response: nothing!

What's up with this? What do you do about a doctor who is simply ignoring his patients? Is this what medical care has come to?

Sign me: Furious in Philadelphia

The Doctor's Reply:

Dear Furious,

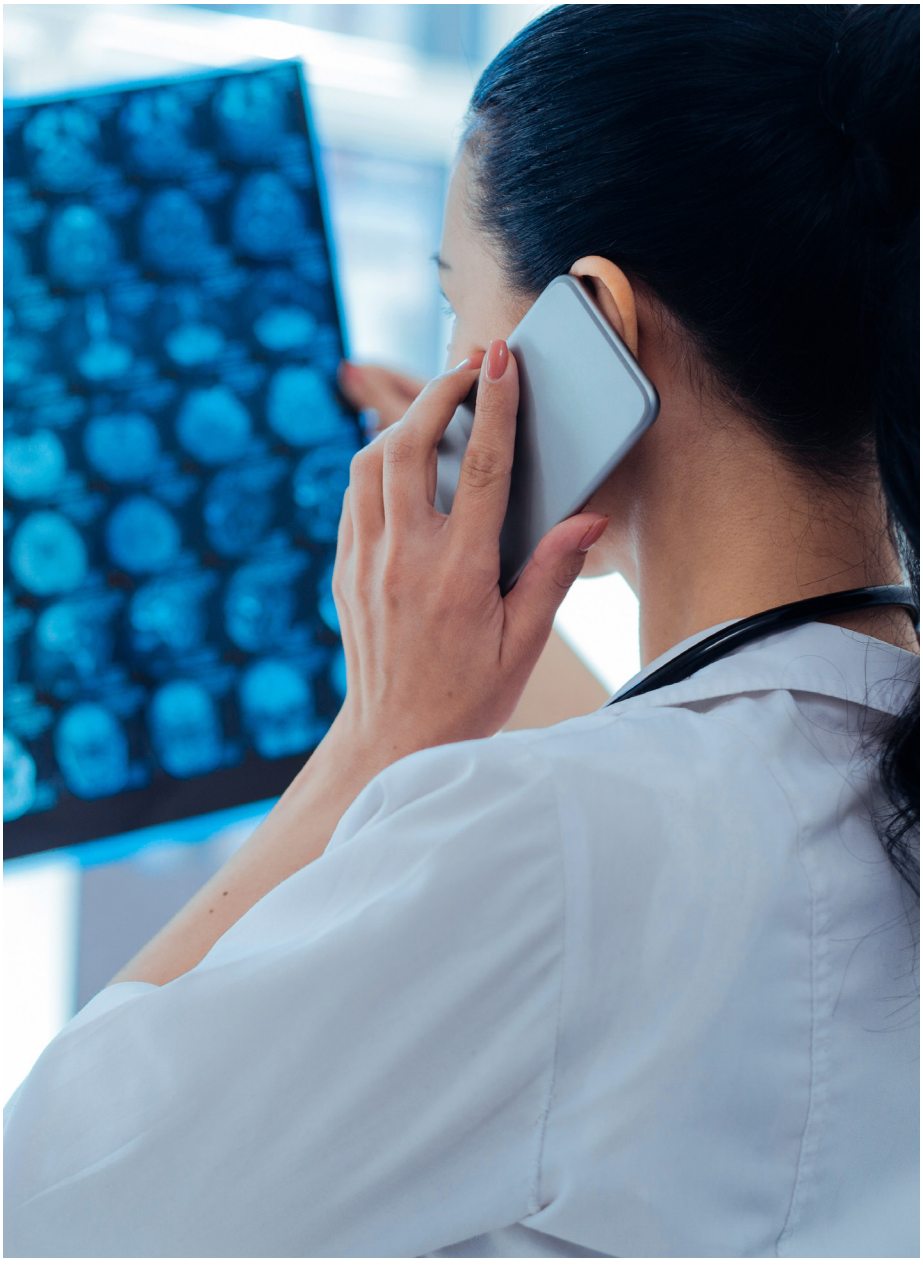
First, I sincerely doubt that your doctor is "ignoring his patients". It is far more likely that your electronic message containing multiple requests arrived when he was in the midst of a busy clinic providing direct care to a large volume of patients, late in the day when he was completing his clinic notes, or in the evening when he was at last spending some time with his family… or asleep.

In theory – and up to a point in practice – the ability for patients to access their medical providers via electronic messaging sounds great. In actual practice, however, it

is fast proving to be the one of the leading banes of existence for many providers.
I assume you are aware that the time providers expend on responding to patients electronically is financially uncompensated. When my research colleagues and I investigated the issue almost 2 years ago, we found that I was spending an average of 28 hours monthly simply responding to messages, *de facto* practicing medicine for free. I'm fairly sure that the time expended has only increased since.

And not truly *free*, really. Those hours represent time I otherwise could devote to providing clinical care to additional new patients, training medical students, residents and fellows, performing research intended to raise the standard of care for headache treatment and education…and, yes, to spending some time on myself to exercise, interact with family and friends, work in my garden, etc. I grant you that electronic messaging is a wonderful deal for patients. For doctors, not so much.

The study I referred to also demonstrated the interesting fact that a small proportion of patients generate a very high percentage of the messages a provider receives. At the extreme, I currently have in my practice one patient whom I've seen a total of 4 times in clinic, and over a period of 6 months I've received from her 67 electronic messages requiring some type of response. Although burdened by a chronic anxiety disorder and a great deal of personal stress related to marital woes and caring for multiple young children, she is by no means a desperately ill patient. In this circumstance, sending 67 messages in 6 months and as many as 8 messages on a single day borders on physician abuse.



I understand your need for a medical letter excusing you from work, but taking the time to compose and send that letter cannot take precedence over providing care to those patients who are sitting in the waiting area or exam room hoping to be evaluated in a timely manner.

As indicated in this issue's "***Tip of the Month***", no extra time has magically fallen out of the sky to assist providers in performing these electronic tasks. Directing patients who have sent electronically questions about their headache disorder and its management to come see me in clinic for a "traditional" evaluation doesn't make much sense when the next available clinic appointment lies months in the future and there is a long waiting list of new patients who wish to establish care with me. Some institutions - notably Johns Hopkins - have begun to advise their patients that within certain parameters electronic, there will be a financial charge for communicating with a provider. If insurers refuse to underwrite that charge, it may be that the patient will be billed directly.
There are no easy solutions, but now that the genie is out of the bottle to which it is unlikely to return, we clearly need to find one.

In the interim, Amelia, please try to understand this difficult situation from the perspective of your doctor. Headache - and migraine particular – is a disorder that inherently is prone to generating a high volume of patient messages. Efficient communication with your headache provider can be a godsend, but please try to maintain a modicum of patience, be selective, and don't overdo it.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