What is the "Best" Migraine Therapy?

Old vs New, New vs New

While 2021 was replete with a variety of woes that any sane person would prefer to see recede and vanish in the rearview mirror, amidst the gloom induced by the endless pandemic the arsenal of effective therapies for migraine continued to blossom and grow.

Since May 2018 there have emerged no less than nine new therapies for migraine: three subcutaneously self-injected anti-CGRP monoclonal antibodies (Mabs), one intravenously infused anti-CGRP Mab, three oral anti-CGRP "gepants", a novel oral serotonin agonist (a "ditan") which is active at a different site than the triptans in the migraine circuitry and an old drug (dihydroergotamine/DHE) available in an interesting new delivery system. That's a lot of newcomers within a short period of time.

Dampening the enthusiasm for these newcomers has been the necessity for patients typically to obtain prior authorization (PA) from their insurers before trying them and thus for providers to spend financially uncompensated time and effort assisting with the PA and appeals process. Often there are hurdles placed by the insurer before authorization will be granted. For example, one may need to try and fail three generic and relatively inexpensive oral prevention therapies before receiving a chance to try an anti-CGRP Mab. Another example:

insurers may require that a client/patient try and fail three oral triptans before authorization is granted for one of the new acute migraine treatments.

These last requirements raise an interesting couple of questions:

- Just how well do the newcomers compare to the older therapies for migraine in terms of safety, tolerability and effectiveness?

- For that matter, how do the newcomers compare to one another?

Well, the honest answers to both questions is…hard to say. With the exception of the triptans, the older therapies were developed for other medical indications and found serendipitously to be useful for treating migraine as well. The medications listed earlier - the CGRP Mabs and the rest – are "designer drugs" which were developed specifically for migraine. Does that make them better? Hmmm. Generally speaking, the mechanism by which they work to reduce migraine has been more clearly identified than is the case with the older therapies, and more to the point clinically they tend to have fewer side effects than the "oldies", but few "active comparator" studies evaluating a given older drug against a given newcomer have been performed. As such, not much is known regarding the effectiveness of "old" versus "new".

There are a few tidbits.

1. Botox (FDA approved for chronic migraine in 2010 and thus not strictly a "newcomer") was directly compared to topiramate in the FORWARD chronic migraine study, and because of significant differences in tolerability favoring Botox it appears to be the more useful therapy.

2. For patients receiving Botox who have experience a partial positive response to injection therapy with the neurotoxin, the addition of erenumab (Aimovig) appears to further reduce migraine burden.

3. When compared to topiramate, Aimovig is more effective for migraine prevention and far better tolerated.

4. Switching from one anti-CGRP Mab to another appears to improve treatment response in some patients…although it still remains unknown whether one Mab is superior to the other three.

And that's about it. Providers complain when insurers require that a patient with chronic migraine try and fail a beta blocker before authorization to receive Botox or an anti-CGRP therapy will be provided. How does "old" propranolol, a beta blocker, compare with Botox or an anti-CGRP medication in treating chronic migraine? No one can say with certainty, but one recent study did demonstrate propranolol can reduce headache burden in chronic migraine, and such data make it difficult to criticize insurers for requiring a trial of (inexpensive) propranolol prior to authorization of (much more expensive) anti-CGRP Mabs.

For better or worse, in welcoming the newcomers we will not be abandoning the older therapies. For now it's best to think of these newcomers as attractive alternatives when the older therapies are ineffective, poorly tolerated or both.

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(atogepant) tablets

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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 the Brief Summary of the full Patient Information on the following 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.

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QULIPTA™ (kew-LIP-tah) (atogepant) tablets, for oral use

CONSUMER BRIEF SUMMARY
Consult Package Insert for
Full Prescribing Information

Patient Information

Read the Patient Information that comes with QULIPTA before you start taking it and each time you get a refill. There may be new information. This brief summary is not comprehensive and does not take the place of talking with your doctor about your medical condition or treatment. For a copy of the full Prescribing Information visit www.QULIPTA.com.

What is QULIPTA?

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

It is not known if QULIPTA is safe and effective in children.

Before you take QULIPTA tell your healthcare provider about all of 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.

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Especially tell your healthcare provider if you take any of the following, as your healthcare provider may need to change the dose of QULIPTA:

• ketoconazole or itraconazole	• rifampin	• St. John's wort
• cyclosporine	• carbamazepine	• efavirenz
• clarithromycin	• phenytoin	• etravirine

Keep a list of medicines you take to show to your healthcare provider or pharmacist when you get a new medicine.

How should I take QULIPTA?

- Take QULIPTA by mouth 1 time each day with or without food.
- Take QULIPTA exactly as your healthcare provider tells you to take it.

What are the possible side effects of QULIPTA?

The most common side effects of QULIPTA include: nausea, constipation, and fatigue.

These are not all of the possible side effects of QULIPTA. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store QULIPTA?

- Store QULIPTA at room temperature between 68ºF to 77ºF (20ºC to 25ºC).

Keep QULIPTA and all medicines out of the reach of children.

General information about the safe and effective use of QULIPTA.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use QULIPTA for a condition for which it was not prescribed. Do not give QULIPTA to other people, even if they have the same symptoms you have. It may harm them. You can ask your pharmacist or healthcare provider for information about QULIPTA that is written for health professionals.

What are the ingredients in QULIPTA?

Active ingredient: atogepant

Inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, mannitol, microcrystalline cellulose, polyvinylpyrrolidone vinyl acetate copolymer, sodium chloride, sodium stearyl fumarate, and vitamin E polyethylene glycol succinate.

Manufactured by:
Forest Laboratories Ireland Ltd.
Dublin, Ireland

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.

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