

# Migraine Treatments of the Month

## *Injectable Sumatriptan and Ubrelvy: The Old and the New*



For this issue I decided to exercise some editorial prerogative and up the ante to feature *two* treatments of the month instead of the usual one. Of the two, one is “old”, the first-ever “designer drug” for migraine, and the other is a newcomer. They are [injectable sumatriptan](#) (initially available under the brand name Imitrex) and [ubrogepant](#) (Ubrelvy).

### **Injectable Sumatriptan: “when the need is for speed”**

Many years ago I was living in San Diego and working at the University of California San Diego, developing a stroke program during my work hours and surfing whenever I could. A colleague from the University of Arizona called one day to urge me to assist in the development of a new medication, GR143175C as it was referred to at that time. As my research was focused on stroke, I asked Joan whether it was a therapy for stroke prevention or for acute stroke treatment.

“It’s not for stroke,” she replied. “It’s for migraine.”

“Nothing works for migraine,” I responded. Prescribing such commonly ineffective therapies as BB-like little spheres of Cafegot and the psychedelic-appearing tablets of wonderfully named “Bellergal Space Tabs” had made me a cynic.

“Do it,” she insisted. “This one is different.” And trusting her, I did so. I joined with a small team of amiable colleagues to evaluate the drug’s safety and effectiveness in human research subjects with migraine, and within a few years subcutaneously injected GR43715C evolved into injectable Imitrex (sumatriptan). Whether for stroke, headache or anything else neurological, no other result from therapeutic research I have assisted with has come close to matching injectable sumatriptan for the benefit conveyed. That drug literally has empowered millions of patients who

otherwise would suffer in silence or endure the misery of the ER to self-treat their most severe migraine episodes. Even after almost 30 years, since it was approved by the FDA in 1992, it remains the most effective self-administered therapy for “rescue” from moderate to severe migraine headache.

Why so effective? Self-administered subcutaneously (under the skin) with an auto-injector that resembles an Epi-pen, sumatriptan reaches a higher blood level that do the oral triptans...and does so far more rapidly. When a migraine headache is rapidly intensifying or already has advanced to a high level of intensity, orally administered medication may be simply too slow to “catch up”. There are inhaled and intranasal formulations that are faster than the oral pills, capsules and powders, but nothing self-administered can equal the rocket-ship rapid delivery of injectable sumatriptan.

Don’t get me wrong. Injectable sumatriptan is not without its downside.

Roughly 30% of migraineurs will either not



respond to the drug or find its side effects more bothersome than the migraine itself. During the early phases of our research, we investigators were rattled by certain of those side effects: chest pressure (*is this a heart attack?!?*), neck squeezing (*is this an anaphylactic reaction?!?*). With time and many millions of usages, however, it became clear that injectable sumatriptan is an exceedingly safe therapy.

Why, then, is this treatment so under-utilized? There are a variety of reasons. For one, with the subsequent advent of five fast-onset oral triptans, two slow-onset and one paired with an anti-inflammatory drug, injectable sumatriptan was quickly placed in the marketing broom closet. Even its most recent brand incarnation, Zembrace, with its lower dose (3 mg) promising equivalent effectiveness/fewer side effects *plus* an especially nifty auto-injector, receives relatively little attention and use.

For another, despite the well-documented safety of injectable sumatriptan, many healthcare providers are leery of the treatment's side effects and thus reluctant to prescribe it. Others assume (often wrongfully) that their patients will refuse to use a self-injected medication.

A shame. Again, injectable sumatriptan is a) safe, and b) the most effective self-administered therapy we have for "rescue" from migraine headache of moderate to severe intensity (especially when nausea and vomiting preclude orally administered treatment). If you experience migraine headaches that get out of hand despite your current management strategy, you owe it to yourself to consider injectable sumatriptan.

### **Ubrogепant (Ubrely): tolerability, effectiveness flexibility**

Such has been the arc of my career that I've had the good fortune to be present both at the birth of injectable sumatriptan, the first "designer drug" for migraine and then, some 27 years later, ubrogепant (Ubrely), one of a new class of medications for acute headache treatment that is distinct from sumatriptan and the other triptans.



The nervous system's biologic circuitry that generates migraine headache depends upon both electricity and chemicals for the transmission of head pain signal. One of the most important chemicals in that circuitry is the protein serotonin, and the triptans exert their therapeutic effect on migraine by acting at certain of the circuitry's receptors for serotonin.

Also important within migraine's circuitry is another protein, calcitonin gene related peptide (CGRP). Not surprisingly, for years CGRP has been a major focus of research involving migraine therapeutics, and within the past several years six new therapies designed to block or disable CGRP have become available for general clinical use. Four of those therapies are monoclonal antibodies, all indicated for migraine prevention and two are "gepants", indicated for the treatment of acute migraine. One of these two gepants is Ubrely.

Ubrely is an orally administered tablet available in two doses, 50 and 100 mg. It treats acute migraine headache by blocking CGRP receptors, "short-circuiting" the migraine circuitry. Like the triptans, Ubrely is a "designer drug" that was developed specifically for the treatment of migraine, but Ubrely is NOT a triptan. Again, the triptans are active at serotonin receptors—not CGRP receptors.

While many migraineurs find the triptans to be effective in treating acute migraine, even those who experience headache relief often complain that the side effects

associated with their use overshadow their benefit. In addition, one of the serotonin receptors which the triptans activate has the potential to cause arteries to constrict, and because of this the use of triptans is discouraged for individuals with a history of vascular disease (egs, heart attack, stroke) or serious vascular risk factors such as poorly controlled hypertension. Ubrely does not produce many of side effects associated with the triptans (egs, chest pressure, neck squeezing), and there is no formal contraindication to its use by patients with a history of vascular disease. Along with being safe and generally low in side effects, Ubrely is effective for a significant proportion of migraineurs who use it to treat acute migraine headache.

The maximum recommended total daily dose of Ubrely is 200 mg, and whether the initial dose of Ubrely administered is 50 mg or 100 mg, a second dose may be taken two or more hours after the first. Migraine can be stubborn, and given its all-too-frequent tendency to re-ignite, this dosing/re-dosing flexibility can be useful for patients who experience only partial headache relief or headache recurrence after their initial dose of Ubrely.

For many migraineurs, Ubrely can offer rapid relief from migraine headache and associated migraine symptoms without provoking unpleasant side effects. Given its high tolerability, efficacy and the option of repeat dosing, Ubrely offers the flexibility of a fast-onset oral triptan without triptan side effects or concerns regarding cardiovascular safety. **17**