Migraine Treatment of the Month

Reyvow (lasmiditan)

Within the past two years 3 new oral medications intended for treatment of acute migraine headache have been approved by the FDA and have become available for general clinical use. Two of these medications, both "gepants", Nurtec (rimegepant) and Ubrelvy (ubrogepant), previously have been featured in this magazine. The featured treatment for this issue is the third of the newcomers, Reyvow (lasmiditan).

In at least several of our prior issues we have discussed the biologic "circuit" in the nervous system which, when activated, generates acute migraine headache. Within that circuit there is electrochemical transmission of head pain signal, and two of the most important chemicals that assist in this transmission are "neurotransmitter" proteins: *serotonin* and *calcitonin gene related peptide* (CGRP).

The gepants "short-circuit" transmission of head pain signal and reduce or eliminate acute migraine headache by blocking the action of CGRP. In contrast, and similar to the triptans (sumatriptan, rizatriptan, eletriptan, etc), Reyvow exerts its therapeutic effect by activating a serotonin receptor (5-HT1F, specifically) that acts like a light switch to turn off transmission of head pain signal.

The triptans do the same by activating the 5-HT1B and 1D receptors which similarly inhibit head pain signal transmission. In doing so, however, they also exert a constrictive effect on cranial arteries and, to a lesser extent, arteries elsewhere in the body (including the coronary arteries which supply heart muscle with oxygen and other nutrients). While both research data and extensive clinical experience suggest that the triptans represent an extremely safe class of medications for acute migraine treatment and specifically have little potential for producing such clinically severe vascular complications as a heart attack or stroke, their theoretical potential for doing so has been a source of concern ever since the introduction of Imitrex (injectable sumatriptan, the first of the triptan line) in 1991.

The ideal serotonin receptor would be capable of blocking transmission of head pain signal without producing any blood vessel constriction. The 5-HT1F receptor meets that requirement, but the process of producing a "designer drug" which would selectively activate that receptor proved to be a long and arduous process. Reyvow (lasmiditan), the first of the so-called "ditans", is the result of that effort, and in October 2019 the FDA approved 3 different doses of Reyvow for the treatment of acute migraine headache (50 mg, 100 mg and 200 mg). In the phase 3 clinical trials that earned Reyvow its FDA approval, all 3 doses were superior to placebo in significantly reducing or eliminating head pain in patients with acute migraine headache of moderate to severe intensity within 2 hours of study drug administration.

As with virtually all medications, Reyvow has its imperfections. Most common amongst its side effects are dizziness and sedation, and it's consequently recommended that one refrain from driving or operating machinery for at least 1 hour following administration even if the medication has terminated the migraine episode. In addition, because of its perceived abuse potential, Reyvow is a federally controlled medication that typically requires a prescription process of the type associated with opioids, benzodiazepines and barbiturates.

That said, Reyvow represents a very promising option for the substantial number of patients who for reasons related to effectiveness or tolerability have failed to respond adequately to the triptans and gepants or for whom triptan therapy is contraindicated.