www.medscape.com

AHS Releases Updated Guidance on New Migraine Treatments

Steve Cimino

July 16, 2021

An updated consensus statement from the American Headache Society (AHS) offers detailed recommendations on the use of novel acute and preventive treatments in adult patients with migraine.

"Because the benefit–risk profiles of newer treatments will continue to evolve as clinical trial and real-world data accrue, the American Headache Society intends to review this statement regularly and update, if appropriate, based on the emergence of evidence with implications for clinical practice," wrote lead author Jessica Ailani, MD, of the department of neurology at Medstar Georgetown University Hospital, Washington, and colleagues. The statement was published in Headache.

To assess recent data on the efficacy, safety, and clinical use of newly introduced acute and preventive migraine treatments, the AHS convened a small task force to review relevant literature published from December 2018 through February 2021. The society's board of directors, along with patients and patient advocates associated with the American Migraine Foundation, also provided pertinent commentary.

New Migraine Treatment

Five recently approved acute migraine treatments were specifically noted: two small-molecule calcitonin gene-related peptide (CGRP) receptor antagonists — rimegepant and ubrogepant — along with the nonsteroidal anti-inflammatory drug celecoxib, the serotonin 5-HT_{1F} agonist lasmiditan, and remote electrical neuromodulation (REN). Highlighted risks include serious cardiovascular thrombotic events in patients on celecoxib, along with driving impairment, sleepiness, and the possibility of overuse in patients on lasmiditan. The authors added, however, that REN "has shown good tolerability and safety in clinical trials" and that frequent use of rimegepant or ubrogepant does not appear to lead to medication-overuse headache.

Regarding acute treatment overall, the statement recommended nonsteroidal anti-inflammatory drugs (NSAIDs), nonopioid analgesics, acetaminophen, or caffeinated analgesic combinations — such as aspirin plus acetaminophen plus caffeine — for mild to moderate attacks. For moderate or severe attacks, they recommended migraine-specific agents such as triptans, small-molecule CGRP receptor antagonists (gepants), or selective serotonin 5-HT_{1F} receptor agonists (ditans). No matter the prescribed treatment, the statement pushed for patients to "treat at the first sign of pain to improve the probability of achieving freedom from pain and reduce attack-related disability."

The authors added that 30% of patients on triptans have an "insufficient response" and as such may benefit from a second triptan or — if certain criteria are met — switching to a gepant, a ditan, or a neuromodulatory device. They also recommended a nonoral formulation for patients whose attacks are often accompanied by severe nausea or vomiting.

More broadly, they addressed the tolerability and safety issues associated with certain treatments, including the gastrointestinal and cardiovascular side effects of NSAIDs and the dangers of using triptans in patients with coronary artery disease or other vascular disorders. And while gepants and ditans appeared in clinical trials to be safe choices for patients with stable cardiovascular disease, "benefit-risk should be assessed in each patient as the real-world database for these therapies grows," they wrote.

Only one recently approved preventive treatment — eptinezumab, an intravenous anti-CGRP ligand monoclonal antibody (MAB) — was highlighted. The authors noted that its benefits can begin within 24 hours, and it can reduce acute medication use and therefore the risk of medication-overuse headache.

Regarding preventive treatments overall, the authors stated that prevention should be offered if patients suffer from 6 or more days of headache per month, or 3-4 days of headache plus some-to-severe disability. Preventive treatments should be considered in patients who range from at least 2 days of headache per month plus severe disability to 4 or 5 days of headache. Prevention should also be considered in patients with uncommon migraine subtypes, including hemiplegic migraine, migraine with brainstem aura, and migraine with prolonged aura.

Initiating Treatment

When considering initiation of treatment with one of the four Food and Drug Administration–approved CGRP MABs — eptinezumab, erenumab, fremanezumab, or galcanezumab — the authors recommend their use if migraine patients show an inability to tolerate or respond to a trial of two or more older oral medications or other established effective therapies.

Though they emphasized that oral preventive medications should be started at a low dose and titrated slowly until the target response is reached or tolerability issues emerge, no such need was specified for the parenteral treatments. They also endorsed the approach of patients staying on oral preventive drugs for a minimum of 8 weeks to determine effectiveness or a lack thereof; at that point, switching to another treatment is recommended.

The dual use of therapies such as neuromodulation, biobehavioral therapies, and gepants were also examined, including gepants' potential as a "continuum between the acute and preventive treatment of migraine" and the limited use of neuromodulatory devices in clinical practice despite clear benefits in patients who prefer to avoid medication or those suffering from frequent attacks and subsequent medication overuse. In addition, it was stated that biobehavioral therapies have "grade A evidence" supporting their use in patients who either prefer nonpharmacologic treatments or have an adverse or poor reaction to the drugs.

From the patient perspective, one of the six reviewers shared concerns about migraine patients being required to try two established preventive medications before starting a recently introduced option, noting that the older drugs have lower efficacy and tolerability. Two reviewers would have liked to see the statement focus more on nonpharmacologic and device-related therapies, and one reviewer noted the possible value in guidance regarding "exploratory approaches" such as cannabis.

Not Everyone Agrees

Commenting on the AHS consensus statement, James A Charles, MD, and Ira Turner, MD, had this to say: "This Consensus Statement incorporates the best available evidence including the newer CGRP therapies as well as the older treatments. The AHS posture is that the CGRP abortive and preventive treatments have a lesser amount of data and experience than the older treatments which have a wealth of literature and data because they have been around longer. As a result, there are 2 statements in these guidelines that the insurance companies quote in their manual of policies:

1. Inadequate response to two or more oral triptans before using a gepant as abortive treatment

2. Inadequate response to an 8-week trial at a dose established to be potentially effective of two or more of the following before using CGRP MAB for preventive treatment: topiramate, divalproex sodium/valproate sodium; beta-blocker: metoprolol, propranolol, timolol, atenolol, nadolol; tricyclic antidepressant: amitriptyline, nortriptyline; serotonin-norepinephrine reuptake inhibitor: venlafaxine, duloxetine; other Level A or B treatments."

Charles, who is affiliated with Holy Name Medical Center in Teaneck N.J., and Turner, who is affiliated with the Center for Headache Care and Research at Island Neurological Associates in Plainview, N.Y., further said that "giving the CGRP MABs and gepants second-class status because they have not been around as long as the old boys is an insult to the research, development, and successful execution of gepant and CGRP MAB therapies in the last several years.

The authors omitted the Hepp study and the long list of adverse effects of triptans leading to high discontinuance rates, and how trying a second triptan will probably not work." Importantly, they said, "the authors have given the insurance carriers a weapon to deny direct access to gepants and CGRP MABs making direct access to these agents difficult for patients and physicians and their staffs."

Charles and Turner point out that the AHS guidelines use the term "cost effective" – that it is better to use the cheaper, older drugs first. "Ineffective treatment of a patient for 8 weeks before using CGRP blocking therapies and using 2 triptans before a gepant is cost ineffective," they said. "Inadequate delayed treatment results in loss of work productivity and loss of school and family participation and excessive use of ER visits. These guidelines forget that we ameliorate current disability and prevent chronification by treating with the most effective abortive and preventive therapies which may not commence with the cheaper old drugs."

They explain: "Of course, we would use a beta-blocker for comorbid hypertension and/or anxiety, and venlafaxine for comorbid depression. And if a patient is pain free in 2 hrs with no adverse effects from a triptan used less than 10 times a month, it would not be appropriate to switch to a gepant. However, a treatment naive migraineur with accelerating migraine should have the option of going directly to a gepant and CGRP blocking MAB."

Charles and Turner concur that the phrase in the AHS consensus statement regarding the staging of therapy — two triptans before a gepant and two oral preventatives for 8 weeks before a CGRP MAB — "should be removed so that the CGRP drugs get the equal credit they deserve, as can be attested to by the migraine voices of lives saved by the sound research that led to their development and approval by the FDA."

Ultimately, Charles and Turner said, "the final decision on treatment should be made by the physician and patient, not the insurance company or consensus statements."

Alan Rapoport, MD, clinical professor of neurology at the University of California, Los Angeles, former president of the International Headache Society, and editor-in-chief of Neurology Reviews, said, "Although I think the consensus statement is well done, and the authors have the right to make the statements they have made, Drs. Charles and Turner are excellent experienced clinicians and they should be heard. They properly state that the restrictive statements highlighted by the authors have already been used by insurance companies to prevent access to the more expensive but more effective therapies with fewer adverse effects."

Rapoport goes on to say, "I believe that the patient's individual headache history and past responses to therapies must be analyzed by the treating physician and an appropriate treatment be agreed upon between the patient and doctor. It is time to let experienced headache-interested doctors make their own correct decision about treatment without the heavy hand of the insurance company, which is often more intent on saving money than helping the patient.

The authors acknowledged numerous potential conflicts of interest, including receiving speaking and consulting fees, grants, personal fees, and honoraria from various pharmaceutical and publishing companies.

Suggested Reading:

Hepp Z et al. Adherence to oral migraine-preventive medications among patients with chronic migraine. Cephalalgia. 2015;35(6):478-88.

Alam A et al. Triptan use and discontinuation in a representative sample of persons with migraine: Results from Migraine in America Symptoms and Treatment (MAST) study. Headache. 2018;58:68-69.

Buse DC et al. Adding additional acute medications to a triptan regimen for migraine and observed changes in headache-related disability: Results from the American Migraine Prevalence and Prevention (AMPP) study. Headache. 2015 Jun;55(6):825-39.

This article originally appeared on MDedge.com, part of the Medscape Professional Network.

Cite this: AHS Releases Updated Guidance on New Migraine Treatments - *Medscape* - Jul 16, 2021.