to account for tolerability and safety issues in prescribing may cause patients to limit, delay, or forego acute treatment.[56]

### Considering self-administered rescue

When acute treatment does not bring relief, patients may require rescue medication. Depending on the initial treatment, options for outpatient rescue include SC sumatriptan, DHE IM or intranasal spray, IM ketorolac, or corticosteroids (e.g., dexamethasone); office-based or inpatient options may include parenteral formulations of triptans, DHE, antiemetics, NSAIDs (e.g., ketorolac), anticonvulsants (e.g., valproate sodium [not in women of childbearing potential who are not using an appropriate method of birth control[63,64]]), corticosteroids, magnesium sulfate, and peripheral nerve blocks. Consider recommending a self-administered rescue treatment for patients with severe attacks and those who have a history of nonresponse or variable response to acute treatment.

### Avoiding medication overuse

Patients with migraine who need to use acute treatments on a regular basis should be instructed to limit medication use to an average of two headache days per week, and patients who exceed this limit should be offered a preventive treatment. Patients who continue to overuse acute medication while receiving preventive therapy may require an escalation in the preventive dose or a change in acute or preventive therapy; expert consensus generally supports the addition of a second preventive treatment in these patients. Among newer medications, repeated treatment with the CGRP receptor antagonists (i.e., ubrogepant and rimegepant) does not appear to be associated with medication-overuse headache[65–67]; preclinical models suggest repeated use of lasmiditan may induce medication-overuse headache through persistent latent peripheral and central sensitization mechanisms, although clinical studies are lacking.[68,69] Acute treatment with an approved neuromodulatory device may reduce the use of acute medication.[70]

## Recently approved acute treatments

Since the publication of the initial Consensus Statement, the FDA has approved or cleared five therapies for the acute treatment of migraine: celecoxib, lasmiditan, REN, rimegepant, and ubrogepant.

### Celecoxib

Celecoxib, which has been used to treat acute pain since 1998, was approved for the acute treatment of migraine; the new formulation is supplied as an oral solution. Efficacy is supported by findings from two randomized controlled clinical trials.[47,71] As with other NSAIDs, the prescribing information for celecoxib oral solution carries a boxed warning about risk of serious cardiovascular thrombotic events (e.g., myocardial infarction and stroke), and the drug is contraindicated in the setting of coronary artery bypass graft surgery.[71] Other safety concerns with celecoxib oral solution include an elevated risk of spontaneous bleeding, ulceration, and perforation of the stomach or intestines, particularly among elderly patients and those with a history of peptic ulcer disease and/or gastrointestinal bleeding.[71]

### Lasmiditan

Lasmiditan was approved based on positive results from two randomized controlled clinical trials evaluating lasmiditan doses of 50, 100, and 200 mg.[40,41] The most common AEs were dizziness, fatigue, paresthesia, sedation, nausea and/or vomiting, and muscle weakness. Lasmiditan has been associated with driving impairment and sleepiness, and it is classified as a Schedule V controlled substance (low potential for abuse).[72] Patients given a prescription for lasmiditan should be cautioned not to drive within 8 h after taking their medication. Frequent use of lasmiditan may potentially cause medication-overuse headache.[68] The safety, tolerability, and efficacy of coadministering lasmiditan with a triptan or a gepant has not been assessed.

### Remote electrical neuromodulation

The REN device achieves therapeutic effects by delivering transcutaneous electrical stimulation to the upper arm, which induces conditioned pain modulation and activates a descending endogenous analgesia.[73] It was FDA-cleared for the acute treatment of migraine in adults based on positive results in a randomized controlled clinical trial[45]; it was cleared for the acute treatment of migraine and chronic migraine in patients aged 12 years and older based on data from an open-label, single-arm, multicenter study.[74] As with many nondrug therapeutic options, REN has shown good tolerability and safety in clinical trials; paresthesia in the area of the device was the most common side effect.[45,46] This novel approach to acute treatment may also reduce the use of medications and consequent risk of medication-overuse headache.[70]

### Rimegepant

Rimegepant has demonstrated efficacy and tolerability in multiple randomized controlled clinical trials.[37–39] It has shown good safety and tolerability when used for up to 1 year, with nausea the most commonly reported AE.[66] The maximum dosage of rimegepant is a single 75 mg dose as needed per 24 h.[75] As stated previously, rimegepant (as with ubrogepant and lasmiditan) does not constrict blood vessels and may have a role in patients with cardiovascular