Migraine: The American Headache Society Update on Integrating New Migraine Treatments into Clinical Practice (2021)

About the Guideline
- This guideline includes the American Headache Society recommendations on the preventive and acute treatment of migraines in adults.
- Expert clinicians and researchers in the field of headache medicine from across North America and the European Union provided input and feedback.

Key Clinical Considerations
Become familiar with the recommendations and best-practice statements provided in this guideline.

Overview
- A migraine is characterized by a throbbing, unilateral headache that is exacerbated by physical activity and associated with photophobia, phonophobia, vomiting, nausea, and cutaneous allodynia.
- Some patients have an aura that precedes or occurs during some attacks. Some have a premonitory phase before the onset of the headache.
- Diagnosis is based on the frequency of monthly migraine days (MMDs) and monthly headache days (MHDs).
  - Migraines are episodic if fewer than 15 MMDs or MHDs occur that are characterized by the following:
    - At least five attacks that fulfill criteria B through D
      - Criteria B: Headache lasts 4 to 72 hours (when untreated or unsuccessfully treated)
      - Criteria C: Headache is characterized by at least two of the following four characteristics:
        - Unilateral location
        - Pulsating quality
        - Moderate or severe pain intensity
        - Aggravation by or causing avoidance of routine physical activity, such as walking or climbing stairs
      - Criteria D: At least one of the following occurs during the headache:
        - Nausea, vomiting, or both
        - Photophobia and phonophobia
    - Symptoms not better accounted for by another diagnosis (criteria E)
  - Migraines are chronic if at least 15 MHDs occur and if at least 8 of them are MMDs. Chronic migraines are characterized by the following:
    - Migraine-like or tension-like headache that occurs 15 or more days/month for more than 3 months and that fulfills criteria B and C:
      - Criteria B: At least five attacks occur that fulfill criteria B through D for migraine without aura, and/or criteria B and C for migraine with aura
      - Criteria C: On 8 or more days/month for more than 3 months, any of the following are present:
        - Criteria C and D for migraine without aura
        - Criteria B and C for migraine with aura
Patient belief that the headache is a migraine at the onset, and headache relief by a triptan or ergot derivative is reported. Symptoms not better accounted for by another diagnosis (criteria D)

- Creation of the treatment plan should include patient education and lifestyle modification, along with guidance about the benefits of the following:
  - Proper nutrition
  - Regular exercise
  - Adequate hydration
  - Proper sleep
  - Stress management
  - Maintaining a migraine diary

- The following should also be considered:
  - Patient preference
  - Status with respect to pregnancy, breastfeeding, or plans to conceive
  - Severity and frequency of attacks
  - Type, presence, and severity of associated symptoms
  - Disability related to attacks
  - Prior treatment response
  - Comorbid and coexisting illness
  - Contraindications
  - Body habitus and physiological measures
  - Concomitant use of medications

Preventive Treatment

- Goals of preventive treatment
  - Reduce the frequency, severity, duration, and disability of attack
  - During acute treatment, improve responsiveness and avoid escalation
  - Improve function and reduce disability
  - Avoid relying on ineffective, poorly tolerated, or unwanted acute treatments
  - Reduce the cost of migraine treatment
  - Enhance personal control and enable patients to manage their disease
  - Improve health-related quality of life (HRQoL)
  - Reduce headache-related distress and psychological symptoms

- Indications for preventive treatment
  - Attacks significantly interfere with daily routines despite acute treatment.
  - Attacks are frequent (four or more MHDs).
  - Acute treatment has failed, is overused, or is contraindicated.
    - Overuse is defined as using medications (such as ergot derivatives, triptans, opioids, combination analgesics, and a combination of medications from different classes) 10 or more days/month to try to control migraines.
  - The patient uses nonopioid analgesics, acetaminophen, and nonsteroidal anti-inflammatory drugs (NSAIDs), including aspirin, for 15 or more days/month.
  - The patient has a history of adverse events (AEs) with acute treatments.
  - The patient prefers preventive treatment.

- Consider preventive therapy to manage uncommon migraine subtypes, including
  - Hemiplegic migraine
• Migraine with brainstem aura
• Migraine with prolonged aura
• Previous migrainous infarction, even if the attack frequency is low

Patient selection for preventive treatment
• Offer preventive treatment to patients with 6 or more headache days per month without disability, 4 or more headache days per month with some disability, or 3 or more headache days per month with severe disability.
• Consider preventive treatment for patients with 4 or 5 headache days per month with no disability, 3 headache days per month with some disability, or 2 headache days per month with moderate disability.

Treatment plan development for traditional oral preventive therapies
• Consider the following when developing a treatment plan:
  ▪ Efficacy evidence
  ▪ Practitioner experience
  ▪ Headache subtype
  ▪ Tolerability
  ▪ Patient preference
  ▪ Comorbidities
  ▪ In women, pregnancy, breastfeeding, or plans to conceive
• Use evidence-based preventive treatments, such as candesartan, divalproex sodium, frovatriptan, metoprolol, propranolol, timolol, topiramate, valproate sodium, and onabotulinumtoxin A.
  ▪ Avoid preventive medications in pregnant and lactating women. Discuss the potential for adverse pregnancy and fetal effects with women of childbearing age.
• Four calcitonin gene-related peptide (CGRP) monoclonal antibody treatments are also available for migraine prevention and include the following:
  ▪ Erenumab, fremanezumab, and galcanezumab are administered as subcutaneous injections.
  ▪ Eptinezumab is available as an IV infusion.
• Start oral medications at a low dose and titrate upward slowly until the target response is achieved, the maximum target dose is reached, or tolerability becomes an issue. Combining preventive medications from different classes may be useful.
• Attempt to reach a therapeutic dose with oral treatments. Set an initial dose and stop titration when the maximum dose is reached, efficacy is optimal, or AEs become intolerable.
• Give an adequate trial of at least 8 weeks using the target or usual effective dose. If no response occurs after 8 weeks at the target dose or usual effective dose, switch the preventive treatment. Teach the patient that cumulative benefits may occur over 6 to 12 months of continued use.
• Establish realistic expectations and define success in migraine prevention to include the following:
  ▪ A 50% reduction in the number of days with headache or migraine
  ▪ Decreased attack duration
  ▪ Decreased attack severity
  ▪ Improved response to acute treatment
  ▪ Improved functioning and reduced migraine-related disability
- Improved HRQoL and reduced psychological distress related to migraines
  - Optimize drug selection
    - Choose treatments known to be effective for a comorbid condition and avoid drugs that may exacerbate a comorbid or coexisting illness or that may interact with coadministered medications.
    - Avoid using a single medication for multiple conditions if a risk of undertreatment exists for any single condition. Optimal treatment may require the use of separate medications.
    - Avoid preventive treatment in pregnant or breastfeeding women and in those who are trying to conceive.
    - Re-evaluate therapeutic responses. Taper or discontinue treatment if the patient no longer meets preventive treatment criteria.
  - Maximize adherence by educating the patient about treatment expectations and dose adjustments, while keeping patient preferences in mind.
- Measure the patient’s response to preventive therapy.
  - The patient usually defines efficacy and tolerability. However, in general, a significant reduction in MHDs is a useful benchmark in clinical trials and in practice.
  - Changes in functional capacity, disability, and quality of life are important for determining whether meaningful change has occurred and often guide clinical decision making and treatment.

**Acute Treatment**

- **Goals of acute treatment**
  - Achieve rapid and consistent freedom from pain and associated symptoms without recurrence
  - Restore functional ability
  - Produce minimal need for repeat dosing or rescue medications
  - Optimize self-care and reduce subsequent use of resources, such as emergency department visits, diagnostic imaging, and health care practitioner and ambulatory infusion center visits
  - Cause minimal or no AEs
- **Indications for acute treatment**
  - All patients with migraines should be offered acute treatment trials.
- **Considerations for treatment plan development**
  - Use evidence-based treatments, such as the following:
    - Offer NSAIDs, nonopioid analgesics, acetaminophen, or caffeinated analgesic combinations (such as aspirin with acetaminophen and caffeine) for mild-to-moderate attacks.
    - Consider migraine-specific agents (triptans and dihydroergotamine [DHE]) for severe attacks and for mild-to-moderate attacks that respond poorly to NSAIDs or caffeinated combinations.
    - If the patient has severe nausea and vomiting, choose a nonoral administration route for medication:
      - Sumatriptan 3 mg, 4 mg, or 6 mg subcutaneously or by the intranasal or inhaled route (powder formulations)
      - Ketorolac by the intranasal or intramuscular (IM) route
      - DHE subcutaneously and by intranasal spray
Medications with established efficacy include:

- Triptans
- Ergotamine derivatives
- NSAIDs such as aspirin, diclofenac, ibuprofen, and naproxen
- Opioids, such as butorphanol
- Combination medications

Medications that may be effective include:

- Ergotamine and other forms of DHE
- NSAIDs, such as ketoprofen, IV and IM ketorolac, and flurbiprofen
- Isometheptene-containing compounds
- IV magnesium
- Combinations, such as codeine-acetaminophen and tramadol-acetaminophen
- Antiemetics, such as prochlorperazine, promethazine, droperidol, chlorpromazine, and metoclopramide

- Account for tolerability and safety issues. Not accounting for safety and tolerability can lead the patient to limit, delay, or forego acute treatment.
- Consider self-administered rescue medications.
  - Medications include subcutaneous sumatriptan, DHE injection or intranasal spray, or corticosteroids such as dexamethasone and IM ketorolac.
- Consider inpatient medications, including parenteral formulations of triptans, DHE, antiemetics, NSAIDs (such as ketorolac), anticonvulsants (such as valproate sodium and topiramate [not for women of childbearing age]), corticosteroids, and magnesium sulfate.
- Avoid medication overuse.
  - Limit treatment to an average of two headache days/week or provide preventive treatment.

- Measure the response to acute treatment.
  - Understand patient preference to increase adherence, discourage treatment discontinuation, and match the patient's treatment needs. Patient-oriented outcome measures help validate meaningful response.

Recently Approved Acute Treatments

- The following are recently approved acute treatments:
  - Celecoxib—comes with a boxed warning regarding the risk of serious cardiovascular thrombotic events and is contraindicated in the setting of coronary artery bypass graft surgery.
  - Lasmiditan—classified as a Schedule V controlled substance (although it has a low potential for abuse) as it is associated with driving impairment and sleepiness. Other side effects may include dizziness, fatigue, paresthesia, sedation, nausea/vomiting, and muscle weakness.
  - Remote electrical neuromodulation (REN)—delivers transcutaneous electrical stimulation to the upper arm that induces conditioned pain modulation and activates a descending endogenous analgesia.
  - Rimegepant—may be useful for patients with contraindications to triptans as it does not constrict blood vessels. Nausea was noted as the most common side effect.
Ubrogepant—found to be safe and tolerable. The most common side effects include nausea, somnolence, and dry mouth.

**Neuromodulation and Biobehavioral Therapies**

- Neuromodulation stimulates the central or peripheral nervous system with an electric current or a magnetic field.
  - Single-pulse transcranial magnetic stimulation may be used for acute and preventive treatment of migraines.
  - Electrical trigeminal nerve stimulation may be used for acute and preventive treatment of migraines.
  - Noninvasive vagus nerve stimulation may be used for acute treatment of migraines.

- Biobehavioral therapies
  - Lifestyle modification includes minimizing exposure to triggers and managing unavoidable triggers. It also includes hydration, exercise, and nutrition advice, which should be individualized for each patient.
  - Biobehavioral therapy, such as cognitive behavioral therapy (CBT), biofeedback, and relaxation therapies, are effective for acute and preventive treatment of migraines.
  - Consortium recommendations for nonpharmacologic treatments may be beneficial to the following patient populations:
    - Those who prefer nonpharmacologic interventions
    - Those with an inadequate response to, poor tolerance of, or medical contraindications to specific pharmacologic treatments
    - Women who are pregnant, breastfeeding, or planning to become pregnant
    - Those with a history of medication overuse
    - Those with significant stress or deficient coping skills
  - Behavioral intervention goals for preventive headache treatment include the following:
    - Reduce the frequency and severity of headache as well as headache-related disability
    - Decrease reliance on poorly tolerated or unwanted medications
    - Enhance personal control of migraine
    - Reduce headache-related distress and psychological symptoms

**Reference**