

# How to Discuss Treatment Options for the Adolescent Patient with Migraine

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## Overview

Migraine is a chronic disease that often requires long-term therapy. While the ultimate goal is to eliminate head pain through lifestyle modifications and therapeutic interventions, this is often difficult to achieve. Setting expectations for pain control with patients and caregivers is essential for successful long-term migraine management. Discussions with patients and caregivers should highlight how the aim of therapeutic intervention is to reduce frequency and severity of migraine attacks to maximize quality of life (i.e. enable an individual to attend and participate in school, perform daily physical and social activities).

The following charts may serve as useful resources for providers to select proper treatment options, guide discussions with patients and caregivers, and provide educational materials regarding prevention and treatment strategies for adolescents with migraine.

## Lifestyle Techniques

Identifying specific triggers, exacerbating and relieving factors unique to each individual is a key aspect of controlling migraine pain. The chart below outlines daily lifestyle measures in an easy to remember SMART mnemonic that may be beneficial in preventing and/or reducing frequency of migraine episodes.



## SMART daily tips to help prevent or decrease frequency of migraine episodes

<b>Sleep</b>	<ul style="list-style-type: none"> <li>Regular bedtime routine with consistent sleep times (even on weekends)</li> <li>Limit naps</li> <li>No screen time 1-2 hours before bedtime</li> <li>Aim for 9-11 hours of sleep each night</li> <li>If difficulty falling asleep, can use melatonin 5-10 mg to help with sleep onset (Note: should be taken 30-60 minutes before desired bedtime)</li> </ul>
<b>Meals (Nutrition and Hydration)</b>	<ul style="list-style-type: none"> <li>Consistent meals daily, no skipping meals (especially breakfast)</li> <li>Snacks as needed</li> <li>Aim to drink body weight equivalent in water per day (kilogram equals ounces of water)</li> <li>Bring a water bottle to school to ensure consistent hydration throughout the day</li> <li>If consuming high sugar electrolyte drink, dilute with half water</li> </ul>
<b>Activity</b>	<ul style="list-style-type: none"> <li>At least 30 minutes of physical activity 3-5 days per week, heart rate should be raised. May increase duration and intensity of exercise as tolerated</li> <li>Limit screen time to 2 hours or less per day</li> </ul>
<b>Relaxation</b>	<ul style="list-style-type: none"> <li>Relaxation training and biofeedback programs reduce stress and/or anxiety (mindfulness apps, deep breathing techniques, yoga, etc.)</li> <li>Counter-stimulation using a strong (more tolerable) stimulus during a migraine to distract from pain and break pain cycle (ex: cold ice pack to forehead or back of neck, strong mint or sour candy on tongue)</li> </ul>
<b>Triggers</b>	<ul style="list-style-type: none"> <li>Recognize and eliminate triggers including dietary, environmental, medication, physical, hormonal, behavioral (ex: specific foods, irregular meals, odors, weather changes, stress, poor sleep habits, menstrual cycle, etc.)</li> <li>Keep a headache log to identify triggers and track response to above measures</li> </ul>

## Acute Therapy

**Rescue medications should be used for patients with migraine (with or without aura) to stop the headache process, shorten duration, decrease severity and prevent progression of migraine symptoms** including pain, nausea/vomiting and photophobia/phonophobia. These medications should be taken at the first indication of migraine, ideally within 30 minutes of onset. In addition to taking medication, resting or sleeping in a dark, quiet room if possible may be beneficial. Medication is most effective when used in combination with lifestyle modifications and proper patient education as outlined in the SMART chart above.

*\*Note: Severe migraine (unresponsive to medications listed below and lasting for more than 24 hours) may require intravenous infusion of medications to stop the migraine attack. Individuals should be seen by headache specialist or facility able to administer medications (infusion center, emergency department, etc).*



## Acute Therapy

### Over-the-counter analgesics

*Medications for initial treatment of migraine (with or without aura) with mild pain and minimal disability*

Medication	Mechanism of action	Dosing and frequency	Side effects	Contraindications and warnings
Nonsteroidal anti-inflammatory drugs (NSAIDs): Ibuprofen (Motrin) Naproxen (Aleve)	Inhibition of the cyclooxygenase enzymes (COX-1 or COX-2) that synthesize prostaglandins	Ibuprofen: 10 mg/kg, max dose 800mg daily limit 2400mg every 6-8 hours as needed  Naproxen: 5-10mg/kg, 220mg pill strength Daily limit 660mg every 8-12 hours as needed	Indigestion Stomach pain Nausea/vomiting Headache Dizziness Drowsiness Bruising Ringing in ears	Do not use if history of renal disease, active GI bleeding or bleeding disorder  Do not use more than 2 days per week to avoid rebound or medication overuse headache
Acetaminophen (Tylenol)	Weak inhibitor of the synthesis of prostaglandins	Acetaminophen: 15 mg/kg, max dose 1 gram daily limit 4 grams every 4-6 hours as needed	Hepatotoxicity Anaphylaxis Skin reactions	Do not use with liver disease or failure  Do not use more than 2 days per week to avoid rebound or medication overuse headache

### Gepants

*Medications for moderate to severe migraine (with or without aura) refractory to or contraindicated usage of triptans*

Medication	Mechanism of action	Dosing and frequency	Side effects	Contraindications and warnings
Ubrogepant (Ubrovelvy)  Rimegepant (Nurtec)	CGRP receptor antagonists	Ubrovelvy: 50 or 100 mg dose max dose 200mg/24hr  Nurtec: 5 mg single dose max dose 75 mg/24hr	Nausea Drowsiness Dry mouth	Do not use with strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin)

### Anti-emetics

*Medications for nausea and/or vomiting with migraine (with or without aura) to be used in combination with analgesics*

Medication	Mechanism of action	Dosing and frequency	Side effects	Contraindications and warnings
Ondansetron (Zofran)  Promethazine (Phenergan)	5-HT <sub>3</sub> receptor antagonist  Dopamine receptor and H <sub>1</sub> receptor antagonist	Ondansetron: 4 or 8 mg per dose max dose 24mg/24hr every 8-12 hours as needed  Promethazine: 0.25-0.5 mg/kg/dose max dose 100mg/24hr every 4-6 hours as needed	Dizziness Drowsiness Headache  Paradoxical effects-excitability restlessness	Avoid if taking other QT interval prolonging agents  Avoid if taking other QT interval prolonging agents or if known hypersensitivity to promethazine

## Acute Therapy

### Triptans

*Medications for moderate to severe migraine (with or without aura) refractory to analgesics*

Medication	Mechanism of action	Dosing and frequency	Side effects	Contraindications and warnings
Rizatriptan (Maxalt)	Serotonin agonists with an affinity for 5-HT <sub>1B</sub> /1D receptors	Rizatriptan: 6-17yr oral 5mg (<40kg), 10mg (>40kg) daily limit 30mg	Dizziness Fatigue Dry mouth Nausea/vomiting Numbness Tingling Weakness Pain/pressure Flushing	Do not use if history of ischemic vascular disease, cerebral vascular abnormalities, arrhythmias associated with accessory conduction pathway disorders or pregnancy  Triptans should not be used in combination with ergotamines  Use with caution in patients with hemiplegic or brainstem aura, theoretical risk of vasospasm  For Rizatriptan, if taking propranolol should reduce dose to 5mg  To prevent the development of medication overuse headache, do not use more than nine days per month
Sumatriptan (Imitrex)		Sumatriptan: 12-17yr oral 25mg (<40kg), 50-100mg (>40kg) daily limit 200mg		
Zolmitriptan (Zomig)		nasal 5mg (<40kg), 10-20mg (>40kg) daily limit 40mg		
Almotriptan (Axert)		Zolmitriptan: 12-17yr oral or nasal 2.5mg (<40 kg), 5mg (>40kg) daily limit 10mg		
Eletriptan (Relpax)		Almotriptan: 12-17yr oral 6.25mg (<40kg), 12.5mg (>40kg) daily limit 25mg		
Frovatriptan (Frova)		Eletriptan: 12-17yr oral 20mg (<40kg), 40-80mg (>40kg) daily limit 80mg		
Naratriptan (Amerge)		Frovatriptan: 12-17yr oral 2.5mg daily limit 7.5mg		
Sumatriptan-naproxen (Treximet)		Naratriptan: 12-17yr oral 1 or 2.5mg daily limit 5mg  Treximet: 12-17yr oral 10/60, 30/180 or 85/500mg daily limit 85/500mg		

### Anti-histamines

*Medications to induce sleep with migraine (with or without aura) to be used in combination with analgesics*

Medication	Mechanism of action	Dosing and frequency	Side effects	Contraindications and warnings
Diphenhydramine (Benadryl)	Histamine H <sub>1</sub> Antagonist	Diphenhydramine: 6.25 or 12.5 mg per dose max 6 doses/24hr every 4 hours as needed	Drowsiness Dizziness Tremor Headache Stomach upset	Avoid use in patients with overactive thyroid, increased eye pressure or previous hypersensitivity reaction

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## Preventive Therapy

For frequent headaches, especially chronic daily headaches (defined as >15 headache days per month), preventive therapies should be tried, in addition to lifestyle modification, co-morbidity management and cognitive behavioral therapy. The goal of these medications is to reduce headache frequency and/or severity and to reduce headache-related functional disability. Historically, the medications used were those known to be effective in reducing headache frequency in adults. In 2013, the findings of the Childhood Headache and Migraine Prevention (CHAMP) trial, which compared the use of topiramate and amitriptyline to placebo over the course of a 24-week treatment period, found no significant difference in reduction of headache frequency or headache-related disability across the 3 groups<sup>1</sup>. The study was stopped early due to futility and the active drugs were associated with increased

adverse events. The medications listed below are those commonly used to help with reducing headache burden in children and adolescents. Much of their use has been extrapolated from studies in adults. Specific medications are often selected based on their potential benefit and/or (positive or negative) side effects and an individual patient's co-morbidities. The lack of evidence supporting pharmacologic therapy and significant placebo effect noted in pediatric migraine studies should be discussed with patients and families prior to any medication trial. Overuse of over the counter or prescribed rescue medications should be addressed. Long term data on the use of CGRP modulators is not yet available. As such, these medications should be used in carefully selected patients with close clinical monitoring<sup>2</sup>.

<b>Preventive Treatments</b> <i>Medications to reduce the frequency and/or severity of chronic daily headache</i>				
Medication	Mechanism of action	Dosing and frequency	Side effects	Contraindications and warnings
<b>Cyproheptadine</b> (Periactin)  4 mg tablets  2 mg/5 mL syrup	Antihistamine (H1 antagonist) and serotonin antagonist with anticholinergic effects	0.2-0.4 mg/kg/day; range 2-8 mg at bedtime	Sedation, increased appetite, weight gain	
<b>Topiramate</b> (Topamax)  15 mg and 25 mg sprinkle capsules  25 mg, 50 mg, 100 mg & 200 mg tablets	Sodium channel blocker, GABA agonist, glutamate antagonist, weak carbonic anhydrase inhibitor	6 to <12y, weight > 20 kg: begin with 15 mg daily and gradually increase weekly up to max of 2-3 mg/kg/day or 100 mg/day ≥12y: begin with 25 mg daily and increase weekly up to 100-200 mg/day; must taper slowly	Flushing, decreased appetite/weight loss, reduced sweating, kidney stones, cognitive slowing, dizziness, paresthesias, fatigue	May cause fetal harm
<b>Amitriptyline</b>  10 mg, 25 mg, 50 mg, 75 mg, 100 mg & 150 mg tablets	Tricyclic antidepressant – serotonin & norepinephrine reuptake inhibitor	Tricyclic antidepressant – serotonin & norepinephrine reuptake inhibitor	Sedation, dry mouth, dizziness, constipation, urinary retention	Increased risk of suicidal thinking and behavior, prolonged QT (obtain ECG if dosing >1 mg/kg/day)
<b>Propranolol</b>  20 mg/5mL & 40 mg/5 mL solutions  10 mg, 20 mg, 40 mg and 80 mg tablets  Extended release also available	Non-selective beta-adrenergic blocker	Children 3 years and adolescents: 0.5-3 mg/kg/day divided BID or TID, max 20-40 mg TID; must taper slowly	Fatigue, exercise intolerance, bradycardia, hypotension, bronchospasm	Do not use in patients with heart block or asthma

## Preventive Treatments

Medications to reduce the frequency and/or severity of chronic daily headache

Medication	Mechanism of action	Dosing and frequency	Side effects	Contraindications and warnings
<b>Verapamil</b>  40 mg, 80 mg and 120 mg tablets  Controlled and extended release also available	Calcium channel blocker	40-120 mg/day divided	Constipation, gingival hyperplasia, hypotension, dizziness, elevated transaminases	Can cause heart block
<b>Valproic Acid</b> (Divalproex sodium/Depakote/Depakene)  250 mg/5mL solution  125 mg and 250 mg sprinkle capsules  Extended release also available  Extended release also available	GABA-agonist, sodium channel blocker	10-15 mg/kg/day divided BID, dose range 250-1,000 mg/day; must monitor CBC, LFTs, vitamin D	Alopecia, hepatotoxicity, hyperammonemia, encephalopathy, leukopenia, thrombocytopenia, drug hypersensitivity, suicidal thoughts/behavior	FDA black box warning for fetal risk and hepatic failure; pancreatitis
<b>CGRP modulators</b>  Erenumab (Aimovig)  Fremanezumab (Aijovy)  Galcanezumab (Emgality)  Eptinezumab	Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonist	70-140 mg SC monthly  225-625 mg SC q3 months  120-240 mg SC monthly  100-300 mg IV q3 months	Injection site reaction, constipation, muscle cramps/spasms  Eptinezumab only: URI, hypersensitivity, fatigue	High cost, lack of long term data, may be beneficial for patients not able to take daily medications
<b>Onabotulinum toxin A</b> (Botox)	Prevents calcium-dependent release of acetylcholine	74-155 Units IM q3 months (5U/site over 31 sites covering forehead, scalp and posterior cervical region)		Spread to other areas, causing weakness, diplopia, ptosis, dysphagia, dysphonia, dysarthria and difficulty breathing
<b>Supplements</b>  Magnesium  Co-enzyme Q10  Riboflavin (B2)  Melatonin	Mitochondrial cofactor, NMDA-glutamate receptor antagonist  CoQ10 and B2 are both mitochondrial enzymatic cofactors  Supplements endogenous melatonin to promote sleep onset	20-80 mEq of elemental magnesium /day  CoQ10: 1-3 mg/kg/day (up to 100 mg TID)  Riboflavin: 25-400 mg daily  1-5 mg at bedtime	Diarrhea  Discoloration of urine, GI upset  Vivid dreams	

## Preventive Treatments

Medications to reduce the frequency and/or severity of chronic daily headache

Medication	Mechanism of action	Dosing and frequency	Side effects	Contraindications and warnings
<b>Non-invasive Neuro-modulatory Devices</b>  Cefaly (tSNS)  eNeura (sTMS)  Gamma Core	Transcutaneous supraorbital neurostimulation applied to forehead  Single pulse transmagnetic stimulation to the back of the head  Non-invasive vagus nerve stimulation to the side of the neck, blocks pain signals	20 minutes daily  4 pulses BID  2 minutes TID	Fatigue, headache, skin irritation  Momentary light headedness, tinnitus  Site-related discomfort/tingling, dizziness	

### References/Resources:

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