

# Preventive Therapy for Adolescents with Migraine



If a patient has frequent migraine (more than four attacks a month) or has chronic migraine (more than 15 attacks per month), preventive therapies could be an option worth exploring. The goal of preventive therapies is to reduce headache frequency and/or severity and to reduce headache-related functional disability. Preventive treatments are most effective alongside lifestyle modification, co-morbidity management and cognitive behavioral therapy.

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.

## Preventative Treatments

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

Medication	Mechanism of Action	Dosing and Frequency	Side Effects	Contraindications & 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 & 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)

*\*Notes: Specific medications are often selected based on their potential benefit and/or (positive or negative) side effects and an individual patient's comorbidities. 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.*

## Preventative Treatments Continued

Medication	Mechanism of Action	Dosing and Frequency	Side Effects	Contraindications & Warnings
<b>Propranolol</b> - 20 mg/5mL & 40 mg/5 mL solutions - 10 mg, 20 mg, 40 mg & 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
<b>Verapamil</b> - 40 mg, 80 mg & 120 mg tablets  Controlled & 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 & 250 mg sprinkle capsules  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> <ul style="list-style-type: none"> <li>Erenumab (Aimovig)</li> <li>Fremanezumab (Ajovy)</li> <li>Galcanezumab (Emgality)</li> <li>Eptinezumab</li> </ul>	Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonist	<ul style="list-style-type: none"> <li>70-140 mg SC monthly</li> <li>225-625 mg SC q3 months</li> <li>120-240 mg SC monthly</li> <li>100-300 mg IV q3 months</li> </ul>	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> <ul style="list-style-type: none"> <li>Magnesium</li> <li>Co-enzyme Q10</li> <li>Riboflavin (B2)</li> <li>Melatonin</li> </ul>	Mitochondrial cofactor, NMDA-glutamate receptor antagonist  CoQ10 and B2 are both mitochondrial enzymatic cofactors  Supplements endogenous melatonin to promote sleep onset	<ul style="list-style-type: none"> <li>20-80 mEq of elemental magnesium /day</li> <li>CoQ10: 1-3 mg/kg/day (up to 100 mg TID)</li> <li>Riboflavin: 25-400 mg daily</li> <li>1-5 mg at bedtime</li> </ul>	Diarrhea  Discoloration of urine, GI upset  Vivid dreams	
<b>Non-invasive Neuro-modulatory Devices</b> <ul style="list-style-type: none"> <li>Cefaly (tSNS)</li> <li>eNeura (sTMS)</li> <li>Gamma Core</li> </ul>	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	<ul style="list-style-type: none"> <li>20 minutes daily</li> <li>4 pulses BID</li> <li>2 minutes TID</li> </ul>	Fatigue, headache, skin irritation  Momentary light headedness, tinnitus  Site-related discomfort/tingling, dizziness	

### References/Resources

1. Powers S, Coffey CS et al. Trial of Amitriptyline, Topiramate and Placebo for Pediatric Migraine. *N Eng J Med*. 2017 Jan 12;376(2): 115-124.
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4. Oskoui M, Pringsheim T et al. Practice guideline update summary: Pharmacologic treatment for pediatric migraine prevention. *Neurology* 2019;93:500-509.
5. Up-to-Date: dosing guidelines (accessed 5/7/20).
6. American Migraine Foundation - Resource Library: Migraine in Children (accessed 5/7/20). <https://americanmigrainefoundation.org/resource-library/?tag=migraine-in-children>.