### Comparison Table: Some Drugs for Migraine Prevention in Adults

<table>
<thead>
<tr>
<th>Drug</th>
<th>Usual Adult Dosage</th>
<th>Efficacy</th>
<th>Precautions</th>
<th>Pregnancy</th>
<th>Comments</th>
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<tbody>
<tr>
<td><strong>Beta Blockers</strong></td>
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<tr>
<td>Metoprolol – generic</td>
<td>50–100 mg bid</td>
<td>≥50%</td>
<td>First-line option&lt;br&gt;Effective and commonly used for prevention of migraine</td>
<td>High doses have caused embryofetal toxicity in animals&lt;br&gt;Preventive therapy is generally not recommended during pregnancy</td>
<td>Improvement may take several weeks&lt;br&gt;Propranolol and timolol are FDA-approved for this indication&lt;br&gt;The dose of rizatriptan should be limited to 5 mg (max 15 mg/day) in adults taking propranolol&lt;br&gt;Nadolol (20-240 mg once/day) and atenolol (25-100 mg once/day) may also be effective</td>
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<tr>
<td>Lopressor (Validus)</td>
<td>100–200 mg once/day</td>
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<tr>
<td>Toprol-XL (AstraZeneca)</td>
<td>40–160 mg/d divided bid</td>
<td>≥50%</td>
<td>First-line option&lt;br&gt;Effective and commonly used for prevention of migraine</td>
<td>Intrauterine growth retardation, small placentas, and congenital abnormalities have been reported in neonates whose mothers received propranolol during pregnancy&lt;br&gt;Preventive treatment is generally not recommended during pregnancy</td>
<td>Brisk fetal heart rate has occurred with maternal use of timolol during pregnancy&lt;br&gt;Preventive therapy is generally not recommended during pregnancy</td>
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<tr>
<td>Propranolol – generic</td>
<td>100–200 mg once/day</td>
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<tr>
<td>Inderal LA (Akrimax)</td>
<td>10–15 mg bid or 20 mg once/day (starting dose 5 mg once/day)</td>
<td></td>
<td>Generally not used for migraine prevention</td>
<td>Decreased fetal heart rate has occurred with maternal use of timolol during pregnancy&lt;br&gt;Preventive therapy is generally not recommended during pregnancy</td>
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<tr>
<td><strong>Antiepileptic Drugs</strong></td>
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<tr>
<td>Valproate3&lt;br&gt;divalproex sodium – generic</td>
<td>250–500 mg bid</td>
<td>≥50%</td>
<td>First-line option&lt;br&gt;Valproate and topiramate are similarly effective for migraine prevention&lt;br&gt;40–50% of patients achieve ≥50% reduction in headache frequency&lt;br&gt;Topiramate has been effective in patients with chronic migraine (&gt;15 headache days/month for ≥3 months)</td>
<td>Common adverse effects: nausea, fatigue, tremor, weight gain, hair loss&lt;br&gt;Polycystic ovary syndrome, hyperinsulinemia, lipid abnormalities, hirsutism, and menstrual disturbances can occur&lt;br&gt;Acute hepatic failure, pancreatitis, and hyperammonemia are rare</td>
<td>Contraindicated for prevention of migraine in pregnant women&lt;br&gt;Associated with an increased risk of major congenital malformations&lt;br&gt;IQ scores were lower in the children of mothers who took the drug during pregnancy&lt;br&gt;Preventive therapy is generally not recommended during pregnancy</td>
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<tr>
<td>Depakote (Abbvie)</td>
<td>500–1000 mg once/day</td>
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<td>Depakote ER</td>
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<tr>
<td>Topiramate – generic</td>
<td>50 mg bid&lt;br&gt;titrate to 100 mg/day over 4 wks: wk 1: 25 mg in the evening; wk 2: 25 mg in the morning and evening; wk 3: 25 mg in the morning and 50 mg in the evening; wk 4: 50 mg in the morning and evening</td>
<td>≥50%</td>
<td>In a trial in pediatric patients, topiramate was no better than placebo5</td>
<td>Adverse effects: paresthesias, fatigue, language and cognitive impairment, taste perversion, weight loss, nephrolithiasis&lt;br&gt;Secondary narrow-angle glaucoma, oligohydrosis, and symptomatic metabolic acidosis are rare</td>
<td>Should not be used in pregnant women; increased risk of cleft lip and cleft palate&lt;br&gt;Preventive therapy is generally not recommended during pregnancy</td>
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<tr>
<td>Topamax (Janssen)</td>
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<td><strong>Tricyclic Antidepressant (TCA)2</strong></td>
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<tr>
<td>Amitriptyline – generic</td>
<td>25–150 mg once/day</td>
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<td>Amitriptyline is the only TCA shown to be effective in clinical trials</td>
<td>Adverse effects: sedation, dry mouth, constipation, blurred vision, urinary retention, tachycardia, palpitations, orthostatic hypotension, weight gain (adverse effects more common with amitriptyline)&lt;br&gt;Confusion can occur, particularly in older adults</td>
<td>TCA use during pregnancy has been associated with jitteriness and convulsions in newborns&lt;br&gt;Preventive therapy is generally not recommended during pregnancy</td>
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<td>Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)²</td>
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| Venlafaxine – generic extended-release – generic Effexor XR (Pfizer)   | 25-50 mg tid 75-150 mg once/day                                                    | • Have been effective for migraine prevention in a few studies, but evidence is weak | • Adverse effects: nausea, vomiting, sweating, tachycardia, urinary retention, increased blood pressure | • Pregnancy studies with SNRIs are limited  
• Fetal malformations are uncommon  
• Increased risks of neonatal behavioral syndrome and perinatal complications  
• Preventive therapy is generally not recommended during pregnancy | • May be an option for patients with comorbid depression, panic disorder, or anxiety disorder | $19.10  
15.00  
422.20  
15.70  
575.00  
675.00  
29.90  
215.10 | Duloxetine – generic Cymbalta                                                      | 30-120 mg once/day                                                                | • Adverse effects: nausea, dry mouth, constipation, insomnia, headache, dizziness, and somnolence | • Small increases in blood pressure and heart rate have been observed |                                                                          |               |
|                                                                       |                                                                                     |          |                                                                             |                          |                                                                          |               |
| Calcitonin Gene-Related Peptide-Blockers⁵,⁷                          |                                                                                     |          |                                                                             |                          |                                                                          |               |
| Erenumab-aooe – Aimovig (Amgen/Novartis)                             | 70 mg SC once/month²                                                                | • Reduced migraine frequency compared to placebo in double-blind trials  
• May be effective when other therapies have failed | • Generally well tolerated; injection-site reactions most common  
• Anti-drug antibodies with in vitro neutralizing activity have developed; clinical significance unknown  
• CGRP suppression could theoretically increase CV risk; patients with significant CV disease excluded from clinical trials  
• Hypersensitivity reactions to fremanezumab and galcanezumab have been reported | • No adequate data in pregnant women  
• No adverse effects reported with animal exposure  
• Long half-life; fetal exposure could occur months after drug discontinuation  
• Preventive therapy is generally not recommended during pregnancy | • Refrigerate during storage; drug should be allowed to sit at room temperature out of sunlight for ≥30 minutes before administration  
• Erenumab: should be injected into upper arm  
• Fremanezumab: should be injected into abdomen, thigh, or upper arm  
• Galcanezumab: should be injected into abdomen, thigh, buttocks, or upper arm | $575.00  
1.50  
277.10  
120.00  
120.00  
120.00  
64.30  
215.10 | Fremanezumab-vfrm – Ajovy (Teva)                                                  | 225 mg SC once/month or 675 mg SC q3 months                                        | • Common adverse effects: headache, and worsening migraines | • Can cause headache and worsening migraines  
• Reductions in body weight and decreased skeletal ossification were observed in the fetuses of pregnant rats and rabbits given the drug  
• Abortions, early deliveries, and maternal death has occurred in pregnant animals given the drug  
• Preventive therapy is generally not recommended during pregnancy |                                                                          |                                                                          |               |
| Gallcanezumab-gnlm – Engalyt (Lilly)                                 | 240 mg SC once, then 120 mg SC once/month                                          | • Evidence supporting the effectiveness of calcium channel blockers for migraine prevention is weak  
• Verapamil was somewhat more effective than placebo in some studies¹³ | • Common adverse effects: headache, gingival hyperplasia, constipation, peripheral edema, hypotension, fatigue  
• Avoid in patients with left ventricular dysfunction  
• May cause AV block and bradycardia | • Limited data on use in pregnant women  
• Preventive therapy is generally not recommended during pregnancy |                                                                          | $1202.00²  
13.90  
277.10  
29.90  
184.10 | Botulinum Toxin Type A⁸                                                      |                                                                                     |          |                                                                             |                          |                                                                          |               |
| OnabotulinumtoxinA – Botox (Allergan)                               | 155 units IM divided over 31 sites in 7 specific head/neck muscle areas every 12 weeks¹⁰ | • Reduced number of migraine days per month in clinical trials¹¹ | • Can cause headache and worsening migraines  
• Reductions in body weight and decreased skeletal ossification were observed in the fetuses of pregnant rats and rabbits given the drug  
• Abortions, early deliveries, and maternal death has occurred in pregnant animals given the drug  
• Preventive therapy is generally not recommended during pregnancy |                                                                          |                                                                          | $1202.00²  
13.90  
277.10  
29.90  
184.10 | Calcium Channel Blocker²                                                   |                                                                                     |          |                                                                             |                          |                                                                          |               |
| Verapamil – generic Calan (Pfizer) extended-release – generic Calan SR | 120-240 mg/day in three divided doses  
120-240 mg/day once or in two divided doses | • Evidence supporting the effectiveness of calcium channel blockers for migraine prevention is weak  
• Verapamil was somewhat more effective than placebo in some studies¹³ | • Common adverse effects: headache, gingival hyperplasia, constipation, peripheral edema, hypotension, fatigue  
• Avoid in patients with left ventricular dysfunction  
• May cause AV block and bradycardia | • Limited data on use in pregnant women  
• Preventive therapy is generally not recommended during pregnancy |                                                                          | $1202.00²  
13.90  
277.10  
29.90  
184.10 | Angiotensin-Converting Enzyme (ACE) Inhibitor and Angiotensin Receptor Blocker (ARB)³ |                                                                                     |          |                                                                             |                          |                                                                          |               |
| Lisinopril – generic Prinivil (Merck)                                | 20 mg once/day                                                                     | • Reduced migraine frequency by about 30-35% in small, double-blind trials¹⁴ | • Can cause angioedema, cough, hypotension (particularly with diuretic use or volume depletion), rash, acute renal failure, hyperkalemia, loss of taste, heptotoxicity, pancreatitis, blood dyscrasias, and renal damage  
• ARBs less likely than ACE inhibitors to cause cough and rarely cause angioedema | • Contraindicated for use during pregnancy  
• Preventive therapy is generally not recommended during pregnancy | • Not frequently used for migraine prevention  
• May be an option in patients who need treatment with an ACE inhibitor or ARB for other reasons | $1.50  
47.70  
64.30  
215.10 | Candesartan – generic Atacand (AstraZeneca)                              | 16 mg once/day                                                                    | • Reduced migraine frequency by about 30-35% in small, double-blind trials¹⁴ | • Can cause angioedema, cough, hypotension (particularly with diuretic use or volume depletion), rash, acute renal failure, hyperkalemia, loss of taste, hepatoxicity, pancreatitis, blood dyscrasias, and renal damage  
• ARBs less likely than ACE inhibitors to cause cough and rarely cause angioedema | • Contraindicated for use during pregnancy  
• Preventive therapy is generally not recommended during pregnancy |                                                                          | $1.50  
47.70  
64.30  
215.10 | Continued on next page
### Comparison Table: Some Drugs for Migraine Prevention in Adults (continued)

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<tr>
<td>Others</td>
<td></td>
<td></td>
<td>▶ Reduced migraine attack frequency by 36-60% in 2 randomized, placebo-controlled trials in ~300 patients[^16]</td>
<td>▶ Has been associated with hepatic toxicity</td>
<td>▶ Should not be used in pregnant women (has emmenagogic, hepatotoxic, genotoxic, and carcinogenic effects)</td>
<td>$65.00[^17]</td>
</tr>
<tr>
<td>Petasites (butterbur) – Petadolex</td>
<td>100–150 mg/day in 2-3 divided doses</td>
<td>▶ Modestly effective in reducing the number of migraine days per month in one small 3-month study[^18]</td>
<td>▶ Adverse effects: local discomfort from electrical stimulation, forehead skin irritation, sleepiness, fatigue, insomnia, and headache after stimulation</td>
<td>▶ Avoid in patients with a cardiac pacemaker, a wearable or implanted defibrillator, or an implanted metallic or electrical device in their head</td>
<td>▶ Preventive therapy is generally not recommended during pregnancy</td>
<td>$65.00[^17]</td>
</tr>
<tr>
<td>Transcutaneous electrical nerve stimulation device – Cefaly (Cefaly Technology)</td>
<td>20 minute treatment once/day</td>
<td>▶ Modestly effective in reducing the number of migraine days per month in one small 3-month study[^18]</td>
<td>▶ Adverse effects: local discomfort from electrical stimulation, forehead skin irritation, sleepiness, fatigue, insomnia, and headache after stimulation</td>
<td>▶ Avoid in patients with a cardiac pacemaker, a wearable or implanted defibrillator, or an implanted metallic or electrical device in their head</td>
<td>▶ Preventive therapy is generally not recommended during pregnancy</td>
<td>374.00[^19]</td>
</tr>
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</table>

[^1]: Approximate WAC for 30 days' treatment at the lowest usual adult dosage. WAC = wholesaler acquisition cost or manufacturer’s published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. October 5, 2018. Reprinted with permission by First Databank, Inc. All rights reserved. ©2018. www.fdbhealth.com/policies/drug-pricing-policy.
[^2]: Not FDA-approved for prevention of migraine. Other tricyclics such as nortriptyline and doxepin are also used for prevention of migraine, but data supporting their efficacy are limited.
[^3]: Marketed as divalproex sodium (Depakote, and generics) and valproic acid (Depakene, and others).
[^6]: Erenumab targets the CGRP receptor. Fremanezumab and galcanezumab target CGRP itself.
[^7]: At time of publication, erenumab and galcanezumab, but not fremanezumab, were on the formulary of the large pharmacy benefit manager Express Scripts (http://lab.express-scripts.com/lab/insights/drug-options/new-migraine-care-value-program-taking-on-the-toughest-headaches).
[^8]: Some patients may benefit from a dosage of 140 mg once/month administered as 2 consecutive 70-mg SC injections.
[^9]: FDA-approved for prophylaxis of headaches in adult patients with chronic migraine.
[^10]: Detailed information provided in the package insert.
[^12]: Cost of one 200-unit vial.
[^19]: Cost to purchase one Cefaly prevention band ($349) and 3 Cefaly multi-use electrodes ($25; each can be used up to 25 times) at www.cefaly.us/en. Accessed October 25, 2018.