## CYPROHEPTADINE

### THERAPEUTICS

**Brands**
- Periactin, Cypromar, Periavit, Pyrohep

**Generic?**
- Yes

**Class**
- Antihistamine

**Commonly Prescribed For**
(FDA approved in bold)
- Allergic reactions
- Migraine/tension type headache prophylaxis (children and adults)
- Insomnia
- Nightmares/posttraumatic stress disorder
- Poor appetite (children)
- Management of moderate to severe cases of serotonin syndrome
- SSRI-induced sexual dysfunction
- Management of carcinoid
- Drug-induced hyperhidrosis
- Cyclical vomiting syndrome

### How the Drug Works
- Antihistamine and anticholinergic activity
- Antiserotonergic agent (5-HT2A/C receptor antagonist) and perhaps a calcium-channel blocker. The relative importance of each action in headache prophylaxis is unclear
- Prevention of cortical spreading depression may be the mechanism of action for all migraine preventive drugs

### How Long until It Works
- Migraines may decrease in as little as 2 weeks, but can take up to 2 months to see full effect

### If It Works
- Migraine: goal is a 50% or greater decrease in migraine frequency or severity. Consider tapering or stopping if headaches remit for more than 6 months or if patient considering pregnancy

### If It Doesn’t Work
- Increase to highest tolerated dose
- Migraine: address other issues, such as medication overuse, other coexisting medical disorders, such as anxiety, and consider changing to another agent or adding a second agent

### Best Augmenting Combos for Partial Response or Treatment Resistance
- Migraine: for some patients with migraine, low-dose polytherapy with 2 or more drugs may be better tolerated and more effective than high-dose monotherapy. May use in combination with AEDs, antidepressants, natural products, and nonmedication treatments, such as biofeedback, to improve headache control

### Tests
- Monitor weight during treatment

### ADVERSE EFFECTS (AEs)

#### How Drug Causes AEs
- Most are related to antihistamine and anticholinergic activity

#### Notable AEs
- Sedation
- Dizziness
- Dry mouth
- Postural hypotension
- Weight gain
- Blurred vision
- Constipation
- Restlessness or akathisia

#### Life-Threatening or Dangerous AEs
- Bradycardia
- ECG changes, including QTc prolongation
- Hypersensitivity reactions

#### Weight Gain
- Problematic

#### Sedation
- Common

#### What to Do about AEs
- Lower dose or switch to another agent. For severe AEs, do not use
**Best Augmenting Agents for AEs**
- No treatment for most AEs other than lowering dose or stopping drug

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## DOSING AND USE

### Usual Dosage Range
- 8–32 mg/day

### Dosage Forms
- Tablet: 4 mg
- Syrup: 2 mg/5mL

### How to Dose
- Migraine/tension-type headache: initial dose is usually 2–4 mg at night.
- Increase by 2–4 mg every 5–7 days until beneficial or AEs develop

#### Dosing Tips
- Take largest dose at night to minimize drowsiness

### Overdose
- CNS depression is most common, but hypotension, cardiac collapse or ECG changes, and respiratory depression may occur. Anticholinergic effects include fixed pupils, flushing, and hyperthermia. Convulsions indicate poor prognosis. Protect against aspiration, correct electrolyte disturbances and acidosis, and give activated charcoal with a cathartic. Give diazepam for convulsions and consider physostigmine for central anticholinergic effects

### Long-Term Use
- Safe for long-term use

### Habit Forming
- No

### How to Stop
- No need to taper, but migraine often returns after stopping

### Pharmacokinetics
- Peak levels at 1–2 hours, duration 4–6 hours
- Hepatic metabolism with renal excretion of metabolites and some unchanged drug

#### Drug Interactions
- Cyproheptadine may lower effectiveness of SSRIs due to serotonin antagonism
- May diminish expected pituitary adrenal response to metyrapone
- Excess sedation with other CNS depressants (alcohol, barbiturates) can occur

#### Other Warnings/Precautions
- Avoid in patients with respiratory disease such as sleep apnea or chronic obstructive pulmonary disease

### Do Not Use
- Hypersensitivity to drug
- Angle-closure glaucoma
- Bladder neck obstruction
- Patients using MAOIs
- Symptomatic prostatic hypertrophy

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## SPECIAL POPULATIONS

### Renal Impairment
- No known effects

### Hepatic Impairment
- May reduce metabolism. Titrate more slowly

### Cardiac Impairment
- Rarely causes arrhythmias and ECG changes. Use with caution

### Elderly
- More likely to experience AEs, especially anticholinergic
- Avoid using for headache prophylaxis

### Children and Adolescents
- Drug is used most often for pediatric headache disorders, but may decrease alertness or produce paradoxical excitation

### Pregnancy
- Category B: use only if potential benefit outweighs risk to the fetus

### Breast-Feeding
- Unknown if excreted in breast milk. Patient should not breast-feed while on drug
THE ART OF PAIN PHARMACOLOGY

Potential Advantages
- Commonly used pediatric migraine preventive, especially for younger children

Potential Disadvantages
- No large studies that demonstrate effectiveness and many AEs that limit use

Primary Target Symptoms
- Headache frequency and severity

Pearls
- In 1 study, superior to placebo but inferior to methysergide
- Antiserotonin effects are most likely responsible for effectiveness, but can cause depression
- Antagonism of 5-HT2A receptors suggests usefulness in the treatment of serotonin syndrome and MAOI toxicity

Suggested Reading


