FLUNARIZINE

THERAPEUTICS

Brands
- Sibelium

Generic?
Yes

Class
- Antihypertensive, calcium channel blocker, antihistamine

Commonly Prescribed For
(FDA approved in bold)
- Migraine prophylaxis
- Vasospasm in subarachnoid hemorrhage
- Adjunctive drug for epilepsy
- Vertigo
- Alternating hemiplegia of childhood
- Tourette syndrome
- Tinnitus

How the Drug Works
- Migraine/cluster: proposed prior mechanisms included inhibition of smooth muscle contraction preventing arterial spasm and hypoxia, prevention of vasoconstriction or platelet aggregation, and alterations of serotonin release and uptake
- Prevention of cortical spreading depression may be the mechanism of action for all migraine preventives
- May also interact with other neurotransmitters, and may inhibit the synthesis and release of nitric oxide
- The drug also appears to act by blocking dopamine D2 receptors in a manner similar to antipsychotics

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

Best Augmenting Combos for Partial Response or Treatment-Resistance
- Migraine: for some patients with migraine, low-dose polytherapy with two 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 ECG for PR interval

ADVERSE EFFECTS (AEs)

How Drug Causes AEs
- Direct effects of calcium receptor antagonism and other CNS receptors
- Antihistaminic properties likely cause weight gain and sedation. D2 blockade can cause movement disorders

Notable AEs
- Sedation, depression, weight gain are most problematic
- Nausea, dry mouth, gingival hyperplasia, weakness, muscle aches, and abdominal pain can occur

Life-Threatening or Dangerous AEs
- Severe depression in a minority
- Extrapyramidal AEs and parkinsonism

Weight Gain
- Problematic

Sedation
- Common
### What to Do About AEs
- Lower dose or switch to another agent. For serious AEs, do not use.

### Best Augmenting Agents for AEs
- None

### DOSING AND USE

#### Usual Dosage Range
- 5–10 mg/day

#### Dosage Forms
- Tablets: 5 mg, 10 mg

#### How to Dose
- Migraine: initial dose is usually 10 mg at night. Start at 5 mg in sensitive patients. The dose is generally not increased for migraine prophylaxis.

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

#### Overdose
- Sedation, weakness, confusion, or agitation may occur. Cardiac AEs, such as bradycardia or tachycardia, have been reported.

#### 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 2–4 hours and more than 90% protein bound. More metabolites are excreted in bile and elimination half-life is about 18 days.

#### Drug Interactions
- Enzyme inducers such as phenytoin or rifampin may increase clearance and lower levels.
- Use with beta-blockers can be synergistic and bradycardia, AV conduction disturbance may occur.
- May increase risk of GI bleeding with NSAIDs.
- May increase levels of carbamazepine.
- Excess sedation with other CNS depressants (alcohol, barbiturates) can occur.

#### Other Warnings/Precautions
- Similar to antipsychotics (D2 receptor blockers) may increase prolactin levels.
- Sick sinus syndrome, greater than 1st degree heart block.
- Severe CHF, cardiogenic shock, severe left ventricular dysfunction, hypotension.
- History of depression, parkinsonism, or porphyria.

### SPECIAL POPULATIONS

#### Renal Impairment
- No known effects.

#### Hepatic Impairment
- Flunarizine is highly metabolized by the liver. Start with lower dose and use with caution.

#### Cardiac Impairment
- Do not use in acute shock, severe CHF, hypotension, and greater than 1st degree heart block.

#### Elderly
- May be more likely to experience AEs (sedation).

#### Children and Adolescents
- Appears to be effective in pediatric migraine at a dose of 5 mg daily.

#### Pregnancy
- Category C (all calcium channel blockers).
- Use only if potential benefit outweighs risk to the fetus.

#### Breast-Feeding
- Flunarizine is found in breast milk at high concentrations. Do not breast-feed on drug.
THE ART OF PAIN PHARMACOLOGY

Potential Advantages

- Effective in both pediatric and adult migraine prophylaxis and possibly effective in epilepsy and schizophrenia

Potential Disadvantages

- Sedation and weight gain can limit use. Not available in the U.S.

Primary Target Symptoms

- Headache frequency and severity
- Seizure frequency and severity
- Hemiplegic attacks

Pearls

- Effective in reducing migraine frequency at rates comparable to other agents (propranolol, pizotifen)
- There have been investigations of using flunarizine for epilepsy, but the effect was weak and AEs were significant
- Unlike many calcium-channel blockers, it does not alter heart rate and is a poor antihypertensive
- Generally more effective than other calcium channel blockers for migraine prophylaxis, but not available in many countries, including the U.S.

Suggested Reading


