**FLURAZEPAM**

### Therapeutics

**Brands** • Dalmane  
*see index for additional brand names*

**Generic?** Yes

**Class**
- Neuroscience-based Nomenclature: GABA  
  positive allosteric modulator (GABA-PAM)  
- Benzodiazepine (hypnotic)

**Commonly Prescribed for**  
*(bold for FDA approved)*
- Insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings, and/or early morning awakening
- Recurring insomnia or poor sleeping habits
- Acute or chronic medical situations requiring restful sleep
- Catatonia

**How the Drug Works**
- Binds to benzodiazepine receptors at the GABA-A ligand-gated chloride channel complex
- Enhances the inhibitory effects of GABA
- Boosts chloride conductance through GABA-regulated channels
- Inhibitory actions in sleep centers may provide sedative hypnotic effects

**How Long Until It Works**
- Generally takes effect in less than an hour

**If It Works**
- Improves quality of sleep
- Effects on total wake-time and number of nighttime awakenings may be decreased over time

**If It Doesn’t Work**
- If insomnia does not improve after 7–10 days, it may be a manifestation of a primary psychiatric or physical illness such as obstructive sleep apnea or restless leg syndrome, which requires independent evaluation
- Increase the dose
- Improve sleep hygiene
- Switch to another agent

### Side Effects

**How Drug Causes Side Effects**
- Same mechanism for side effects as for therapeutic effects – namely due to excessive actions at benzodiazepine receptors
- Actions at benzodiazepine receptors that carry over to the next day can cause daytime sedation, amnesia, and ataxia
- Long-term adaptations in benzodiazepine receptors may explain the development of dependence, tolerance, and withdrawal

**Notable Side Effects**
- Sedation, fatigue, depression
- Dizziness, ataxia, slurred speech, weakness
- Forgetfulness, confusion
- Hyperexcitability, nervousness
- Rare hallucinations, mania
- Rare hypotension
- Hypersalivation, dry mouth
- Rebound insomnia when withdrawing from long-term treatment

**Life-Threatening or Dangerous Side Effects**
- Respiratory depression, especially when taken with CNS depressants in overdose
- Rare hepatic dysfunction, renal dysfunction, blood dyscrasias

**Weight Gain**
- Reported but not expected

**Best Augmenting Combos for Partial Response or Treatment Resistance**
- Generally, best to switch to another agent
- Trazodone
- Agents with antihistamine actions (e.g., diphenhydramine, TCAs)

**Tests**
- In patients with seizure disorders, concomitant medical illness, and/or those with multiple concomitant long-term medications, periodic liver tests and blood counts may be prudent
Sedation

- Many experience and/or can be significant in amount

What to Do About Side Effects

- Wait
- To avoid problems with memory, only take flurazepam if planning to have a full night’s sleep
- Lower the dose
- Switch to a shorter-acting sedative hypnotic
- Switch to a non-benzodiazepine hypnotic
- Administer flumazenil if side effects are severe or life-threatening

Best Augmenting Agents for Side Effects

- Many side effects cannot be improved with an augmenting agent

Overdose

- No death reported in monotherapy; sedation, slurred speech, poor coordination, confusion, coma, respiratory depression

Long-Term Use

- Not generally intended for long-term use
- Because of its relatively longer half-life, flurazepam may cause some daytime sedation and/or impaired motor/cognitive function, and may do so progressively over time

Habit Forming

- Flurazepam is a Schedule IV drug
- Some patients may develop dependence and/or tolerance; risk may be greater with higher doses
- History of drug addiction may increase risk of dependence

How to Stop

- If taken for more than a few weeks, taper to reduce chances of withdrawal effects
- Patients with seizure history may seize upon sudden withdrawal
- Rebound insomnia may occur the first 1–2 nights after stopping
- For patients with severe problems discontinuing a benzodiazepine, dosing may need to be tapered over many months (i.e., reduce dose by 1% every 3 days by crushing tablet and suspending or dissolving in 100 mL of fruit juice and then disposing of 1 mL while drinking the rest; 3–7 days later, dispose of 2 mL, and so on). This is both a form of very slow biological tapering and a form of behavioral desensitization

Pharmacokinetics

- Elimination half-life approximately 24–100 hours
- Active metabolites

Drug Interactions

- Cimetidine may decrease flurazepam clearance and thus raise flurazepam levels
- Flurazepam and kava combined use may affect clearance of either drug
- Increased depressive effects when taken with other CNS depressants (see Warnings below)
Other Warnings/Precautions

- Boxed warning regarding the increased risk of CNS depressant effects when benzodiazepines and opioid medications are used together, including specifically the risk of slowed or difficulty breathing and death
- If alternatives to the combined use of benzodiazepines and opioids are not available, clinicians should limit the dosage and duration of each drug to the minimum possible while still achieving therapeutic efficacy
- Patients and their caregivers should be warned to seek medical attention if unusual dizziness, lightheadedness, sedation, slowed or difficulty breathing, or unresponsiveness occur
- Insomnia may be a symptom of a primary disorder, rather than a primary disorder itself
- Some patients may exhibit abnormal thinking or behavioral changes similar to those caused by other CNS depressants (i.e., either depressant actions or disinhibiting actions)
- Some depressed patients may experience a worsening of suicidal ideation
- Use only with extreme caution in patients with impaired respiratory function or obstructive sleep apnea
- Flurazepam should be administered only at bedtime

Do Not Use

- If patient is pregnant
- If patient has angle-closure glaucoma
- If there is a proven allergy to flurazepam or any benzodiazepine

Elderly

- Recommended dose: 15 mg/day

Children and Adolescents

- Safety and efficacy have not been established
- Long-term effects of flurazepam in children/adolescents are unknown
- Should generally receive lower doses and be more closely monitored

Pregnancy

- Contraindicated for use in pregnancy
- Effective June 30, 2015, the US FDA requires changes to the content and format of pregnancy and lactation information in prescription drug labels, including the elimination of the pregnancy letter categories; the Pregnancy and Lactation Labeling Rule (PLLR or final rule) applies only to prescription drugs and will be phased in gradually for drugs approved on or after June 30, 2001
- Infants whose mothers received a benzodiazepine late in pregnancy may experience withdrawal effects
- Neonatal flaccidity has been reported in infants whose mothers took a benzodiazepine during pregnancy

Breast Feeding

- Unknown if flurazepam is secreted in human breast milk, but all psychotropics assumed to be secreted in breast milk
- Recommended either to discontinue drug or bottle feed
- Effects on infant have been observed and include feeding difficulties, sedation, and weight loss

SPECIAL POPULATIONS

Renal Impairment

- Recommended dose: 15 mg/day

Hepatic Impairment

- Recommended dose: 15 mg/day

Cardiac Impairment

- Benzodiazepines have been used to treat insomnia associated with acute myocardial infarction

THE ART OF PSYCHOPHARMACOLOGY

Potential Advantages

- Transient insomnia

Potential Disadvantages

- Chronic nightly insomnia

Primary Target Symptoms

- Time to sleep onset
- Total sleep time
- Nighttime awakenings
Suggested Reading


Pearls

Flurazepam has a longer half-life than some other sedative hypnotics, so it may be less likely to cause rebound insomnia on discontinuation.

- Flurazepam may not be as effective on the first night as it is on subsequent nights.
- Was once one of the most widely used hypnotics.

Long-term accumulation of flurazepam and its active metabolites may cause insidious onset of confusion or falls, especially in the elderly.

- Though not systematically studied, benzodiazepines have been used effectively to treat catatonia and are the initial recommended treatment.