## ZALEPLON

### THERAPEUTICS

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

**Generic?** Yes

**Class**
- Neuroscience-based Nomenclature: GABA positive allosteric modulator (GABA-PAM)
- Non-benzodiazepine hypnotic; alpha 1 isoform agonist of GABA-A/benzodiazepine receptors

**Commonly Prescribed for**
*bold for FDA approved*
- Short-term treatment of insomnia

### How the Drug Works

- Binds selectively to a subtype of the benzodiazepine receptor, the alpha 1 isoform
- May enhance GABA inhibitory actions that provide sedative hypnotic effects more selectively than other actions 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

### Best Augmenting Combos for Partial Response or Treatment Resistance
- Generally, best to switch to another agent
- Trazodone

### SIDE EFFECTS

#### How Drug Causes Side Effects

- Actions at benzodiazepine receptors that carry over to the next day can cause daytime sedation, amnesia, and ataxia
- Long-term adaptations of zaleplon not well studied, but chronic studies of other alpha 1 selective non-benzodiazepine hypnotics suggest lack of notable tolerance or dependence developing over time

#### Notable Side Effects
- ✽ Sedation
- ✽ Dizziness, ataxia
- ✽ Dose-dependent amnesia
- ✽ Hyperexcitability, nervousness
- ✽ Rare hallucinations
- ✽ Headache
- ✽ Decreased appetite

#### Life-Threatening or Dangerous Side Effects
- Respiratory depression, especially when taken with other CNS depressants in overdose
- Rare angioedema

#### Weight Gain
- Reported but not expected

#### Sedation
- Many experience and/or can be significant in amount

#### What to Do About Side Effects
- Wait
- To avoid problems with memory, do not take zaleplon if planning to sleep for less than 4 hours
- Lower the dose
- 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

**DOSING AND USE**

**Usual Dosage Range**
- 10 mg/day at bedtime for 7–10 days

**Dosage Forms**
- Capsule 5 mg, 10 mg

**How to Dose**
- Initial 10 mg/day at bedtime; may increase to 20 mg/day at bedtime if ineffective; maximum dose generally 20 mg/day

**Dosing Tips**
- Patients with lower body weights may require only a 5-mg dose
- Zaleplon should generally not be prescribed in quantities greater than a 1-month supply
- Risk of dependence may increase with dose and duration of treatment
- However, treatment with alpha 1 selective non-benzodiazepine hypnotics may cause less tolerance or dependence than benzodiazepine hypnotics

**Overdose**
- No fatalities reported with zaleplon; fatalities have occurred with other sedative hypnotics; sedation, confusion, ataxia, hypotension, respiratory depression, coma

**Long-Term Use**
- Not generally intended for long-term use
- Increased wakefulness during the latter part of night (wearing off) or an increase in daytime anxiety (rebound) may occur because of short half-life

**Habit Forming**
- Zaleplon 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**
- Rebound insomnia may occur the first night after stopping
- If taken for more than a few weeks, taper to reduce chances of withdrawal effects

**Pharmacokinetics**
- Terminal phase elimination half-life approximately 1 hour (ultra-short half-life)

**Drug Interactions**
- Increased depressive effects when taken with other CNS depressants
- Cimetidine may increase plasma concentrations of zaleplon, requiring a lower initial dose of zaleplon (5 mg/day)
- CYP450 3A4 inducers such as carbamazepine may reduce the effectiveness of zaleplon

**Other Warnings/Precautions**
- 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
- Zaleplon should be administered only at bedtime
- Rare angioedema has occurred with sedative hypnotic use and could potentially cause fatal airway obstruction if it involves the throat, glottis, or larynx; thus if angioedema occurs treatment should be discontinued
- Sleep driving and other complex behaviors, such as eating and preparing food and making phone calls, have been reported in patients taking sedative hypnotics

**Do Not Use**
- If there is a proven allergy to zaleplon
THE ART OF PSYCHOPHARMACOLOGY

**Potential Advantages**
- Those needing short duration of action

**Potential Disadvantages**
- Those needing longer duration of action
- More expensive than some other sedative hypnotics

**Primary Target Symptoms**
- Time to sleep onset
- Total sleep time
- Nighttime awakenings

**Pearls**
- Zaleplon has not been shown to increase the total time asleep or to decrease the number of awakenings
- May be preferred over benzodiazepines because of its rapid onset of action, short duration of effect, and safety profile
- Popular for uses requiring short half-life (e.g., dosing in the middle of the night, sleeping on airplanes, jet lag)
- May not be ideal for patients who desire immediate hypnotic onset and eat just prior to bedtime
- Not a benzodiazepine itself, but binds to benzodiazepine receptors
- May have fewer carryover side effects than some other sedative hypnotics
- May not have sufficient efficacy in patients with severe chronic insomnia resistant to some other sedative hypnotics
- May cause less dependence than some other sedative hypnotics, especially in those without a history of substance abuse
- Zaleplon is not absorbed as quickly if taken with high-fat foods, which may reduce onset of action

**SPECIAL POPULATIONS**

**Renal Impairment**
- No dose adjustment necessary
- Use with caution in patients with severe impairment

**Hepatic Impairment**
- Mild to moderate impairment: recommended dose 5 mg
- Not recommended for use in patients with severe impairment

**Cardiac Impairment**
- Zaleplon has not been studied in patients with cardiac impairment, but dose adjustment may not be necessary

**Elderly**
- Recommended dose: 5 mg

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

**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
- Controlled studies have not been conducted in pregnant women
- Infants whose mothers took sedative hypnotics during pregnancy may experience some withdrawal symptoms
- Neonatal flaccidity has been reported in infants whose mothers took sedative hypnotics during pregnancy

**Breast Feeding**
- Some drug is found in mother’s breast milk
- Recommended either to discontinue drug or bottle feed
Suggested Reading


