**SIDE EFFECTS**

**How Drug Causes Side Effects**
- Theoretically due to downstream effects of blocking orexin receptors

**Notable Side Effects**
- Sedation, headache, dizziness, abnormal dreams

**Life-Threatening or Dangerous Side Effects**
- Sleep paralysis and hypnagogic/hypnopompic hallucinations (rare)
- Dose-dependent symptoms similar to mild cataplexy (rare)

**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, take suvorexant only if planning to have a full night’s sleep
- Lower the dose
- Switch to a different hypnotic

**Best Augmenting Agents for Side Effects**
- Many side effects cannot be improved with an augmenting agent

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**THERAPEUTICS**

**Brands**
- Belsomra

**Generic?**
- No

**Class**
- Orexin receptor antagonist; hypnotic

**Commonly Prescribed for**
- Insomnia (problems with sleep onset and/or sleep maintenance)

**How the Drug Works**
- Orexin serves to stabilize and promote wakefulness; suvorexant binds to orexin 1 and orexin 2 receptors, blocking orexin from binding there and thus preventing it from promoting wakefulness

**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 could theoretically 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**
- No controlled trials of combinations with other hypnotics or psychotropic drugs
- Generally, best to switch to another agent

**Tests**
- None for healthy individuals

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**DOISING AND USE**

**Usual Dosage Range**
- 10 mg/night

**Dosage Forms**
- Tablet 5 mg, 10 mg, 15 mg, 20 mg

**How to Dose**
- Starting dose is 10 mg, no more than once per night and within 30 minutes of bedtime
• Should not take unless there are at least 7 hours remaining of sleep time

**Dosing Tips**

• Patients who tolerate but do not respond to 10 mg may receive 15 mg or 20 mg doses; 20 mg is the maximum recommended dose
• Use the lowest dose effective for the patient
• Taking suvorexant with or soon after a meal can delay the time to effect
• Not restricted to short-term use

**Overdose**

• Limited data; sedation

**Long-Term Use**

• Has been evaluated and found effective in trials up to 1 year

**Habit Forming**

• Suvorexant is a Schedule IV drug
• There was no evidence of physiological dependence or withdrawal symptoms with prolonged use of suvorexant

**How to Stop**

• Taper not necessary

**Pharmacokinetics**

• Metabolized by CYP450 3A4
• Mean terminal half-life approximately 12 hours

**Drug Interactions**

• Not recommended in patients taking concomitant strong CYP450 3A4 inhibitors
• Patients taking moderate CYP3A4 inhibitors should receive a 5-mg dose; dose can be increased to 10 mg if needed
• Patients taking CYP3A4 inducers may experience reduced efficacy of suvorexant

**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 caution in patients with impaired respiratory function or obstructive sleep apnea
• Suvorexant should only be administered at bedtime
• Label contains warning for risk of next-day impaired alertness and motor coordination

**Do Not Use**

• If patient has narcolepsy
• If patient is taking strong CYP450 3A4 inhibitors
• If there is a proven allergy to suvorexant

**SPECIAL POPULATIONS**

**Renal Impairment**

• Dose adjustment not necessary

**Hepatic Impairment**

• Dose adjustment not necessary in mild to moderate hepatic impairment
• Not recommended in patients with severe hepatic impairment

**Cardiac Impairment**

• Not studied in patients with cardiac impairment

**Elderly**

• Some patients may tolerate lower doses better

**Children and Adolescents**

• Safety and efficacy have not been established

**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
**Breast Feeding**
- Unknown if suvorexant is secreted in human breast milk, but all psychotropics assumed to be secreted in breast milk
- Recommended to either discontinue drug or bottle feed

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

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**Pearls**
- Targeting insomnia may prevent the onset of major depressive disorder or GAD and help maintain remission after recovery from major depressive disorder or GAD
- Rebound insomnia does not appear to be common
- Suvorexant may be safe for long-term use, with little or no suggestion of tolerance, dependence, or abuse
- May even be safe to consider in patients with a past history of substance abuse who require treatment with a hypnotic
- May be effective in patients with insomnia unresponsive to medications with other mechanisms of action (e.g., Z-drug hypnotics, benzodiazepines)

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**Suggested Reading**

Citrome L. Suvorexant for insomnia: a systematic review of the efficacy and safety profile for this newly approved hypnotic – what is the number needed to treat, number needed to harm and likelihood to be helped or harmed? Int J Clin Pract 2014;68(12):1429–41.