HYPNOTIC | C-IV

Suvorexant

Belsomra

First dual orexin receptor antagonist; blocks wake drive rather than sedating, for sleep onset and maintenance insomnia.

USUAL ADULT RANGE	HALF-LIFE	METABOLISM	ONSET
10 mg PO qhs (max 20 mg)	~12 h	CYP3A4 (minor CYP2C19)	~30 min; peak ~2 h

No FDA boxed warning on the current US label.

INDICATIONS

- FDA-approved for the treatment of insomnia characterized by difficulties with sleep onset, sleep maintenance, or both, in adults.
- Efficacy was maintained over 3-month randomized trials, so it is suitable for longer courses than the traditional short-term hypnotics.
- The American Academy of Sleep Medicine gives a weak recommendation for suvorexant in sleep maintenance insomnia.
- Off-label interest in delirium prevention in hospitalized older adults exists, with small trials suggesting reduced incidence.
- It is an option when benzodiazepines and Z-drugs are undesirable, though it remains a schedule IV controlled substance.
- Contraindicated in narcolepsy, since orexin signaling is already deficient in that disorder and further blockade worsens it.

DOSING & TITRATION

- Adults: **10 mg PO once nightly** within 30 minutes of going to bed, with at least 7 hours remaining before planned awakening.
- If 10 mg is tolerated but not effective, the dose may be increased to 15 or **20 mg**, which is the labeled maximum.
- With a moderate CYP3A4 inhibitor such as diltiazem, verapamil or fluconazole, use 5 mg nightly and do not exceed 10 mg.
- Not recommended with strong CYP3A4 inhibitors such as ketoconazole, itraconazole, clarithromycin or ritonavir.
- Take no more than one dose per night, and avoid dosing with or soon after a meal since food delays the onset of effect.
- No taper is required, and rebound insomnia after discontinuation is minimal compared with benzodiazepines and Z-drugs.

MECHANISM OF ACTION

- Dual orexin receptor antagonist blocking OX1R and OX2R, the receptors for the wake-promoting neuropeptides orexin A and orexin B.
- Rather than enhancing GABAergic sedation, it removes the arousal signal from lateral hypothalamic orexin neurons to monoaminergic nuclei.
- Because it targets wakefulness rather than global CNS depression, sleep architecture is largely preserved with increases in REM sleep.
- Loss of orexin signaling is the lesion in narcolepsy, which explains both the contraindication and the sleep paralysis and cataplexy-like effects.
- Absence of GABA-A activity means no muscle relaxation, no anticonvulsant effect, and less amnesia than benzodiazepine hypnotics.

PHARMACOKINETICS

- Absorbed with peak levels near 2 hours and bioavailability about 82 percent; a high-fat meal delays the peak by roughly 1.5 hours.
- Elimination half-life is about **12 hours**, long enough that next-day residual effects are the main dose-limiting problem.
- Metabolized almost entirely by **CYP3A4** with a minor CYP2C19 contribution; the major circulating metabolite is inactive.
- Exposure is higher in obese patients and particularly in obese women, who should be watched closely for next-day sedation.
- No adjustment is needed for renal impairment or mild to moderate hepatic impairment; severe hepatic disease has not been studied.

ADVERSE EFFECTS

- Somnolence in about 7 percent versus 3 percent on placebo, headache 7 percent, dizziness 3 percent and abnormal dreams.
- Next-day driving impairment demonstrated at 20 mg in both men and women, with the effect present even when patients feel alert.
- Sleep paralysis, hypnagogic and hypnopompic hallucinations, and mild cataplexy-like leg weakness reflecting orexin blockade.
- Complex sleep behaviors including sleepwalking have been reported, and the drug should be stopped if any such episode occurs.
- Worsening of depression and suicidal ideation, reported more often at 20 mg; assess mood before and during treatment.
- Respiratory depression risk in patients with compromised respiratory function, and additive impairment with alcohol and opioids.

MONITORING

- Assess next-morning alertness and driving safety, particularly at 15 and 20 mg, and in obese patients where exposure is higher.
- Ask about sleep paralysis, hallucinations on falling asleep, leg weakness and any complex sleep behaviors at follow-up visits.
- Screen for depression and suicidal ideation before starting and at each visit, since worsening mood has been reported.
- Evaluate for obstructive sleep apnea and COPD before use, since respiratory effects in those groups are incompletely characterized.
- Check the prescription monitoring program before prescribing this schedule IV agent and reassess ongoing need periodically.

INTERACTIONS & CAUTIONS

- Strong CYP3A4 inhibitors are not recommended for co-administration; moderate inhibitors require the reduced 5 mg starting dose.
- Strong CYP3A4 inducers such as rifampin, carbamazepine and St. John's wort substantially reduce exposure and may abolish benefit.
- Additive sedation and respiratory depression with opioids, alcohol, benzodiazepines, gabapentinoids and sedating antihistamines.
- Contraindicated in narcolepsy; use caution in obstructive sleep apnea, severe COPD and any condition compromising respiration.
- Suvorexant is a weak inhibitor of intestinal P-glycoprotein and can modestly raise digoxin levels, so monitor digoxin concentrations.

SPECIAL POPULATIONS

- Pregnancy: human data are insufficient; a pregnancy exposure registry exists and the drug should be used only if clearly needed.
- Lactation: it is not known whether suvorexant passes into human milk; monitor the nursing infant for sedation and poor feeding.
- Pediatrics: safety and effectiveness under age 18 are not established and use is not recommended in that age group.
- Older adults: not among the agents the AGS Beers Criteria flag for avoidance, but next-day sedation and fall risk still apply.
- Hepatic and renal impairment: no adjustment for renal disease or mild to moderate hepatic disease; not studied in severe hepatic disease.

PRESCRIBING PEARLS

- Blocks the wake signal instead of sedating, so sleep architecture is largely preserved.
- Absolutely contraindicated in narcolepsy, where orexin signaling is already lost.
- Next-day driving is measurably impaired at 20 mg even when the patient reports feeling fine.

References

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NOTE

References follow APA 7th edition style. Dosing, boxed warnings, and interaction data change; confirm every clinical decision against the current FDA prescribing information (DailyMed) and your institution's formulary. This sheet is an educational quick reference and does not replace the full label or clinical judgment.