ZOLPIDEM (Ambien, Edluar, Intermezzo, Zolpimist) Fact Sheet [G]

Bottom Line:

Ambien is the original Z-drug, having been initially FDA approved in 1992. It is a good hypnotic that can also help with sleep maintenance, particularly in the ER formulation. The lower-dose sublingual version (Intermezzo) has a shorter duration of action and can be taken in the middle of the night—but we recommend using cheaper generic zaleplon instead for middle-of-the-night awakening.

FDA Indications:

Insomnia (IR: short term, sleep onset; CR: sleep onset and maintenance; Intermezzo: difficulty falling asleep after middle-of-the-night awakening).

Dosage Forms:

- **Tablets (G):** 5 mg, 10 mg.
- **ER tablets (G):** 6.25 mg, 12.5 mg.
- **SL tablets (Edluar [G]):** 5 mg, 10 mg.
- **SL tablets (Intermezzo, [G]):** 1.75 mg, 3.5 mg.
- **Oral spray (Zolpimist, [G]):** 5 mg/spray.

Dosage Guidance:

- Start 10 mg QHS (5 mg in women). ER: Start 12.5 mg QHS (6.25 mg in women). Take immediately before bed, with at least seven to eight hours remaining before planned awakening time. Dose may be increased to max 10 mg (or 12.5 mg ER) QHS if no daytime grogginess. Higher doses may lead to greater abuse potential. Use lower doses in elderly.
- Lower doses (3.5 mg in men, 1.75 mg in women) SL QHS can be used with at least four hours remaining before wake time.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: $; Intermezzo, Zolpimist: $$; Edluar: $$$

Side Effects:

- Most common: Headache, somnolence, dizziness, diarrhea.
- Serious but rare: Complex sleep-related behavior (sleep driving, cooking, eating, phone calls).
- Pregnancy/breastfeeding: Limited data suggest relatively safe in pregnancy and breastfeeding.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Selective $GABA_A$ alpha-1 subunit agonist.
- Metabolized primarily through CYP3A4; t ½: 2.5–3 hours.
- Avoid concomitant use with other CNS depressants, including alcohol and opioids (additive effects). Potent CYP3A4 inhibitors may increase effects of zolpidem, whereas CYP3A4 inducers (eg, carbamazepine) may decrease zolpidem levels; adjust zolpidem dosing.

Clinical Pearls:

- Schedule IV controlled substance.
- Unlike benzodiazepines, zolpidem does not disrupt normal sleep stages.
- At therapeutic doses, abuse potential is somewhat less than with benzodiazepines.
- Less withdrawal effects than with benzodiazepines, but abrupt discontinuation, particularly from higher doses, can cause withdrawal symptoms (mostly rebound insomnia).
- The CR formulation's dual layer allows some medication to be released immediately, with the rest released gradually, resulting in higher levels through the night.

Fun Fact:

Biovail Labs received FDA approval for an orally disintegrating tablet form of zolpidem called Tovalt in 2007. It has since been discontinued due to poor sales.