

Short-term treatment with Edluar[®] may help your patients with insomnia characterized by difficulty falling asleep¹

- Sublingual administration with rapid absorption¹

INDICATIONS AND USAGE

Edluar (zolpidem tartrate) sublingual tablets are indicated for the short-term treatment of insomnia characterized by difficulties with sleep initiation.

The clinical trials performed with zolpidem tartrate in support of efficacy were 4-5 weeks in duration with the final formal assessments of sleep latency performed at the end of treatment.

SELECTED IMPORTANT SAFETY INFORMATION

WARNING: COMPLEX SLEEP BEHAVIORS

Complex sleep behaviors including sleep-walking, sleep-driving, and engaging in other activities while not fully awake may occur following use of Edluar. Some of these events may result in serious injuries, including death. Discontinue Edluar immediately if a patient experiences a complex sleep behavior.

EDLUAR[®]

Zolpidem Tartrate Sublingual Tablets (IV)
5 mg and 10 mg

IMPORTANT SAFETY INFORMATION (CONTINUED)

CONTRAINDICATIONS

- Edluar is contraindicated in patients who have experienced complex sleep behaviors after taking Edluar and with known hypersensitivity to zolpidem. Observed reactions include anaphylaxis and angioedema.

WARNINGS AND PRECAUTIONS

- **Complex Sleep Behaviors:**

Complex sleep behaviors including sleep-walking, sleep-driving, and engaging in other activities (e.g., preparing and eating food, making phone calls, or having sex) while not fully awake may occur following use of zolpidem. Patients can be seriously injured or injure others during complex sleep behaviors. Such injuries may result in a fatal outcome. Patients usually do not remember these events. Complex sleep behaviors may occur with zolpidem alone at recommended dosages, with or without concomitant use of alcohol or other CNS depressants. Discontinue Edluar immediately if a patient experiences a complex sleep behavior.

- **CNS Depressant Effects and Next-Day Impairment:**

Edluar, like other sedative-hypnotic drugs, has CNS depressant effects. Co-administration with other CNS depressants (e.g., benzodiazepines, opioids, tricyclic antidepressants, alcohol) increases the risk of CNS depression. Dosage adjustments of Edluar and concomitant CNS depressants may be necessary when administered together. The use of Edluar with other sedative-hypnotics (including other zolpidem products) at bedtime or the middle of the night is not recommended.

The risk of next-day psychomotor impairment, including impaired driving, is increased if Edluar is taken with less than a full night of sleep remaining (7 to 8 hours); if a higher than the recommended dose is taken; if co-administered with other CNS depressants; or if co-administered with other drugs that increase the blood level of zolpidem. Patients should be cautioned against driving and other activities requiring complete mental alertness.

Because Edluar can cause drowsiness and a decreased level of consciousness, patients, particularly the elderly, are at higher risk of falls.

- **Need to Evaluate for Co-morbid Diagnoses:**

Treatment of insomnia should be initiated only after a careful evaluation of the patient. Re-evaluate for comorbid conditions if insomnia persists or worsens after 7 to 10 days of treatment. Worsening of insomnia or the emergence of new thinking or behavior abnormalities may be the consequence of an unrecognized psychiatric or physical disorder and can emerge during the course of treatment with sedative/hypnotic drugs, including zolpidem.

- **Severe Anaphylactic and Anaphylactoid Reactions:**

Cases of angioedema involving the tongue, glottis or larynx have been reported in patients after taking the first or subsequent doses of sedative-hypnotics, including zolpidem tartrate. Some patients have had additional symptoms such as dyspnea, throat closing or nausea and vomiting that suggest anaphylaxis. Some patients have required medical therapy in the emergency department. If angioedema involves the throat, glottis or larynx, airway obstruction may occur and be fatal. Patients who develop angioedema after treatment with Edluar should not be rechallenged with the drug.

- **Abnormal Thinking and Behavioral Changes:**

Abnormal thinking and behavior changes have been reported in patients treated with sedative/hypnotics, including zolpidem. Some of these changes included decreased inhibition (e.g., aggressiveness and extroversion that seemed out of character), bizarre behavior, agitation and depersonalization. Visual and auditory hallucinations have been reported. Emergence of any new behavioral sign or symptom of concern requires careful and immediate evaluation.

- **Use in Patients with Depression:**

In primarily depressed patients treated with sedative-hypnotics, worsening of depression, and suicidal thoughts and actions (including completed suicides), have been reported. Suicidal tendencies may be present in such patients and protective measures may be required. Intentional overdose is more common in this group of patients; therefore, the least amount of drug that is feasible should be

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (Cont'd)

prescribed for the patient at any one time.

- **Respiratory Depression:**

Studies with 10 mg zolpidem tartrate did not reveal respiratory depressant effects at hypnotic doses in healthy subjects or in patients with mild-to-moderate chronic obstructive pulmonary disease (COPD). A reduction in the Total Arousal Index, together with a reduction in lowest oxygen saturation and increase in the time of oxygen desaturation below 80% and 90%, was observed in patients with mild-to-moderate sleep apnea when treated with zolpidem compared to placebo. Since sedative hypnotics have the capacity to depress respiratory drive, precautions should be taken if Edluar is prescribed to patients with compromised respiratory function. The risks of respiratory depression should be considered prior to prescribing Edluar in patients with respiratory impairment including sleep apnea and myasthenia gravis.

- **Withdrawal Effects:**

There have been reports of withdrawal signs and symptoms following the rapid dose decrease or abrupt discontinuation of zolpidem. Monitor patients for tolerance, abuse, and dependence.

ADVERSE EVENTS

- During short-term treatment (up to 10 nights) at doses up to 10 mg, the most common adverse reactions in controlled clinical trials were drowsiness (2%), dizziness (1%), and diarrhea (1%). During longer-term treatment (28 to 35 nights) at doses up to 10 mg, the most common adverse reactions that were also statistically different from placebo were dizziness (5%) and drugged feelings (3%)

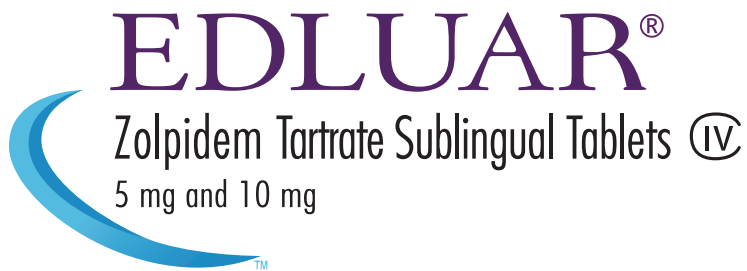
DRUG INTERACTIONS

- Co-administration of zolpidem with other CNS depressants increases the risk of CNS depression
- Imipramine used in combination with zolpidem produced an additive effect of decreased alertness. Similarly, chlorpromazine used in combination with zolpidem produced impaired alertness and psychomotor performance

- An additive adverse effect on psychomotor performance between alcohol and oral zolpidem was demonstrated
- Concomitant administration of zolpidem and sertraline increases exposure to zolpidem and may increase the pharmacodynamics effect of zolpidem
- Rifampin, a CYP3A4 inducer, in combination with zolpidem may decrease the efficacy of zolpidem
- Ketoconazole, a potent CYP3A4 inhibitor, in combination with zolpidem increased the pharmacodynamics effects of zolpidem. Consideration should be given to using a lower dose of zolpidem when ketoconazole and zolpidem are given together

USE IN SPECIAL POPULATIONS

- **Pregnancy:** Published data on the use of zolpidem during pregnancy have not identified a drug-associated risk of major birth defects. Neonates born to mothers using zolpidem late in the third trimester of pregnancy have been reported to experience symptoms of respiratory depression and sedation. Fetal/neonatal adverse reactions: Zolpidem crosses the placenta and may produce respiratory depression and sedation in neonates. Monitor neonates exposed to Edluar during pregnancy and labor for signs of excess sedation, hypotonia, and respiratory depression and manage accordingly.
- **Lactation:** Infants exposed to Edluar through breastmilk should be monitored for excess sedation, hypotonia, and respiratory depression. A lactating woman may consider interrupting breastfeeding and pumping and discarding breast milk during treatment and for 23 hours (approximately 5 elimination half-lives) after Edluar administration in order to minimize drug exposure to a breast fed infant.
- **Pediatric Use:** Edluar is not recommended for use in children. Safety and effectiveness in pediatric patients have not been established in pediatric patients below the age of 18
- **Geriatric Use:** The dose of Edluar in elderly patients is 5 mg to minimize adverse effects related to impaired motor and/or cognitive performance and unusual sensitivity to sedative/hypnotic drugs



IMPORTANT SAFETY INFORMATION (CONTINUED)

USE IN SPECIAL POPULATIONS (Cont'd)

- **Gender Differences in Pharmacokinetics:** Women clear zolpidem tartrate from the body at a lower rate than men, therefore the recommended dose of Edluar for adult women is 5 mg and 5 or 10 mg for adult men.

DRUG ABUSE AND DEPENDENCE

- Edluar contains zolpidem tartrate which is classified as a Schedule IV controlled substance by federal regulation.
- Because persons with a history of addiction to or abuse of, drugs or alcohol are at increased risk for misuse, abuse, and addiction of Edluar, they should be monitored carefully when receiving Edluar or any other hypnotic.
- Use the lowest effective dose for the patient.
- Sedative/hypnotics have produced withdrawal signs and symptoms following abrupt discontinuation. These reported symptoms range from mild dysphoria and insomnia to a withdrawal syndrome that may include abdominal and muscle cramps, vomiting, sweating, tremors, and convulsions.

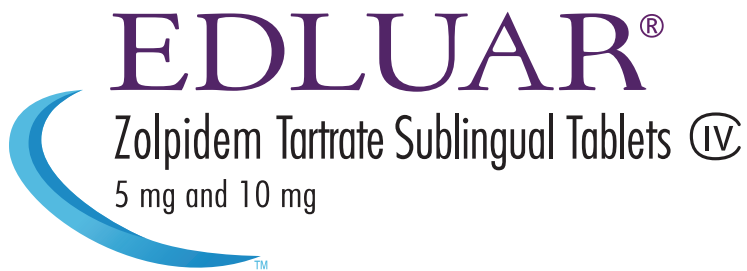
OVERDOSAGE

• Recommended Treatment

General symptomatic and supportive measures for overdose with Edluar should be used along with immediate gastric lavage where appropriate. Intravenous fluids should be administered as needed. Flumazenil reduces zolpidem's sedative/hypnotic effect however, flumazenil administration may contribute to the appearance of neurological symptoms (convulsions). As in all cases of drug overdose, respiration, pulse, blood pressure, and other appropriate signs should be monitored, and general supportive measures employed. Hypotension and CNS depression should be monitored and treated by appropriate medical intervention. Sedating drugs should be withheld following zolpidem overdose, even if excitation occurs. The value of dialysis in the treatment of overdose has not been determined, although hemodialysis studies in patients with renal failure receiving therapeutic doses have demonstrated that zolpidem is not dialyzable.

The possibility of multiple drug ingestion should be considered and the physician may consider contacting a poison control center for up-to-date information on the management of hypnotic drug product overdose.

See full Prescribing Information, including **Boxed WARNING regarding **Complex Sleep Behaviors**.**



Established clinical efficacy in patients with insomnia characterized by sleep latency^{1*}

In normal adults with transient and chronic insomnia, zolpidem tartrate oral tablets were superior to placebo on the objective polysomnographic measure of sleep latency.¹

*Normal adults experiencing transient insomnia (n = 462) during the first night in a sleep laboratory were evaluated in a double-blind, parallel-group, single-night trial comparing two doses of zolpidem tartrate oral tablets and placebo. Normal elderly adults (mean age 68) experiencing transient insomnia (n = 35) during the first 2 nights in a sleep laboratory were evaluated in a double-blind, crossover, two-night trial comparing four doses of zolpidem and placebo. All doses of zolpidem tartrate were superior to placebo when compared for the primary endpoint of the polysomnographic (PSG) sleep latency measure in both trials.

Zolpidem was evaluated in two double-blind, parallel-group, controlled studies for the treatment of patients with chronic insomnia. One study included adult outpatients (n = 75) in a 5-week trial and another study had adult outpatients (n = 141) in a 4-week trial comparing two doses of zolpidem tartrate and placebo. Zolpidem 10 mg tablets were superior to placebo on the PSG parameter of sleep latency for the first 4 out of 5-week trial and were superior to placebo on a subjective measure of sleep latency for all 4 weeks of the 4-week trial.

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Please see Important Safety Information on pages 2-4. [Click here](#) for Full Prescribing Information, including Boxed WARNING.

Safety profile for sedative/hypnotic concerns¹

Placebo-controlled studies evaluating safety concerns of zolpidem tartrate oral tablets in adult patients showed¹:



Next-day residual effects

- Next-day residual effects of zolpidem tartrate were evaluated in 7 studies involving normal subjects. In three studies in adults and one study in elderly subjects, a small but statistically significant decrease in performance was observed in the Digital Symbol Substitution Test (DSST) when compared to placebo¹
- No evidence of next-day residual effects in non-elderly patients with insomnia was detected in studies using the DSST, the Multiple Sleep Latency Test and patient ratings of alertness¹



Rebound effects

- No objective (polysomnographic) evidence of rebound insomnia at recommended doses seen in studies evaluating sleep on the nights following discontinuation of zolpidem tartrate¹
- There is subjective evidence of impaired sleep in the elderly on the first post-treatment night at doses above the recommended elderly dose of 5 mg¹



Memory impairment

- No consistent evidence of next-day memory impairment following the administration of zolpidem tartrate¹
- However, in one study involving zolpidem doses of 10 mg and 20 mg, there was a significant decrease in next-morning recall of information presented to subjects during the peak drug effect (90 minutes post-dose, these subjects experienced anterograde amnesia)¹
- There is also subjective evidence from adverse event data for anterograde amnesia occurring in association with administration of zolpidem tartrate (predominantly at doses above 10 mg)¹



Effect on sleep stages

- Generally has been shown to preserve sleep stages¹

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (CONTINUED)

- **CNS Depressant Effects and Next-Day Impairment (Cont'd):**

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Clinical safety for Edluar[®]1

Table 1. Incidence of Treatment-Emergent Adverse Experiences in Placebo-Controlled Clinical Trials with Zolpidem Tartrate Lasting up to 10 Nights (Percentage of Patients Reporting)¹

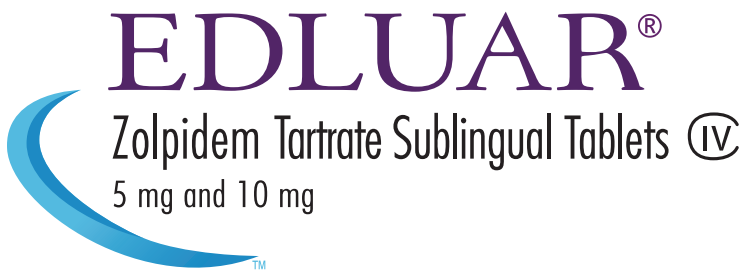
Body system/Adverse Event*	Zolpidem tartrate (≤10 mg) (N = 685)	Placebo (N = 473)
Central and Peripheral Nervous System		
Headache	7	6
Drowsiness	2	-
Dizziness	1	-
Gastrointestinal System		
Diarrhea	1	-

*Reactions reported by at least 1% of patients treated with oral zolpidem and at a greater frequency than placebo.

Table 2. Incidence of Treatment-Emergent Adverse Experiences in Placebo-Controlled Clinical Trials with Zolpidem Tartrate Lasting up to 35 nights (Percentage of Patients Reporting)¹

Body System/Adverse Event*	Zolpidem tartrate (≤10 mg) (N = 152)	Placebo (N = 161)
Autonomic Nervous System		
Dry mouth	3	1
Body as a Whole		
Allergy	4	1
Back Pain	3	2
Influenza-like symptoms	2	-
Chest pain	1	-
Cardiovascular System		
Palpitation	2	-
Central and Peripheral Nervous System		
Drowsiness	8	5
Dizziness	5	1
Lethargy	3	1
Drugged feeling	3	-
Lightheadedness	2	1
Depression	2	1
Abnormal dreams	1	-
Amnesia	1	-
Sleep disorder	1	-
Gastrointestinal System		
Diarrhea	3	2
Abdominal pain	2	2
Constipation	2	1
Respiratory System		
Sinusitis	4	2
Pharyngitis	3	1
Skin and Appendages		
Rash	2	1

*Reactions were reported by at least 1% of patients treated with oral zolpidem and at a greater frequency than placebo.



Edluar®: For the short-term treatment of your insomnia patients who have trouble falling asleep¹

- Sublingual administration with rapid absorption¹

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (CONTINUED)

- **Need to Evaluate for Co-morbid Diagnoses:**

Treatment of insomnia should be initiated only after a careful evaluation of the patient. Re-evaluate for comorbid conditions if insomnia persists or worsens after 7 to 10 days of treatment. Worsening of insomnia or the emergence of new thinking or behavior abnormalities may be the consequence of an unrecognized psychiatric or physical disorder and can emerge during the course of treatment with sedative/hypnotic drugs, including zolpidem.

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Reference:

1. EDLUAR [prescribing information]. Somerset, NJ: Meda Pharmaceuticals Inc.; 2021.

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