

least 3% for zolpidem tartrate and for which the zolpidem incidence was at least twice the placebo incidence (i.e., they could be considered drug related).

Adverse Reaction	Zolpidem	Placebo
Dizziness	3%	0%
Drowsiness	5%	2%
Diarrhea	3%	1%

A total of 30/1,959 (1.5%) non-U.S. patients receiving zolpidem reported falls, including 28/30 (93%) who were ≥ 70 years of age. Of these 28 patients, 23 (82%) were receiving zolpidem doses >10 mg. A total of 24/1,959 (1.2%) non-U.S. patients receiving zolpidem reported confusion, including 18/24 (75%) who were ≥ 70 years of age. Of these 18 patients, 14 (78%) were receiving zolpidem doses >10 mg.

The dose of Zolpimist in elderly patients is 5 mg to minimize the adverse effects related to impaired motor and/or cognitive performance and unusual sensitivity to sedative-hypnotic drugs [see *Warnings and Precautions (5.6)*].

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled substance

Zolpidem tartrate is classified as a Schedule IV controlled substance by federal regulation.

9.2 Abuse

Abuse and addiction are separate and distinct from physical dependence and tolerance. Abuse is characterized by misuse of the drug for non-medical purposes, often in combination with other psychoactive substances. Tolerance is a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug effects over time. Tolerance may occur to both desired and undesired effects of drugs and may develop at different rates for different effects.

Addiction is a primary, chronic, neurobiological disease with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving. Drug addiction is a treatable disease, using a multidisciplinary approach, but relapse is common.

Studies of abuse potential in former drug abusers found that the effects of single doses of zolpidem tartrate 40 mg were similar, but not identical, to diazepam 20 mg, while zolpidem tartrate 10 mg was difficult to distinguish from placebo.

Because persons with a history of addiction to, or abuse of, drugs or alcohol are at increased risk for misuse, abuse and addiction of zolpidem, they should be monitored carefully when receiving zolpidem or any other hypnotic.

9.3 Dependence

Physical dependence is a state of adaptation that is manifested by a specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist.

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. The following adverse reactions which are considered to meet the DSM-III-R criteria for uncomplicated sedative-hypnotic withdrawal were reported during U.S. clinical trials following placebo substitution occurring within 48 hours following last zolpidem treatment: fatigue, nausea, flushing, lightheadedness, uncontrolled crying, emesis, stomach cramps, panic attack, nervousness, and abdominal discomfort. These reported adverse reactions occurred at an incidence of 1% or less. However, available data cannot provide a reliable estimate of the incidence, if any, of dependence during treatment at recommended doses. Post-marketing reports of abuse, dependence, and withdrawal have been received.

10 OVERDOSAGE

10.1 Signs and symptoms

In postmarketing experience of overdose with zolpidem tartrate alone, or in combination with CNS-depressant agents, impairment of consciousness ranging from somnolence to coma, cardiovascular and/or respiratory compromise, and fatal outcomes have been reported.

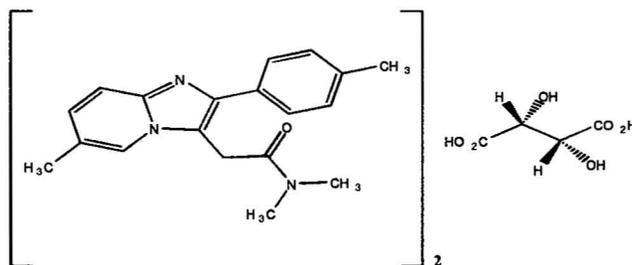
10.2 Recommended treatment

General symptomatic and supportive measures should be used along with immediate gastric lavage where appropriate. Intravenous fluids should be administered as needed. Zolpidem's sedative-hypnotic effect was shown to be reduced by flumazenil and therefore may be useful; 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.

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

11 DESCRIPTION

Zolpimist contains zolpidem tartrate, a non-benzodiazepine hypnotic of the imidazopyridine class. Chemically, zolpidem is *N,N,6-trimethyl-2-p-tolylimidazo[1,2-*a*]pyridine-3-acetamide L-(+)*tartrate (2:1). It has the following structure:



Zolpidem tartrate is a white to off-white crystalline powder that is sparingly soluble in water, alcohol, and propylene glycol. It has a molecular weight of 764.89.

Zolpimist is available as an oral solution designed to be sprayed directly into the mouth over the tongue. Each metered actuation of Zolpimist delivers 5 mg of zolpidem tartrate in 100 μ L. Two actuations deliver 10 mg of zolpidem tartrate. Zolpimist includes the following inactive ingredients: artificial cherry flavor, benzoic acid, citric acid monohydrate, hydrochloric acid, neotame, propylene glycol, and purified water.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of action

Zolpidem, the active moiety of zolpidem tartrate, is a hypnotic agent with a chemical structure unrelated to benzodiazepines, barbiturates, or other drugs with known hypnotic properties. It interacts with a GABA-BZ receptor complex and shares some of the pharmacological properties of the benzodiazepines. In contrast to the benzodiazepines which non-selectively bind to and activate all BZ receptor subtypes, zolpidem *in vitro* binds the BZ₁ receptor preferentially with a high affinity ratio of the α_1/α_5 subunits. This selective binding of zolpidem on the BZ₁ receptor is not absolute, but it may explain the relative absence of myorelaxant and anticonvulsant effects in animal studies as well as the preservation of deep sleep (stages 3 and 4) in human studies of zolpidem at hypnotic doses.

12.3 Pharmacokinetics

Zolpimist (zolpidem tartrate) Oral Spray is bioequivalent to Ambien® tablets (Sanofi-Aventis). The pharmacokinetic profile of Zolpimist is characterized by rapid absorption from the oral mucosa and gastrointestinal tract, and a short $t_{1/2}$ in healthy subjects.

In a single-dose crossover study in 10 healthy young (18-40 years of age) male subjects administered 2.5, 5, and 10 mg Zolpimist, the results demonstrated a linear relationship to dose for mean C_{max} and $AUC_{0-\infty}$ over the range of doses administered in the study.

In a single-dose crossover study in 43 healthy young (18-45 years of age) subjects administered 5 and 10 mg Zolpimist, the means for C_{max} were 114 (range: 19 to 197) and 210 ng/mL (range: 77 to 401), respectively, occurring at a mean T_{max} of approximately 0.9 hours for both. The mean zolpidem $t_{1/2}$ was 2.7 (range: 1.7 to 5.0) and 3.0 hours (range: 1.7 to 8.4), for 5 and 10 mg Zolpimist, respectively. In the same study, the means for C_{max} were 123 (range: 53 to 221) and 219 ng/mL (range: 101 to 446) for 5 and 10 mg Ambien® tablets, respectively, occurring at a mean T_{max} of 0.9 and 1.0 hours, respectively. The mean zolpidem $t_{1/2}$ was 2.8 (range: 1.5 to 6.0) and 3.1 hours (range: 1.1 to 8.6) for the 5 and 10 mg Ambien® tablets, respectively.

Zolpidem is converted to inactive metabolites that are eliminated primarily by renal excretion. Total protein binding for zolpidem was found to be $92.5 \pm 0.1\%$ and remained constant, independent of concentration between 40 and 790 ng/mL. Zolpidem did not accumulate in young adults following nightly dosing with 20 mg zolpidem tartrate for 2 weeks.

A food-effect crossover study in 14 healthy young (18-45 years of age) male subjects compared the pharmacokinetics of Zolpimist 10 mg when administered while fasting at least 8 hours or 5 minutes after eating a standard high-fat meal. Results demonstrated that with food, mean $AUC_{0-\infty}$ and C_{max} were decreased by 27% and 58%, respectively, while mean T_{max} was prolonged by 225% (from 0.8 to 2.6 hours). These results suggest that, for faster sleep onset, as with all zolpidem products, Zolpimist should not be administered with or immediately after a meal.

Special Populations:

Elderly: In the elderly, the dose for zolpidem tartrate should be 5 mg [see *Warnings and Precautions (5) and Dosage and Administration (2)*]. This recommendation is based on several studies in which the mean C_{max} , $t_{1/2}$, and AUC were significantly increased when compared to results in young adults administered zolpidem tartrate. In a pharmacokinetic study of 24 elderly (≥ 65 years of age) subjects administered 5 mg Zolpimist, the means for C_{max} and AUC were 134 ng/mL and 493 ng*hr/mL respectively, following administration of a single 5 mg oral dose of Zolpimist. Zolpidem tartrate did not accumulate in elderly subjects following nightly oral dosing of 10 mg for 1 week.

Hepatic Impairment: The pharmacokinetics of zolpidem in eight patients with chronic hepatic insufficiency were compared to results in healthy subjects. Following a single 20 mg oral zolpidem tartrate dose, mean C_{max} and AUC were found to be two times (250 vs 499 ng/mL) and five times (788 vs 4,203 ng*hr/mL) higher, respectively, in hepatically compromised patients. T_{max} did not change. The mean $t_{1/2}$ in cirrhotic patients of 9.9 hours (range: 4.1 to 25.8 hours) was greater than that observed in normal subjects of 2.2 hours (range: 1.6 to 2.4 hours). Dosing should be modified accordingly in patients with hepatic insufficiency [see *Dosage and Administration (2.2) and Warnings and Precautions (5.6)*].

Renal Impairment: The pharmacokinetics of zolpidem were studied in 11 patients with end-stage renal failure (mean $Cl_{Cr} = 6.5 \pm 1.5$ mL/min) undergoing hemodialysis three times a week, who were dosed with zolpidem tartrate 10 mg orally each day for 14 or 21 days. No statistically significant differences were observed for C_{max} , T_{max} , $t_{1/2}$, and AUC between the first and last day of drug administration when baseline concentration adjustments were made. On Day 1, C_{max} was 172 ± 29 ng/mL (range: 46 to 344 ng/mL). After repeated dosing for 14 or 21 days, C_{max} was 203 ± 32 ng/mL (range: 28 to 316 ng/mL). On Day 1, T_{max} was 1.7 ± 0.3 hours (range: 0.5 to 3.0 hours); after repeated dosing T_{max} was 0.8 ± 0.2 hour (range: 0.5 to 2.0 hours). This variation is accounted for by noting that last-day serum sampling began 10 hours after the previous dose, rather than after 24 hours. This resulted in residual drug concentration and a shorter period to reach maximal serum concentration. On Day 1, $t_{1/2}$ was 2.4 ± 0.4 hours (range: 0.4 to 5.1 hours). After repeated dosing, $t_{1/2}$ was 2.5 ± 0.4 hours (range: 0.7 to 4.2 hours). AUC was 796 ± 159 ng*hr/mL after the first dose and 818 ± 170 ng*hr/mL after repeated dosing. Zolpidem was not hemodialyzable. No accumulation of unchanged drug appeared after 14 or 21 days. Zolpidem pharmacokinetics were not significantly different in renally impaired patients.

No dosage adjustment is necessary in patients with compromised renal function. However, as a general precaution, these patients should be closely monitored.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, mutagenesis, impairment of fertility

Carcinogenesis: Zolpidem was administered to mice and rats for 2 years at dietary dosages of 4, 18, and 80 mg base/kg. In mice, these doses are ≈ 2.5 , 10, and 50 times the maximum recommended human dose (MRHD) of 10 mg/day (8 mg zolpidem base) on mg/m^2 basis. In rats, these doses are ≈ 5 , 20, and 100 times the MRHD on a mg/m^2 basis. No evidence of carcinogenic potential was observed in mice. In rats, renal tumors (lipoma, liposarcoma) were seen at the mid- and high doses.

Mutagenesis: Zolpidem was negative in *in vitro* (bacterial reverse mutation, mouse lymphoma, and chromosomal aberration) and *in vivo* (mouse micronucleus) genetic toxicology assays.

Impairment of fertility: Oral administration of zolpidem (doses of 4, 20, and 100 mg base/kg or ≈ 5 , 24, and 120 times the MRHD on a mg/m^2 basis) to rats prior to and during mating, and continuing in females through postpartum day 25, resulted in irregular estrus cycles and prolonged precoital intervals. The no-effect dose for these findings is ≈ 24 times the MRHD on a mg/m^2 basis. There was no impairment of fertility at any dose tested.

CLINICAL STUDIES

14.1 Transient insomnia

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 (7.5 and 10 mg) and placebo. Both zolpidem doses were superior to placebo on objective (polysomnographic) measures of sleep latency, sleep duration, and number of awakenings.

Normal elderly adults (mean age 68) experiencing transient insomnia (n=35) during the first two nights in a sleep laboratory were evaluated in a double-blind, crossover, 2-night trial comparing four doses of zolpidem (5, 10, 15, and 20 mg) and placebo. All zolpidem doses were superior to placebo on the two primary PSG parameters (sleep latency and efficiency) and all four subjective outcome measures (sleep duration, sleep latency, number of awakenings, and sleep quality).

14.2 Chronic insomnia

Zolpidem was evaluated in two controlled studies for the treatment of patients with chronic insomnia (most closely resembling primary insomnia, as defined in the APA Diagnostic and Statistical Manual of Mental Disorders, DSM-IVTM). Adult outpatients with chronic insomnia (n=75) were evaluated in a double-blind, parallel group, 5-week trial comparing two doses of zolpidem tartrate and placebo. On objective (polysomnographic) measures of sleep latency and sleep efficiency, zolpidem 10 mg was superior to placebo on sleep latency for the first 4 weeks and on sleep efficiency for weeks 2 and 4. Zolpidem was comparable to placebo on number of awakenings at both doses studied.

Adult outpatients (n=141) with chronic insomnia were also evaluated, in a double-blind, parallel group, 4-week trial comparing two doses of zolpidem and placebo. Zolpidem 10 mg was superior to placebo on a subjective measure of sleep latency for all 4 weeks, and on subjective measures of total sleep time, number of awakenings, and sleep quality for the first treatment week.

Increased wakefulness during the last third of the night as measured by polysomnography has not been observed in clinical trials with zolpidem.

14.3 Studies pertinent to safety concerns for sedative-hypnotic drugs

Next-day residual effects: Next-day residual effects of zolpidem tartrate were evaluated in seven studies involving normal subjects. In three studies in adults (including one study in a phase advance model of transient insomnia) and in one study in elderly subjects, a small but statistically significant decrease in performance was observed in the Digit Symbol Substitution Test (DSST) when compared to placebo. Studies of zolpidem tartrate in non-elderly patients with insomnia did not detect evidence of next-day residual effects using the DSST, the Multiple Sleep Latency Test (MSLT), and patient ratings of alertness.

Rebound effects: There was no objective (polysomnographic) evidence of rebound insomnia at recommended doses seen in studies evaluating sleep on the nights following discontinuation of zolpidem tartrate. There was subjective evidence of impaired sleep in the elderly on the first post-treatment night at doses above the recommended elderly dose of 5 mg.

Memory impairment: Controlled studies in adults utilizing objective measures of memory yielded no consistent evidence of next-day memory impairment following the administration of zolpidem tartrate. However, in one study involving zolpidem doses of 10 and 20 mg, there was a significant decrease in next-morning recall of information presented to subjects during peak drug effect (90 minutes post-dose) (i.e., these subjects experienced anterograde amnesia). There was also subjective evidence from adverse event data for anterograde amnesia occurring in association with the administration of zolpidem tartrate, predominantly at doses above 10 mg.

Effects on sleep stages: In studies that measured the percentage of sleep time spent in each sleep stage, zolpidem tartrate has generally been shown to preserve sleep stages. Sleep time spent in stages 3 and 4 (deep sleep) was found comparable to placebo with only inconsistent, minor changes in REM (paradoxical) sleep at the recommended dose.

16 HOW SUPPLIED/STORAGE AND HANDLING

Zolpimist is available in a child-resistant container. Each container includes a child-resistant cap and base with a metered-dose pump assembly and clear over cap. Each container contains 8.2 g of product formulation. One and two actuations of Zolpimist are equal to 5 and 10 mg of zolpidem tartrate, respectively. There are 60 metered actuations per container after 5 initial priming actuations. Zolpimist is supplied as:

NDC Number
XXXXXX-001-01

Size
Carton includes a child-resistant container with 8.2 g of product formulation; 60 metered actuations per container

Store upright at 25 °C (77 °F) with excursions permitted to 15-30 °C (59-86 °F) (*USP Controlled Room Temperature*). Do not freeze. Avoid prolonged product exposure to temperatures above 30 °C (86 °F). The child-resistant container should be discarded when the labeled number of actuations (60 sprays) have been used.

KEEP OUT OF REACH OF CHILDREN.

17 PATIENT COUNSELING INFORMATION

Prescribers or other healthcare professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with sedative-hypnotics, should counsel them in its appropriate use, and should instruct them to read the accompanying Medication Guide and Patient Instructions for Use [*see Section 17.4 Medication Guide and Patient Instructions for Use*].

17.1 Severe anaphylactic and anaphylactoid reactions

Inform patients that severe anaphylactic and anaphylactoid reactions have occurred with zolpidem. Describe the signs/symptoms of these reactions and advise patients to seek medical attention immediately if any of them occur.

17.2 Sleep-driving and other complex behaviors

There have been reports of people getting out of bed after taking a sedative-hypnotic and driving their cars while not fully awake, often with no memory of the event. If a patient experiences such an episode, it should be reported to his or her doctor immediately, since “sleep-driving” can be dangerous. This behavior is more likely to occur when Zolpimist is taken with alcohol or other central nervous system depressants [*see Warnings and Precautions (5.3)*]. Other complex behaviors (e.g., preparing and eating food, making phone calls, or having sex) have been reported in patients who are not fully awake after taking a sedative-hypnotic. As with “sleep-driving”, patients usually do not remember these events.

In addition patients should be advised to report all concomitant medications to the prescriber. Patients should be instructed to report events such as “sleep-driving” and other complex behaviors immediately to the prescriber.

17.3 Administration instructions

See the Dosage and Administration section [*see Administration (2.4)*]. Zolpimist is packaged in a child-resistant container. Patients should be referred to the Patient Instructions for Use (following the Medication Guide) for detailed instructions on how to use Zolpimist. Patients should be counseled to take Zolpimist right before they get into bed and only when they are able to stay in bed a full night (7-8 hours) before being active again. Zolpimist should not be taken with or immediately after a meal. Advise patients NOT to take Zolpimist when drinking alcohol.

17.4 Medication Guide and Patient Instructions for Use

MEDICATION GUIDE
Zolpimist Oral Spray (C-IV)
(zolpidem tartrate)
Spray, Metered for Oral Use

Read the Medication Guide that comes with Zolpimist before you start taking it and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking to your doctor about your medical condition or treatment.

What is the most important information I should know about Zolpimist?

After taking Zolpimist, you may get up out of bed while not being fully awake and do an activity that you do not know you are doing. The next morning, you may not remember that you did anything during the night. You have a higher chance for doing these activities if you drink alcohol or take other medicines that make you sleepy with Zolpimist. Reported activities include:

- driving a car ("sleep-driving")
- making and eating food
- talking on the phone
- having sex
- sleep-walking

Call your doctor right away if you find out that you have done any of the above activities after taking Zolpimist.

Important:

1. Take Zolpimist exactly as prescribed

- Do not take more Zolpimist than prescribed.
- Take Zolpimist right before you get in bed, not sooner.

2. Do not take Zolpimist if you:

- drink alcohol
- take other medicines that can make you sleepy. Talk to your doctor about all of

your medicines. Your doctor will tell you if you can take Zolpimist with your other medicines.

- cannot get a full night sleep

What is Zolpimist?

Zolpimist is a sedative-hypnotic (sleep) medicine. Zolpimist is used in adults for the short-term treatment of a sleep problem called insomnia. Symptoms of insomnia include:

- trouble falling asleep

Zolpimist is not for children.

Zolpimist is a federally controlled substance (C-IV) because it can be abused and lead to dependence. Keep Zolpimist in a safe place to prevent misuse and abuse. Selling or giving away Zolpimist may harm others, and is against the law. Tell your doctor if you have ever abused or have been dependent on alcohol, prescription medicines, or street drugs.

Who should not take Zolpimist? Do not take Zolpimist if you have had an allergic reaction to zolpidem (Ambien, Ambien CR, Zolpimist). Some signs of allergic reaction may be swelling of the face, a feeling of the throat closing, or difficulty breathing shortly after taking Zolpidem.

See the end of this Medication Guide for a complete list of ingredients in Zolpimist.

Zolpimist may not be right for you. Before starting Zolpimist, tell your doctor about all of your health conditions, including if you:

- have a history of depression, mental illness, or suicidal thoughts
- have a history of drug or alcohol abuse or addiction
- have kidney or liver disease
- have a lung disease or breathing problems
- are pregnant, planning to become pregnant, or breastfeeding

Tell your doctor about all the medicines you take including prescription and nonprescription medicines, vitamins, and herbal supplements. Medicines can interact with each other, sometimes causing serious side effects. **Do not take Zolpimist with other medicines that can make you sleepy.**

Know the medicines you take. Keep a list of your medicines with you to show your doctor and pharmacist each time you get a new medicine.

How should I take Zolpimist?

- Take Zolpimist exactly as prescribed. Do not take more Zolpimist than prescribed for you.
- **Take Zolpimist right before you get into bed.**
- **Do not take Zolpimist unless you are able to stay in bed a full night (7-8 hours) before you must be active again.**
- For faster sleep onset, Zolpimist should NOT be taken with or immediately after a meal.
- Call your doctor if your insomnia worsens or is not better within 7 to 10 days. This may mean that there is

another condition causing your sleep problem.

- If you take too much Zolpimist or overdose, call your doctor or poison control center right away, or get emergency treatment.

What are the possible side effects of Zolpimist?

Serious side effects of Zolpimist include:

- **getting out of bed while not being fully awake and doing an activity that you do not know you are doing.** (See "What is the most important information I should know about Zolpimist?")
- **abnormal thoughts and behavior.** Symptoms include more outgoing or aggressive behavior than normal, confusion, agitation, hallucinations, worsening of depression, and suicidal thoughts or actions.
- **memory loss**
- **anxiety**
- **severe allergic reactions.** Symptoms include swelling of the tongue or throat, trouble breathing, and nausea and vomiting. Get emergency medical help if you get these symptoms after taking Zolpimist.

Call your doctor right away if you have any of the above side effects or any other side effects that worry you while using Zolpimist.

The most common side effects of Zolpimist are:

- drowsiness
- dizziness
- diarrhea
- "drugged feelings"
- You may still feel drowsy the next day after taking Zolpimist. **Do not drive or do other dangerous activities after**

taking Zolpimist until you feel fully awake.

After you stop taking a sleep medicine, you may have symptoms for 1 or 2 days such as: tiredness, trouble sleeping, nausea, flushing, lightheadedness, uncontrolled crying, vomiting, stomach cramps, panic attack, nervousness, and stomach area pain.

These are not all the side effects of Zolpimist. Ask your doctor or pharmacist for more information.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store Zolpimist?

- Store Zolpimist in an upright position at 59 °F to 86 °F (15 °C to 30 °C).
- Do not freeze.
- Avoid prolonged product exposure above 86 °F (30 °C).
- The child-resistant container should be thrown away when the 60 sprays have been used.

Keep Zolpimist and all medicines out of reach of children.

General Information about Zolpimist

- Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide.

- Do not use Zolpimist for a condition for which it was not prescribed.
- Do not share Zolpimist with other people, even if you think they may have the same symptoms that you have. It may harm them and it is against the law.

This Medication Guide summarizes the most important information about Zolpimist. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about Zolpimist that is written for healthcare professionals. For more information about Zolpimist, call 1-800-XXX-XXXX.

What are the ingredients in Zolpimist?

Active Ingredient: Zolpidem tartrate

Inactive Ingredients: artificial cherry flavor, benzoic acid, citric acid monohydrate, hydrochloric acid, neotame, propylene glycol, and purified water.

Rx Only

Revised December 2008

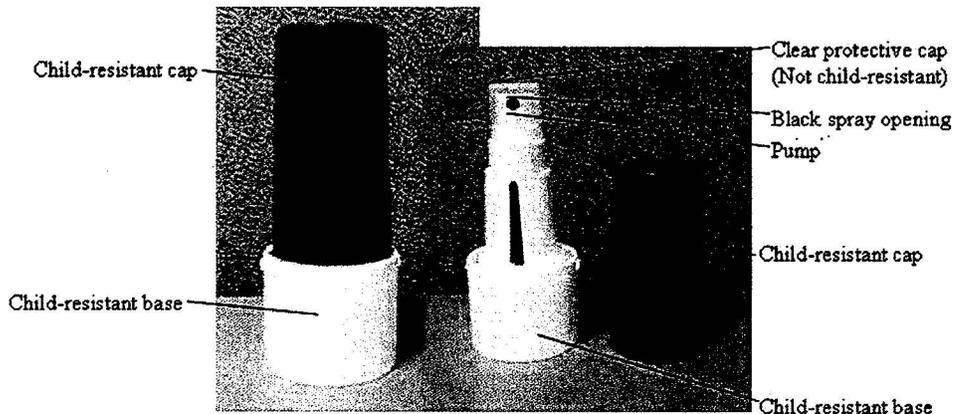
This Medication Guide has been approved by U.S. Food and Drug Administration.

NovaDel Pharma Inc.
Flemington, NJ 08822

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Patient Instructions for Use Zolpimist (zolpidem tartrate) Spray, Metered for Oral Use

Be sure to carefully read, understand, and follow these instructions so that you use Zolpimist the right way. Ask your doctor or pharmacist if you have any questions about how to use Zolpimist.



Priming:

Before you use Zolpimist for the first time or if you have not used Zolpimist for 14 days, you will need to prime the pump (Steps 1-6). Otherwise go directly to Step 7.

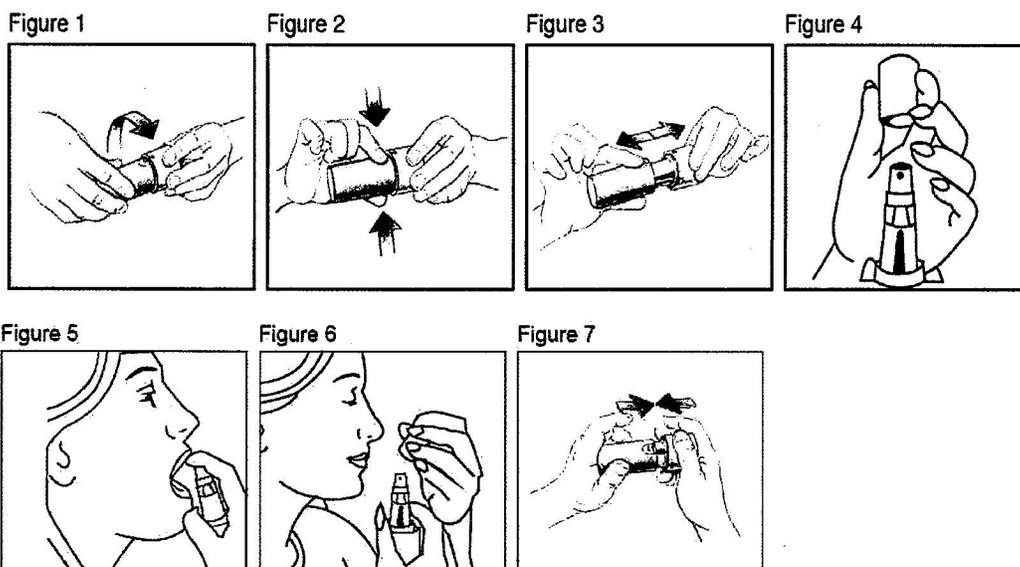
To prime the pump:

1. Line up the arrows on the child-resistant cap and base (see Figure 1).
2. Squeeze the cap at arrows (see Figure 2).
3. Pull the cap and base to separate (see Figure 3).
4. Remove the clear protective cap from the pump (see Figure 4).
5. Hold the container upright. Point the black spray opening in a safe direction away from your face and other people. Fully press down on the pump with your forefinger. Release the pump and let the pump return to the starting position.
6. Follow step 5 and press down on the pump 4 more times. You should see a fine spray. Zolpimist is now ready to use. Now go directly to Step 11.

Taking a dose of Zolpimist:

- **If you are using Zolpimist for the first time or you have not used Zolpimist for 14 days, you will need to prime the pump (Steps 1-6). Otherwise, there is no need to prime the pump.**
- **Take Zolpimist exactly as prescribed. Do not take more Zolpimist than prescribed for you.** Your doctor will tell you whether to take 1 or 2 sprays of Zolpimist.
- **Take Zolpimist right before you get into bed.**

- **Do not take Zolpimist unless you are able to stay in bed a full night (7-8 hours) before you must be active again.**
7. Line up the arrows on the child-resistant cap and base (see Figure 1).
 8. Squeeze the cap at arrows (see Figure 2).
 9. Pull the cap and base to separate (see Figure 3).
 10. Remove the clear protective cap from the pump (see Figure 4).
 11. Hold the container upright with the black spray opening pointed directly into your mouth. Fully press down on the pump to make sure that a full dose of Zolpimist is sprayed directly into your open mouth over your tongue (see Figure 5).
 12. Let the pump return to the starting position. If your doctor prescribed only one spray of Zolpimist (5 mg dose), go directly to Step 14.
 13. If your doctor prescribes a second spray of Zolpimist (10 mg dose), repeat Step 11.
 14. Put the clear protective cap back over the pump at the top of the child-resistant base after each use (see Figure 6).
 15. Snap the child-resistant cap back onto the base and rotate the child-resistant cap and the child-resistant base so that the arrows are not lined up (see Figure 7).
 16. The child-resistant container should be thrown away when the 60 sprays have been used.



There are no special requirements for cleaning and maintaining Zolpimist. Professional assistance regarding questions about product performance or use can be obtained by calling 1-800-XXX-XXXX.

See Medication Guide section “How should I store Zolpimist?” for instructions about how to store Zolpimist.

Manufactured for
NovaDel Pharma Inc.
Flemington, NJ 08822
by

NovaDel Pharma Inc.
Zolpimist (zolpidem tartrate) Oral Spray

New Drug Application
NDA 022196, SN 0021
December 2008

Rechon Life Sciences AB
SE-216 10 Limhamn, Sweden

Prepared December 2008

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