1. Product and Company Identification

PRODUCT NAME: ZOLPIDEM TATRATE EXTENDED RELEASE IV Tablets
6.25 mg, 12.5 mg

Supplier:
Winthrop U.S.
A business of Sanofi U.S.
55 Corporate Drive
Bridgewater, NJ 08807

24-Hour Transport Emergency, US (Chemtrec):	**(800) 424-9300**
24-Hour Transport Emergency, outside US (Chemtrec):	**(703) 527-3887**
US Customer Service	**(800) 207-8049**
24-Hour Emergency, sanofi-aventis US:	**(908) 981-5550**

Product use: Pharmaceutical product.

2. Hazards Identification

2.1 Classification in accordance with 29 CFR 1910.1200

Classification of the finished drug product is not required according to OSHA 29 CFR 1910.1200. The following information is provided for the drug substance, zolpidem tartrate:

Classification:
Acute toxicity, Category 4
Specific target organ toxicity - single exposure, Category 3

2.2 Label elements in accordance with 29 CFR 1910.1200

Labeling of the finished drug product is not required according to OSHA 29 CFR 1910.1200. The following information is provided for the drug substance, zolpidem tartrate:

Signal Word: Warning

Hazard Statement(s): Harmful if swallowed. May cause drowsiness or dizziness.

Symbol(s): Exclamation mark

Precautionary Statement(s):

- Prevention: Avoid breathing dust. Use only in a well-ventilated area. Wash hands thoroughly after handling. Do not eat, drink or smoke while using this product.
- Response: If inhaled: Remove person to fresh air and keep comfortable for breathing. If swallowed: Call a poison center if you feel unwell. Rinse mouth.
- Storage: Store in a well-ventilated place. Keep container tightly closed. Store locked up.
- Disposal: Dispose of in accordance with applicable regional, national and local laws and regulations.

2.3 Hazards Not Otherwise Classified (HNOC)

Not classified.

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3. Composition/Information on Ingredients

Chemical Name:	**Common Name:**	**CAS #:**	**Percentage or concentration range**
N,N,6-trimethyl-2-p-tolylimidazo[1,2-a] pyridine-3-acetamide L-(+)-tartrate (2:1)	Zolpidem tartrate	99294-93-6	5 mg or 10 mg per tablet

Inactive Ingredients: hydroxypropyl methylcellulose, lactose, magnesium stearate, micro-crystalline cellulose, polyethylene glycol, sodium starch glycolate, and titanium dioxide. The 5 mg tablet also contains FD&C Red No. 40, iron oxide colorant, and polysorbate 80.

4. First Aid Measures

4.1 First aid procedures

Eye contact: In case of contact with dust from broken tablets or capsules, immediately flush eyes with plenty of water for at least 15 minutes. If easy to do, remove contact lenses if worn. Get medical attention.

Skin contact: In case of contact with broken tablets or capsules, immediately flush skin with plenty of water. Remove contaminated clothing and shoes. Get medical attention if irritation develops and persists.

Ingestion: If swallowed, call a poison center or physician if you feel unwell. Do NOT induce vomiting unless directed to do so by a physician. Never give anything by mouth to an unconscious person. Rinse mouth thoroughly with water.

Inhalation: If dust from broken tablets or capsules is inhaled, remove to fresh air. If breathing is difficult, trained personnel should give oxygen. Get medical attention.

4.2 Most important symptoms and effects, both acute and delayed

Mental confusion, drowsiness, dizziness, sedation and possible loss of consciousness, diarrhea.

4.3 Indication of any immediate medical attention and special treatment needed

General symptomatic and supportive measures should be used along with immediate gastric lavage where appropriate.

5. Fire Fighting Measures

5.1 Extinguishing media

Suitable extinguishing media: All means: water, carbon dioxide, foam or dry chemical.

Unsuitable extinguishing media: Strong water jet.

5.2 Specific hazards arising from the chemical

Hazardous combustion products: Carbon monoxide, carbon dioxide, oxides of nitrogen.

5.3 Special Protective Equipment and Precautions for Fire-fighters

In case of fire, use full firefighting turnout (bunker) gear and self-contained breathing apparatus (SCBA). Keep personnel upwind and away from fire. Move container from fire area if you can do it without risk. Do not scatter spilled material with high-pressure water streams. Dike fire-control water for later disposal.

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6. Accidental Release Measures

6.1 Personal precautions and Protective Equipment:

Eye protection, respiratory protective equipment, and suitable protective clothing should be worn if significant dust emissions are generated from broken or crushed tablets or capsules.

6.2 Emergency Procedures:

Follow local workplace procedures. Prevent the product from entering the environment. Avoid discharges to sewers, drains, waterways, or onto the ground.

6.3 Methods for containment:

Vacuum or scoop up, moisten any dust with water before collection with a shovel or broom.

6.4 Methods for clean-up:

Place material in suitable container for disposal. Wash the floor with plenty of water, absorb or retain the cleaning water for disposal.

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7. Handling and Storage

7.1 Precautions for Safe Handling

Use with adequate ventilation. Avoid breathing dust if tablets are crushed or spilled. Do not get dust in eyes or on skin. Wash thoroughly after handling.

7.2 Conditions for Safe Storage

Keep container tightly closed. Protect from light. Store in a cool, well-ventilated area. Store at room temperature, 68°F to 77°F (20°C to 25°C).

8. Exposure Controls/Personal Protection

8.1 Exposure Limits

Sanofi-aventis occupational exposure limit, zolpidem tartrate: 0.02 mg/m^3, 8-hour TWA.

8.2 Appropriate Engineering Controls

Provide adequate ventilation. No other specific controls are needed under normal handling conditions.

8.3 Individual Protection Measures

Eye/face protection: Safety glasses or safety goggles should be worn if there is a potential for dust exposure from broken or crushed tablets.

Skin protection: Suitable protective gloves should be worn if handling the unfinished product or broken or crushed tablets.

Respiratory protection: None normally required. Approved respiratory protection should be worn if there is a potential for exposure to dust from handling operations or from broken or crushed tablets.

General hygiene considerations: Suitable work clothes. Wash hands before breaks and at the end of the work shift.

9. Physical and Chemical Properties

Appearance: pink or white film-coated tablets.
Odor: Not available.
Odor threshold: Not available.
pH: Not available.
Melting point/ Freezing point: Not applicable.
Initial boiling point/boiling point range: Not applicable.
Flash point: Not available.
Evaporation rate: Not applicable.
Flammability: Not available.
Upper/lower flammability or explosive limits: Not available.
Vapor pressure: Not applicable.
Vapor density: Not applicable.
Relative density: Not available.
Solubility: Not available.

Partition coefficient: n-octanol/water (zolpidem tartrate): Log Kow = 2.42 (experimental)
Auto-ignition temperature: Not available.
Decomposition temperature: Not available.
Viscosity: Not available.

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10. Stability and Reactivity

10.1 Reactivity

Not a reactive material under normal handling conditions.

10.2 Chemical Stability

Stable under normal handling conditions.

10.3 Possibility of hazardous reactions

None known.

10.4 Conditions to Avoid

Keep away from heat, sparks and flames.

10.5 Incompatible materials

Strong oxidizing and reducing agents.

10.6 Hazardous decomposition products

Carbon monoxide, carbon dioxide, oxides of nitrogen.

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11. Toxicological Information

The following information is for the active ingredient zolpidem tartrate unless otherwise noted:

Information on likely routes of exposure: Exposure not expected under normal use. Dust from broken or crushed tablets could result in exposure to eyes, skin and respiratory tract.

Symptoms related to the physical, chemical and toxicological characteristics: Central nervous system sedative (depressant). Effects of excessive exposure include mental confusion, sedation and possible loss of consciousness.

Effects of short-term (acute) exposure: Drowsiness, dizziness, and diarrhea.

Effects of long-term (chronic) exposure: Dizziness and drugged feelings.

Acute toxicity (LD50):
Oral route, rat: 695 – 1,030 mg/kg

Skin corrosion/irritation: Non-irritant.

Serious eye damage/irritation: Non-irritant.

Sensitization: Negative for dermal sensitization in the guinea pig maximization study.

Specific target organ toxicity – single exposure (STOT-SE): In chronic toxicity studies (52 weeks) in rats and monkeys, dosages as low as 5 mg/kg produced central nervous system depression, but no other signs of toxicity.

Specific target organ toxicity – repeated exposure (STOT-RE): Exposure of rats to concentrations of 1 mg/m^3 for six weeks in an inhalation study did not result in any signs of toxicity.

Carcinogenicity: Zolpidem was administered to mice and rats for 2 years at oral doses of 4, 18, and 80 mg base/kg. In mice, these doses are approximately 2, 9, and 40 times the maximum recommended human dose (MRHD) of 12.5 mg/day (10 mg zolpidem base) on mg/m^2 basis. In rats, these doses are approximately 4, 18, and 80 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.

Not listed by NTP, not found to be a potential carcinogen by IARC or OSHA.

Titanium dioxide has been classified by IARC as 2B: Possibly carcinogenic to humans. Tumors were observed at high dose in animal studies by inhalation and intratracheal administration. Tumors were not observed by other routes.

Reproductive toxicity and teratogenicity: Administration of zolpidem to pregnant rats and rabbits resulted in adverse effects on offspring development at doses greater than the Ambien maximum recommended human dose (MRHD) of 10 mg/day (approximately 8 mg/day zolpidem base); however, teratogenicity was not observed.

When zolpidem was administered at oral doses of 4, 20, and 100 mg base/kg/day to pregnant rats during the period of organogenesis, dose-related decreases in fetal skull ossification occurred at all but the lowest dose, which is approximately 5 times the MRHD on a mg/m2 basis. In rabbits treated during organogenesis with zolpidem at oral doses of 1, 4, and 16 mg base/kg/day increased embryo-fetal death and incomplete fetal skeletal ossification occurred at the highest dose tested. The no-effect dose for embryo-fetal toxicity in rabbits is approximately 10 times the MRHD on a mg/m^2 basis. Administration of zolpidem to rats at oral doses of 4, 20, and 100 mg base/kg/day during the latter part of pregnancy and throughout lactation produced decreased

offspring growth and survival at all but the lowest dose, which is approximately 5 times the MRHD on a mg/m^2 basis.

In a rat reproduction study, the high dose (100 mg/base/kg) of zolpidem resulted in irregular estrus cycles and prolonged pre-coital intervals, but there was no effect on male or female fertility after daily oral doses of 4 to 100 mg base/mg or 5 to 130 times the recommended human dose in mg/m^2. No effects on any other fertility parameters were noted.

Lactation: Zolpidem is excreted in human milk.

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

Aspiration hazard: Not applicable.

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12. Ecological Information

The following information is for the active ingredient zolpidem tartrate unless otherwise noted:

12.1. Ecotoxicity
Fish toxicity (LC50): 22 mg/l
Species: Oncorhynchus mykiss
Exposure duration: 96 h

Toxicity on invertebrates (EC50): 120 mg/l
Species: Daphnia magna
Exposure duration: 48 h

Algae toxicity (IC50): 2.2 mg/l
Species: Selenastrum capricornutum
Exposure duration: 96 h

Bacteria toxicity (EC50): 2,900 mg/l
Species: Activated sludge.

12.2. Persistence and degradability

Biological degradability: 26 - 33 %
Testing period: 28 d
The product is not readily biodegradable according to OECD criteria.

12.3. Bioaccumulative potential

Unlikely to be bioaccumulable in living organisms (Log Kow < 3).

12.4 Mobility in soil

Not determined.

12.5 Other adverse effects

Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

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13. Disposal Considerations

13.1 Disposal of product waste

Disposal should be in accordance with applicable regional, national and local laws and regulations. Local regulations may be more stringent than regional or national requirements.

13.2 Disposal of packaging waste

Dispose of in a safe manner in accordance with federal, state and local environmental regulations. Empty packages, containers or liners may contain product residue.

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14. Transport Information

14.1 Basic shipping information, finished product

U.S. DOT	Not a regulated material.
ICAO/IATA	Not a regulated material.
IMDG	Not a regulated material.

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15. Regulatory Information

Information for zolpidem tartrate:

DEA Controlled Substances
Zolpidem tartrate, the active ingredient, is regulated by the US Drug Enforcement Agency (DEA) via the Controlled Substance Act as a Schedule IV controlled substance.

US Regulations
CERCLA Hazardous Substance List (40 CFR 302.4): Not listed.
Clean Water Act Section 311 Hazardous Substances (40 CFR 117.3): Not listed.
Clean Air Act (CAA) Section 112(r) Accidental Release Prevention (40 CFR 68.130): Not listed.

SARA Title III:
Section 302 Extremely Hazardous Substance (40 CFR 355, Appendix A): Not listed.
Section 313 Toxic Release Inventory (40 CFR 372): Not listed.

State Regulations
California Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65): Titanium dioxide (airborne, unbound particles of respirable size).
Massachusetts Right-To-Know List: Titanium dioxide.
New Jersey Right-To-Know List: Titanium dioxide.
Pennsylvania Right-To-Know List: Titanium dioxide.

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16. Other Information

Other Information: The information contained herein is based upon data considered true and accurate. Winthrop U.S. makes no warranties, express or implied, as to the adequacy of the information contained herein. This information is offered solely for the user's consideration, investigation and verification. Report to the manufacturer any allegations of health effects resulting from handling or accidental contact with this material.

Abbreviations and Acronyms
CAS: Chemical Abstracts Service
DEA: Drug Enforcement Agency
DOT: U.S. Department of Transportation
EST: Eastern standard time (U.S.)
IATA: International Air Transport Association
IMDG: International Maritime Dangerous Goods Code
LC50: Lethal concentration, 50%
LD50: Lethal dose, 50%
OEL: Occupational Exposure Limit
PPE: Personal Protection Equipment
SDS: Safety Data Sheet
STEL: Short-term exposure limit
TWA: Time-weighted average
U.S.: United States

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Third version.