1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Sanofi-Synthelabo Inc.
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EMERGENCY TELEPHONE NUMBER (CHEMTREC – Chemical Referral Service): (800) 424-9300
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PRODUCT NAME: AMBIEN®

CHEMICAL NAME: N,N,6-trimethyl-2-p-tolyl-imidazo[1,2-a]pyridine-3-acetamide L-(+)-tartrate (2:1)

SYNONYMS: Stilnox®, Zolpidem hemitartrate, SL80.0750-23N, SA02224

CHEMICAL FAMILY: Non-benzodiazepine hypnotic of the imidazopyridine class

2. COMPOSITION/INFORMATION ON INGREDIENTS

ACTIVE INGREDIENT: zolpidem tartrate (% by weight) 4.1% for 5 mg. tablet, 7.9% for 10 mg. tablet
CAS NUMBER: 99294-93-6

PRINCIPAL INACTIVE INGREDIENTS: (% by weight) 95.9% for 5 mg. tablet, 92.1% for 10 mg. tablet

INGREDIENT	CAS NUMBER
Lactose NF	63-42-3
Microcrystalline Cellulose	9004-34-6
Hydroxypropyl Methylcellulose	9004-65-3
Sodium Starch Glycolate	9063-38-1

3. HAZARDS IDENTIFICATION

WARNING: This is a pharmaceutical material available only with a prescription - use only as directed.

The product is supplied as a capsule shaped film coated tablet in 5 mg. and 10 mg. strengths. The 5 mg. tablet is pink colored with AMB 5 debossed on one side and 5401 on the other. The 10 mg. tablet is white colored with AMB 10 debossed on one side and 5421 on the other.

TARGET ORGANS Central nervous system sedative.

POTENTIAL HEALTH EFFECTS
Effects of excessive exposure include mental confusion, sedation and possible loss of consciousness.

Ambien® is a schedule IV controlled substance.

4. FIRST AID MEASURES

EYES
In case of contact with dust from crushed or broken tablets, flush eyes with water for at least 15 minutes. Seek medical attention if irritation develops.

SKIN
If dust from broken or crushed tablets comes in contact with skin and clothing, remove contaminated clothing and wash thoroughly with running water for at least 15 minutes. Use soap if available. Seek medical attention if irritation develops.

INGESTION
In case of acute overdose by ingestion, seek immediate medical attention or contact the Poison Control Center for further instructions.

INHALATION
Dust containing drug substance could be inhaled if tablets are crushed or broken. If dust is inhaled, remove to fresh air. Seek medical attention.

NOTE TO PHYSICIAN Persons allergic or hypersensitive to zolpidem tartrate and individuals with hepatitic insufficiency, mental depression, psychosis or who take other psychoactive drugs are at increased risk from overexposure to zolpidem tartrate.

5. FIRE FIGHTING MEASURES

If drug product handling produces significant dust, a risk assessment of the procedure should be performed.

FIRE AND EXPLOSION HAZARDS
May emit nitrogen oxides under fire conditions.

EXTINGUISHING MEDIA
Carbon dioxide, dry chemical powder, water spray or foam.

FIRE FIGHTING INSTRUCTIONS
Use pressure demand self-contained breathing apparatus (SCBA), and protective clothing to prevent contact with skin and eyes. Use water spray to keep fire-exposed containers cool.

6. ACCIDENTAL RELEASE MEASURES

If tablets are crushed or broken, dust containing drug substance may be released. Minimize dust generation and accumulation. Do not breathe dust.

Necessary personal protective equipment should be worn when cleaning up a spill [See Section 8].

Wet dusts and soak up contents of broken tablets with an absorbent material. Use HEPA vacuum or carefully collect materials and place in a properly labeled waste container for disposal. Wash area of spill with water to remove residual from surfaces. Wash thoroughly after handling.

7. HANDLING AND STORAGE

HANDLING AND STORAGE PRECAUTIONS
CAUTION: This product is a Controlled Substance and should be handled in accordance with US Drug Enforcement Agency regulations. Keep this and all drugs out of the reach of children.

WORK/HYGIENIC PRACTICES
If tablets are crushed or broken, dust containing drug substance may be released. Avoid breathing dust and avoid contact with skin, eyes and clothing. Use local exhaust ventilation, supplementary ventilation or respiratory protection for operations which generate dust. Wash thoroughly after handling.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

If product handling produces dusts, a risk assessment of the procedure should be performed.

ENGINEERING CONTROLS
If tablets are crushed or broken, dust containing drug substance may be released. If dust is generated, supplementary ventilation may be required.

EYE/FACE PROTECTION
Avoid eye contact with dust. Wear safety glasses with side shields or goggles where risk of eye exposure exists.

SKIN PROTECTION
Avoid skin contact with dust. Impervious gloves should be worn.

RESPIRATORY PROTECTION
None normally required. However, if dust is generated, respirators may need to be worn. Respiratory protection must be in compliance with the OSHA Respiratory Protection Program, 29 CFR 1910.134 and ANSI Z88.2 whenever workplace conditions warrant respirator usage.

9. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE
The product is supplied as a capsule-shaped, film coated tablet. The 5 mg. tablet is pink colored and the 10 mg. tablet is white.

BASIC PHYSICAL PROPERTIES
The following physical properties apply to the active ingredient zolpidem tartrate.

CHEMICAL FORMULA: $[C_{19}H_{21}N_3O]_2\ C_4H_6O_6$
MOLECULAR WEIGHT:764.88
pH: N/A
MELTING POINT: 193-197 C
BOILING POINT: N/A
SPECIFIC GRAVITY: N/A
SOLUBILITY: Water: 23 mg/ml at 20 °C
Alcohol and propylene glycol: sparingly soluble

10. STABILITY AND REACTIVITY

The following information applies to the active ingredient zolpidem tartrate.

STABILITY
Stable under normal conditions.

INCOMPATIBLE MATERIALS
N/A

HAZARDOUS DECOMPOSITION PRODUCTS
Oxides of Nitrogen

HAZARDOUS POLYMERIZATION
Will not occur.

11. TOXICOLOGICAL INFORMATION

HUMAN CLINICAL DATA

The following information applies to the active ingredient zolpidem tartrate.

POTENTIAL HEALTH EFFECTS

INGESTION
Zolpidem tartrate is a hypnotic agent and accidental ingestion of small quatities will lead to confusion, sedation and eventual loss of consciousness.

INHALATION
The effects of inhaling dust from crushed or broken tablets has not been determined. Effects may be presumed to be similar to those which may occur following ingestion.

SKIN AND EYE CONTACT
Not irritant to skin and eyes.
Absorption from skin contact is not expected to cause pharmacological effects.

ANIMAL STUDIES

Unless otherwise stated, the following data describes the active ingredient, zolpidem tartrate.

Test	Species	Dose
Oral LD50	Male Rat	695 mg/kg
	Female Rat	1030 mg/kg
LC50	Rat	> 11 mg/m^3 (for 6 hrs)

SKIN AND EYE CONTACT
Negative for dermal sensitization in the guinea pig maximization study.

EFFECTS OF CHRONIC EXPOSURE
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. 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.

REPRODUCTIVE TOXICITY
In a rat reproduction study, the high dose (100 mg/base/kg) of zolpidem resulted in irregular estrus cycles and prolonged precoital 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/m2. No effects on any other fertility parameters were noted.

DEVELOPMENTAL TOXICITY
Animal studies have shown no embryotoxic or teratogenic effects.

Testing in rats and rabbits indicated dose related maternal sedation and lethargy, decreased weight gain and ataxia. The no-effect dose for fetal toxicity resulting from maternal sedation was 4 mg base/kg or 7 times the maximum human dose on a mg/m2 basis.

MUTAGENICITY
Zolpidem tartrate did not have mutagenic activity in several tests including the Ames test, genotoxicity in mouse lymphoma cells in vitro, chromosomal aberration in cultured human lymphocytes, unscheduled DNA synthesis in rat hepatocytes in vitro, and the micronucleus test in mice.

CARCINOGENICITY
Zolpidem tartrate was administered to rats and mice for 2 years at dietary dosages of 4, 18, and 80 mg/kg/day. In mice, these doses are 26 to 520 times or 2 to 35 times the maximum 10 mg human dose on a mg/kg or mg/m2 basis, respectively. In rats these doses are 43 to 876 times or 6 to 115 times the maximum 10 mg human dose on a mg/kg or mg/m2 basis, respectively. No evidence of carcinogenic potential was observed in mice. Renal lipocarcinomas were seen in 4/100 rats (3 males, 1 female) receiving 80 mg/kg/day and a renal lipoma was observed in one male rat at the 18 mg/kg/day dose. Incidence rates of lipoma and liposarcoma for zolpidem were comparable to those seen in historical controls and the tumor findings are thought be a spontaneous occurrence.

12. ECOLOGICAL INFORMATION

The following information applies to the active ingredient zolpidem tartrate.

Zolpidem tartrate is practically non-toxic to fish, slightly toxic to daphnia, moderately toxic to algae and insignificantly hazardous to active sludge.

Species	LC50 (mg/L)	NOEC (mg/L)
Rainbow Trout	48 hrs. > 120	16
Daphnia	48 hrs. 22	6.2
Freshwater Algae	96 hrs. 2.2	0.32
Activated Sludge	96 hrs. 2900	

Zolpidem tartrate readily biodegrades and photodegrades in the presence of light. Hydrolysis occurs at a moderately slow rate.

Hydrolysis: Half-life of 6.1 months (80 C).
Photolysis: 35% degradation after one month exposure.
Biodegradation: 26-33% degradation after 28 days.

13. DISPOSAL CONSIDERATIONS

Discharge, treatment and disposal are subject to federal, state and/or local laws. This product is a schedule IV controlled substance. Dispose of in accordance with U.S. Drug Enforcement Agency regulations.

It is recommended that bulk wastes, contaminated clean up materials and disposable personal protective equipment should be double contained (e.g. double sealed bags), marked and disposed by incineration. Outer waste containers should be labeled or marked to indicate contents and hazards for safe handling and disposal. Contents should be burned in an incinerator with environmental control devices operating under applicable regulatory requirements.

14. TRANSPORT INFORMATION

This product is a controlled substance. Per U.S. Drug Enforcement Agency regulations, specific recordkeeping requirements for shipping this product apply.

Not regulated by USDOT as a hazardous material.
Not regulated by IATA as a dangerous good.

15. REGULATORY INFORMATION

U.S. FEDERAL REGULATORY INFORMATION
This product does not contain any ingredients which are regulated on the U.S. EPA List of Toxic Chemicals (40 CFR 372), and is therefore not subject to release reporting under section 313 of EPCRA, (SARA Title III).

TARGET ORGANS Central nervous system sedative.

REGULATED SUBSTANCES
Ambien® is regulated by the US Drug Enforcement Agency (DEA) via the Controlled Substance Act as a schedule IV controlled substance.

16. OTHER INFORMATION

N/A = Not Applicable N/D = Not Determined ~ = Approximately Equal To

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