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## 1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

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Sanofi-Synthelabo Inc.  
90 Park Avenue  
New York, NY 10016

Technical Information Telephone Number (Sanofi-Synthelabo Inc.): (800) 446-6267

EMERGENCY TELEPHONE NUMBER (CHEMTREC – Chemical Referral Service): (800) 424-9300  
International Transportation Emergency Number (CHEMTREC – Chemical Referral Service): (703) 527-3887

PRODUCT NAME: AMBIEN<sup>®</sup>

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

SYNONYMS: Stilnox<sup>®</sup>, Zolpidem hemitartrate, SL80.0750-23N, SA02224

CHEMICAL FAMILY: Non-benzodiazepine hypnotic of the imidazopyridine class

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## 2. COMPOSITION/INFORMATION ON INGREDIENTS

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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

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

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## 3. HAZARDS IDENTIFICATION

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**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<sup>®</sup> is a schedule IV controlled substance.

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#### 4. FIRST AID MEASURES

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##### 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 hepatic insufficiency, mental depression, psychosis or who take other psychoactive drugs are at increased risk from overexposure to zolpidem tartrate.

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#### 5. FIRE FIGHTING MEASURES

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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.

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#### 6. ACCIDENTAL RELEASE MEASURES

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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.

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## 7. HANDLING AND STORAGE

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### 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.

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## 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

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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.

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## 9. PHYSICAL AND CHEMICAL PROPERTIES

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### 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

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## 10. STABILITY AND REACTIVITY

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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.

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## 11. TOXICOLOGICAL INFORMATION

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### 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 quantities 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.

<u>Test</u>	<u>Species</u>	<u>Dose</u>
Oral LD50	Male Rat	695 mg/kg
	Female Rat	1030 mg/kg
LC50	Rat	> 11 mg/m <sup>3</sup> (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<sup>3</sup> 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/m<sup>2</sup>. 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/m<sup>2</sup> 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/m<sup>2</sup> 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/m<sup>2</sup> 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 to be a spontaneous occurrence.

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## 12. ECOLOGICAL INFORMATION

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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.

<u>Species</u>	<u>LC50 (mg/L)</u>	<u>NOEC (mg/L)</u>
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.

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### 13. DISPOSAL CONSIDERATIONS

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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.

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### 14. TRANSPORT INFORMATION

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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.

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### 15. REGULATORY INFORMATION

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#### 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<sup>®</sup> is regulated by the US Drug Enforcement Agency (DEA) via the Controlled Substance Act as a schedule IV controlled substance.

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### 16. OTHER INFORMATION

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

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