Olanzapine for Injection

Effective Date: 10-Nov-2006

Eli Lilly and Company
Material Safety Data Sheet

Section 1 - Chemical Product and Company

Manufacturer:
Eli Lilly and Company
Lilly Corporate Center
Indianapolis, IN 46285

Manufacturer's Emergency Phone:
1-317-276-2000
CHEMTREC:
1-800-424-9300 (North America)
1-703-527-3887 (International)

Common Name: Olanzapine for Injection

Chemical Name: 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-
Chemical Name 2: 2-Methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine
Synonym(s): 170053 Formulation; Olanzapine Formulation; Olanzapine IM; Olanzapine Intramuscular; Olanzapine Vials; Vial Olanzapine for Injection
Trademarks(s): Ciprex; Elzyprex; Lanexa; Lansek; Lanzek; Lilly Zyprex; Olansek; Ziprexa; Zypep; Zyprex; Zyprex and Two; Zyprexa; Zyprexa and Design; Zyprexa and Katakana; Zyprexin
Lilly Item Code(s): CA1494; MS8336; MS8338; MS9613; MS9620; VL7592; VL7597

See attached glossary for abbreviations.

Section 2 - Composition / Information on Ingredients

Ingredient	CAS	Concentration %
Olanzapine	132539-06-1	10 - 20
Excipients	NA	80 - 90

Contains no hazardous components (one percent or greater) or carcinogens (one-tenth percent or greater) not listed above.

Exposure Guidelines:
Olanzapine - LEG 38 micrograms/m3 TWA for 12 hours, LEG 50 micrograms/m3 TWA for 8 hours, 114 micrograms/m3 TWA for 15 minutes STEG.

Section 3 - Hazards Identification

Appearance: Off-white to yellow freeze-dried powder
Physical State: Solid
Odor: Odorless

Emergency Overview

Special
A = Allergen

Emergency Overview Effective Date: 04-May-2000

Lilly Laboratory Labeling Codes:
Health 2 **Fire** 1 **Reactivity** 0 **Special** A

Primary Physical and Health Hazards: Irritant (eyes, skin). Allergen. Nervous System and Hormonal Effects.

Caution Statement: Olanzapine for Injection may be irritating to the eyes and skin and causes allergic reactions. Effects of exposure may include drowsiness and increased serum prolactin.

Routes of Entry: Inhalation and skin contact.

Effects of Overexposure:
Olanzapine - Confirmed cases of allergic contact dermatitis have been reported. Symptoms have included rash with redness, swelling, and scaling of the affected skin areas. Positive reactions have been verified by patch testing with olanzapine (0.1%). Based on the clinical dose, olanzapine is highly potent. May be irritating to the eyes based on animal studies.
Adverse effects associated with therapeutic use of olanzapine include sleepiness, weight gain, mild temporary increase in serum prolactin, dizziness, weakness, restlessness, increased appetite, swelling of hands and feet, decreased blood pressure when standing, dry mouth and constipation. Mild temporary increases in glucose and liver enzyme levels and blood effects have been seen occasionally. Symptoms reported in olanzapine overdose include changes in heart rate and rhythm, slurred speech, reduced level of consciousness ranging from sedation to coma, convulsion, and muscle rigidity.

Medical Conditions Aggravated by Exposure:
Olanzapine - Sensitivity to olanzapine.

Carcinogenicity:
Olanzapine - Not listed by IARC, NTP, ACGIH, or OSHA. Olanzapine produced mammary tumors in female rats and female mice. This is consistent with effects of compounds that elevate prolactin levels in rodents. There is no clear understanding of the role of elevated prolactin in human mammary carcinogenesis.

Section 4 - First Aid Measures

Eyes: Hold eyelids open and flush with a steady, gentle stream of water for 15 minutes. See an ophthalmologist (eye doctor) or other physician immediately.

Skin: Remove contaminated clothing and clean before reuse. Wash all exposed areas of skin with

plenty of soap and water. Get medical attention if irritation develops.

Inhalation: Move individual to fresh air. Get medical attention if breathing difficulty occurs. If not breathing, provide artificial respiration assistance (mouth-to-mouth) and call a physician immediately.

Ingestion: Do not induce vomiting. Call a physician or poison control center. If available, administer activated charcoal (6-8 heaping teaspoons) with two to three glasses of water. Do not give anything by mouth to an unconscious person. Immediately transport to a medical care facility and see a physician.

Notes to Physician:
Olanzapine - There is no specific antidote for olanzapine. Induction of emesis is not recommended. Standard procedures for management of overdose may be indicated (i.e. gastric lavage, administration of activated charcoal). The concomitant administration of activated charcoal was shown to reduce the oral bioavailability of olanzapine by 50 to 60%. Symptomatic treatment and monitoring of vital organ function should be instituted according to clinical presentation, including treatment of hypotension and circulatory collapse and support of respiratory function. Do not use epinephrine, dopamine, or other sympathomimetic agents with beta-agonist activity since beta stimulation may worsen hypotension.

Section 5 - Fire Fighting Measures

Flash Point: No applicable information found
UEL: No applicable information found
LEL: No applicable information found

Extinguishing Media: Use water, carbon dioxide, dry chemical, foam, or Halon.

Unusual Fire and Explosion Hazards: As a finely divided material, may form dust mixtures in air which could explode if subjected to an ignition source.

Hazardous Combustion Products: May emit toxic fumes when exposed to heat or fire.

Section 6 - Accidental Release Measures

Spills: Wear protective equipment, including eye protection, to avoid exposure (see Section 8 for specific handling precautions). Vacuum material with appropriate dust collection filter in place. Be aware of potential for dust explosion when using electrical equipment. If vacuum is not available, lightly mist material and remove by sweeping or wet wiping.

Section 7 - Handling and Storage

Storage Conditions: Controlled Room Temperature: 15 to 30 C (59 to 86 F). Protect from light. Do not freeze.

Section 8 - Exposure Controls / Personal Protection

See Section 2 for Exposure Guideline information.

Under normal use and handling conditions, no protective equipment is required. The following is recommended for a production setting:

Respiratory Protection: Use an approved respirator.

Eye Protection: Chemical goggles and/or face shield.

Ventilation: Laboratory fume hood or local exhaust ventilation.

Other Protective Equipment: Chemical-resistant gloves and body covering to minimize skin contact. If handled in a ventilated enclosure, as in a laboratory setting, respirator and goggles or face shield may not be required. Safety glasses are always required.

Additional Exposure Precautions: In production settings, airline-supplied, hood-type respirators are preferred. Shower and change clothing if skin contact occurs.

Section 9 - Physical and Chemical Properties

Appearance: Off-white to yellow freeze-dried powder
Odor: Odorless
Boiling Point: No applicable information found
Melting Point: No applicable information found
Specific Gravity: No applicable information found
pH: No applicable information found
Evaporation Rate: No applicable information found
Water Solubility: No applicable information found
Vapor Density: No applicable information found
Vapor Pressure: No applicable information found

Section 10 - Stability and Reactivity

Stability: Stable at normal temperatures and pressures.

Incompatibility: May react with strong oxidizing agents (e.g., peroxides, permanganates, nitric acid, etc.).

Hazardous Decomposition: May emit toxic fumes when heated to decomposition.

Hazardous Polymerization: Will not occur.

Section 11 - Toxicological Information

Acute Exposure

No data available for mixture or formulation. Data for ingredient(s) or related material(s) are

presented.

Oral:
Olanzapine - Rat, median lethal dose 177 mg/kg, reduced activity, lethargy, coma, tremors, convulsions, drooping eyelids, salivation.
Monkey, 100 mg/kg, no deaths, sedation, prostration, reduced activity, anorexia.

Skin:
Olanzapine - Rabbit, 200 mg/kg, no deaths or toxicity.

Inhalation:
Olanzapine - Rat, 880 mg/m3 for 4 hours, no deaths, reduced activity, lethargy, labored breathing, prostration.

Skin Contact:
Olanzapine - Rabbit, nonirritant

Eye Contact:
Olanzapine - Rabbit, irritant

Chronic Exposure

No data available for mixture or formulation. Data for ingredient(s) or related material(s) are presented.

Target Organ Effects:
Olanzapine - Nervous system effects (sedation, reduced activity, salivation, pupil constriction), heart effects (increased heart rate), blood effects (decreased circulating blood cell counts).

Reproduction:
Olanzapine - Decreased mating activity due to sedation. Decreased fertility, abnormal reproductive cycles, and reproductive tissue changes can be linked to elevations of prolactin levels. The clinical effects of such elevations are unknown for humans. Embryo and fetal toxicity occurred only at maternally toxic doses.

Sensitization:
Olanzapine - Guinea pig, subcutaneous, intravenous, dermal - negative systemic response.

Mutagenicity:
Olanzapine - Not mutagenic in bacterial or mammalian cells.

Section 12 - Ecological Information

No environmental data for the mixture or formulation. The environmental information for ingredient(s) or related material(s) are presented.

Ecotoxicity Data:
Olanzapine
Rainbow trout 96-hour median lethal concentration: 1.74 mg/L

Daphnia magna 48-hour median effective concentration: 8.0 mg/L
Green algae (S. capricornutum) median effective concentration: >14.1 mg/L (average specific growth rate)
Microorganisms:
fungus (Chaetomium globosum): MIC = 400 mg/L
mold (Aspergillus flavus): MIC = 1000 mg/L
soil bacteria (Comamonas acidovorans): MIC > 1000 mg/L
N-fixing bacteria (Azotobacter chroococcum): MIC > 1000 mg/L
blue-green algae (Nostoc sp.): MIC = 255 mg/L

Environmental Fate:
Olanzapine
Dissociation constants (pKa): 7.37, 4.69
Log Kow: 0.3, 1.7, 2.1 (pH 5, 7, 9)
Log Koc: 0.04, 1.48, 1.94 (pH 5, 7, 9)
Bioconcentration Factor: 11 (pH 7)
Solubility (g/L): 87.4, 0.1926, 0.0165 (pH 5, 7, 9)
Light absorption (nm): none between 290 and 800
Hydrolysis half-life (days): 65.30, 75.97, 77.93 (pH 5, 7, 9)
Hydrolysis rate (1/day): 0.0106, 0.00912, 0.00889 (pH 5, 7, 9)
Aerobic biodegradation half-life (days): 7.4

Environmental Summary:
Olanzapine - Moderately toxic to fish and invertebrates. No more than slightly toxic to green algae. Practically non-toxic to microorganisms. No volatility expected. Low potential to bioconcentrate in aquatic organisms. Persistence in the environment not expected due to biodegradation and hydrolysis.

Lilly Aquatic Exposure Guideline (LAEG):
Olanzapine
LAEG for Drinking Water: 2.5 micrograms/L
LAEG for Chronic Exposure of Aquatic Organisms: 7.4 micrograms/L
LAEG for Acute Exposure of Aquatic Organisms: 67 micrograms/L

Section 13 - Disposal Considerations

Waste Disposal: Dispose of any cleanup materials and waste residue according to all applicable laws and regulations.

Section 14 - Transport Information

Regulatory Organizations:

DOT: Not Regulated

ICAO/IATA: Not Regulated

IMO: Not Regulated

Section 15 - Regulatory Information

Below is selected regulatory information chosen primarily for possible Eli Lilly and Company usage. This section is not a complete analysis or reference to all applicable regulatory information. Please consider all applicable laws and regulations for your country/state.

U.S. Regulations

Olanzapine
TSCA - No
CERCLA - Not on this list
SARA 302 - Not on this list
SARA 313 - Not on this list
OSHA Substance Specific - No

EU Regulations

EC Classification
Contains olanzapine (C = 10 to 20%).
Xn (Harmful)
Xi (Irritant)

Risk Phrases
R 22 - Harmful if swallowed.
R 36/38 - Irritating to eyes and skin.
R 43 - May cause sensitization by skin contact.
R 52 - Harmful to aquatic organisms.

Safety Phrases
S 36/37/39 - Wear suitable protective clothing, gloves and eye/face protection.
S 61 - Avoid release to the environment. Refer to special instructions/Safety data sheets.

Section 16 - Other Information

MSDS Sections Revised: Sections 2 and 4.

As of the date of issuance, we are providing available information relevant to the handling of this material in the workplace. All information contained herein is offered with the good faith belief that it is accurate. THIS MATERIAL SAFETY DATA SHEET SHALL NOT BE DEEMED TO CREATE ANY WARRANTY OF ANY KIND (INCLUDING WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE). In the event of an adverse incident associated with this material, this safety data sheet is not intended to be a substitute for consultation with appropriately trained personnel. Nor is this safety data sheet intended to be a substitute for product literature which may accompany the finished product.

For additional information contact:
Eli Lilly and Company
Hazard Communication

317-651-9533

GLOSSARY:

ACGIH = American Conference of Governmental Industrial Hygienists
AIHA = American Industrial Hygiene Association
BEI = Biological Exposure Index
CAS Number = Chemical Abstract Service Registry Number
CERCLA = Comprehensive Environmental Response Compensation and Liability Act (of 1980)
CHAN = Chemical Hazard Alert Notice
CHEMTREC = Chemical Transportation Emergency Center
DOT = Department of Transportation
EC = European Community
EINECS = European Inventory of Existing Chemical Substances
ELINCS = European List of New Chemical Substances
EPA = Environmental Protection Agency
HEPA = High Efficiency Particulate Air (Filter)
IARC = International Agency for Research on Cancer
ICAO/IATA = International Civil Aviation Organization/International Air Transport Association
IEG = Lilly Interim Exposure Guideline
IMO = International Maritime Organization
Kow = Octanol/Water Partition Coefficient
LEG = Lilly Exposure Guideline
LEL = Lower Explosive Limit
MSDS = Material Safety Data Sheet
MSHA = Mine Safety and Health Administration
NA = Not Applicable, except in Section 14 where NA = North America
NADA = New Animal Drug Application
NAIF = No Applicable Information Found
NCI = National Cancer Institute
NIOSH = National Institute for Occupational Safety and Health
NOS = Not Otherwise Specified
NTP = National Toxicology Program
OSHA = Occupational Safety and Health Administration
PEL = Permissible Exposure Limit (OSHA)
RCRA = Resource Conservation and Recovery Act
RQ = Reportable Quantity
RTECS = Registry of Toxic Effects of Chemical Substances
SARA = Superfund Amendments and Reauthorization Act
STEG = Lilly Short Term Exposure Guideline
STEL = Short Term Exposure Limit
TLV = Threshold Limit Value (ACGIH)
TPQ = Threshold Planning Quantity
TSCA = Toxic Substances Control Act
TWA = Time Weighted Average/8 Hours Unless Otherwise Noted
UEL = Upper Explosive Limit
UN = United Nations
WEEL = Workplace Environmental Exposure Level (AIHA)