



# Olanzapine Capsules, Granules, and Tablets

Eli Lilly and Company  
Material Safety Data Sheet

Effective Date: 11-Jan-2008

## 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 Capsules, Granules, and Tablets

**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):** Granules olanzapine, 1%; Olanzapan, 20 mg; Olanzapine granulation for 2.5 mg tablets; Olanzapine, 15 mg; Olanzapine orally disintegrating tablets; Olanzapine oral lyophilizate; Olanzapine granulation for 5 and 10 mg tablets; Olanzapine fine granules; Olanzapine; Olanzapine capsule mix; Olanzapine tablet mix; 170053 formulation; Olanzapine capsules; Olanzapine tablets

**Trademarks(s):** Ciprex; Elzyprex; Lansek; Lilly zyprex; Olansek; Midax; Zyprex; Zypep; Lanzek; Lanexa; Zyprexin; Zyprexa and katakana; Zyprexa and design; Zyprex and two; Zyprexa; Ziprexa

**Lilly Item Code(s):** MS5152; MS5153; MS5154; MS5155; MS5156; MS8293; MS9621; ND0997; ND0998; ND1009; ND1011; ND1013; ND1022; ND1023; ND1029; ND1034; ND1038; ND1096; ND1097; ND1098; ND1099; ND1100; QA435B; QA479W; QA480U; TA4111; TA4112; TA4115; TA4116; TA4117; TA4415; TA4420; TA4425; TA4453; TA4454; TA4455; TA4456; TA4756; TA4757; TA4758; VF0336; VF0337; VF0356

See attached glossary for abbreviations.

## Section 2 - Composition / Information on Ingredients

<u>Ingredient</u>	<u>CAS</u>	<u>Concentration %</u>
Olanzapine	132539-06-1	0.3 - 34
Excipients	NA	66 - 99

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

**Exposure Guidelines:**

Olanzapine - LEG 38 micrograms/m<sup>3</sup> TWA for 12 hours, LEG 50 micrograms/m<sup>3</sup> TWA for 8 hours, 114 micrograms/m<sup>3</sup> TWA for 15 minutes STEG.

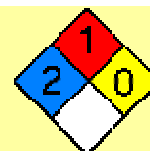
## Section 3 - Hazards Identification

**Appearance:** Off-white to yellow powder finished as capsules, granules, coated tablets, or uncoated tablets

**Physical State:** Solid

**Odor:** Odorless

### Emergency Overview



Special  
A = Allergen

**Emergency Overview Effective Date:** 30-Nov-2000

**Lilly Laboratory Labeling Codes:**

**Health** 2

**Fire** 1

**Reactivity** 0

**Special** A

**Primary Physical and Health Hazards:** Not hazardous if intact. Irritant (eyes, skin). Allergen. Nervous System and Hormonal Effects.

**Caution Statement:** Intact Olanzapine Capsules, Granules, and Tablets are not considered to be a health hazard. The contents of Olanzapine Capsules, Granules, and Tablets 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:** Capsules, granules, and tablets are intended for human consumption under guidance of a physician. Intact olanzapine capsules and coated tablets are not considered hazardous under normal handling procedures. 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.

<h2>Section 4 - First Aid Measures</h2>
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**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:** Store at 20 - 25 C (68 - 77 F).

## Section 8 - Exposure Controls / Personal Protection

See Section 2 for Exposure Guideline information.

Filled capsules and coated compressed tablets are not considered hazardous under normal handling procedures and protective equipment is not required. The following are recommended for manufacturing or other situations where exposure to the capsule contents or tablet powder may occur.

**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 powder finished as capsules, granules, coated tablets, or uncoated tablets

**Odor:** Odorless

**Boiling Point:** Not applicable.

**Melting Point:** No applicable information found.

**Specific Gravity:** No applicable information found.

**pH:** Neutral

**Evaporation Rate:** No applicable information found.

**Water Solubility:** Slightly soluble

**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/m<sup>3</sup> 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

Fathead minnow (*P. promelas*) 33-day no observed effect concentration: 11 micrograms/L

Fathead minnow (*P. promelas*) 33-day lowest observed effect concentration: 27 micrograms/L  
Daphnia magna 48-hour median effective concentration: 8.0 mg/L  
Daphnia magna 21-day median effective concentration (survival): > 1004 micrograms/L  
Daphnia magna 21-day median effective concentration (reproduction): 599 micrograms/L  
Daphnia magna 21-day no observed effect concentration: 27 micrograms/L  
Daphnia magna 21-day lowest observed effect concentration: 66 micrograms/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  
Activated Sludge Respiration Inhibition median effective concentration: >100 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

Degradation in water-sediment system (100 days under aerobic conditions):

    DT50 from overlying water: 2.6 days (no olanzapine observed in water or sediment by 14 days)

    Numerous transformation products observed

    4.3% of the radiolabel evolved as CO<sub>2</sub>

### **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 = 0.3 - 34%).

Xi (Irritant)

#### Risk Phrases

R 36/38 - Irritating to eyes and skin.

R 43 - May cause sensitization by skin contact.

R 51 - Toxic to aquatic organisms.

**Safety Phrases**

S 36/37/39 - Wear suitable protective clothing, gloves and eye/face protection.

S 45 - In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).

S 61 - Avoid release to the environment. Refer to special instructions/Safety data sheets.

<b>Section 16 - Other Information</b>
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**MSDS Sections Revised:** Section 12.

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

For additional copies contact:

Eli Lilly and Company  
1-800-LILLY-Rx (1-800-545-5979)

**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)