



Raloxifene Hydrochloride Tablets

Eli Lilly and Company
Material Safety Data Sheet

Effective Date: 15-Dec-2004

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: Raloxifene Hydrochloride Tablets

Chemical Name: Methanone, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]-, hydrochloride

Synonym(s): Evista Tab 60mg; 139481 Hydrochloride Formulation; 156758 Formulation; Raloxifene Hydrochloride Formulation; Raloxifene Tablet Mix; Keoxifene

Trademarks(s): Evista

Lilly Item Code(s): B02059; ND1002; SA1006; TA4012; TA4013; TA4164; TA4165; TA4166; TA4466; VF0297; VF0298; VF0316; VF0317; VF0338; VF0374

See attached glossary for abbreviations.

Section 2 - Composition / Information on Ingredients

Ingredient	CAS	Concentration %
Raloxifene Hydrochloride	82640-04-8	10 - 65
Excipients	NA	35 - 90

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

Exposure Guidelines:

Raloxifene hydrochloride - LEG 5 micrograms/m³ TWA for 12 hours. LEG 8 micrograms/m³ TWA for 8 hours. Excursion Limit is 130 micrograms/m³ for 15 minutes, allowable up to 2 times per workshift.

Section 3 - Hazards Identification

Appearance: Off-white to pale yellow or greenish-yellow powder finished as film-coated tablets

Physical State: Solid

Odor: Odorless



Emergency Overview

Special
R = Reproductive
P = Potent

Emergency Overview Effective Date: 09-Sep-2003

Lilly Laboratory Labeling Codes:

Health 2

Fire 1

Reactivity 0

Special R, P

Primary Physical and Health Hazards: Not hazardous if intact. Irritant (skin). Highly Potent. Reproductive Effects.

Caution Statement: Intact Raloxifene Hydrochloride Tablets are not considered to be a health hazard. The contents of Raloxifene Hydrochloride Tablets may be irritating to the skin and is highly potent. Effects of exposure to raloxifene hydrochloride may include decreased fertility in females, adverse female reproductive tissue changes, and adverse fetal changes.

Routes of Entry: Inhalation and skin contact.

Effects of Overexposure: Tablets are intended for human consumption under guidance of a physician. Intact coated tablets are not considered hazardous under normal handling procedures. In the manufacturing setting, care should be used to avoid exposure to dust from tablets. Exposure to raloxifene hydrochloride resulted in skin rash/redness. Raloxifene hydrochloride is a Selective Estrogen Receptor Modulator (SERM) and is highly potent. Reproductive effects in females and developmental effects are associated with compounds in this pharmacological class, including raloxifene hydrochloride. Effects of exposure with therapeutic use in postmenopausal women not taking estrogen replacement therapy may include blood clots in veins, leg cramps, and hot flashes.

Medical Conditions Aggravated by Exposure: None known.

Carcinogenicity: Raloxifene hydrochloride - Not listed by IARC, NTP, ACGIH, or OSHA. Not considered carcinogenic in animal studies conducted by Lilly Research Laboratories.

Section 4 - First Aid Measures

Eyes: Flush eyes with plenty of water. Get medical attention.

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.

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 chloride 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).

Section 8 - Exposure Controls / Personal Protection

See Section 2 for Exposure Guideline information.

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 powder may occur.

Respiratory Protection: Use an approved HEPA-filtered or supplied-air respirator.

Eye Protection: Safety glasses.

Ventilation: Extensive local exhaust or enclosed process equipment.

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 pale yellow or greenish-yellow powder finished as film-coated tablets

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: Insoluble

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 chloride fumes when heated to decomposition.

Hazardous Polymerization: Will not occur.

Section 11 - Toxicological Information

Acute Exposure

Data for the active ingredient, raloxifene hydrochloride, are reported.

Oral: Raloxifene hydrochloride - Rat, 5000 mg/kg, no deaths, leg weakness, soft stools.
Monkey, 1000 mg raloxifene/kg, no deaths.

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

Inhalation: Raloxifene hydrochloride - Monkey, 27 mg raloxifene/m³ for 8 hours, no deaths or toxicity.

Intraperitoneal: Raloxifene hydrochloride - Rat, median lethal dose estimated greater than 2000 mg/kg, mortality, reduced activity.

Skin Contact: Raloxifene hydrochloride - Rabbit, slight irritant

Eye Contact: Raloxifene hydrochloride - Rabbit, slight irritant

Chronic Exposure

Data for the active ingredient, raloxifene hydrochloride, are reported.

Target Organ Effects: No applicable information found.

Other Effects: Raloxifene hydrochloride - Decreased body weight gain, decreased food consumption, diarrhea.

Reproduction: Raloxifene hydrochloride - No pregnancies occurred when male and female rats were given daily doses of 5 mg/kg prior to and during mating. In female rats, disrupted estrous cycles and inhibited ovulation (all reversible), and delayed and disrupted embryo implantation resulting in prolonged gestation and reduced litter size were reported. Developmental effects reported included decreased fetal weight and delayed skeletal development, growth retardation, malformations of the heart, edema, and hydrocephaly in offspring. In male rats, daily doses up to 100 mg/kg for at least 2 weeks did not affect sperm production/quality or reproductive performance. Decreased prostate weights and a single case of aspermatogenesis were observed in dogs given 30 mg/kg for 6-months. No significant observations in sperm count/motility and morphology were observed in humans during a 3-month clinical trial when given daily doses of 120 mg.

Sensitization: Raloxifene hydrochloride - Guinea pig, subcutaneous, negative systemic response.

Mutagenicity: Raloxifene hydrochloride - Not mutagenic in bacterial or mammalian cells.

Section 12 - Ecological Information

Environmental data for raloxifene hydrochloride and raloxifene are reported where indicated.

Ecotoxicity Data: Raloxifene hydrochloride

Rainbow trout 96-hr median lethal concentration: 1.45 mg/L

Daphnia magna 48-hr median effective concentration: 2.43 mg/L

Daphnia magna 23-day no-observed-effect concentration: 0.165 mg/L

Green algae (*S. capricornutum*) median effective concentration: 1.21 mg/L (average specific growth rate)

Microorganisms:

fungus (*Chaetomium globosum*): MIC > 1000 mg/L

mold (*Aspergillus flavus*): MIC > 1000 mg/L

soil bacteria (*Comamonas acidovorans*): MIC > 1000 mg/L

N-fixing bact. (*Azotobacter chroococcum*): MIC > 1000 mg/L

blue-green algae (*Nostoc sp.*): MIC = 875 mg/L

Environmental Fate: Raloxifene hydrochloride

Log Kow: 2.71, 3.12, 3.19, (pH 5, 7, 9)

Water solubility (mg/L): 345.2, 13.3, 0.9 (pH 5, 7, 9)

Light absorption maxima (nm): 287, 287, 297 (pH 5, 7, 9)

Molar extinction coefficient: 34,245; 34,087; 33,967 (pH 5, 7, 9)

Hydrolysis half-life (days): 1001, 410, 90 (pH 5, 7, 9)

Sewage sludge 24-hour Kd (7 g/L total suspended solids): 2700 to 3100

Sewage sludge degradation half-life (0.47 g/L total suspended solids): 7.17 hours

Aerobic biodegradation half-life (0.03 g/L total suspended solids): 37 days

Bioconcentration factor (calculated from Log Kow at pH 7): 65

Environmental Summary: Raloxifene - Moderately toxic to fish, invertebrates and green algae. Practically non-toxic to microorganisms. No volatility expected due to a high melting point. Low potential to bioconcentrate in aquatic organisms. Adsorbs to organic particles. Not persistent in the environment due to biodegradation and possible photolysis.

Lilly Aquatic Exposure Guideline (LAEG): Raloxifene hydrochloride

LAEG for Drinking Water: 3.5 micrograms/L

LAEG for Chronic Exposure of Aquatic Organisms: 0.01 micrograms/L

LAEG for Acute Exposure of Aquatic Organisms: 0.01 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

Raloxifene hydrochloride

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 raloxifene hydrochloride (C = 10 to 65%)

T (Toxic)

Reproductive Category 1

Risk Phrases

R 52 - Harmful to aquatic organisms.

R 60 - May impair fertility.

R 61 - May cause harm to the unborn child.

Safety Phrases

S 22 - Do not breathe dust.

S 36/37 - Wear suitable protective clothing and gloves.

S 57 - Use appropriate containment to avoid environmental contamination.

Section 16 - Other Information

MSDS Sections Revised: Section 1.

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
317-277-6029

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)