



# Duloxetine Hydrochloride Capsules

Eli Lilly and Company  
Material Safety Data Sheet

Effective Date: 21-Sep-2005

## 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:** Duloxetine Hydrochloride Capsules

**Chemical Name:** 2-Thiophenepropanamine, N-methyl-gamma-(1-naphthalenyloxy)-, hydrochloride, (gammaS)-

**Synonym(s):** 10% W/W duloxetine pellets; 20% W/W duloxetine pellets; 5% W/W duloxetine pellets; Duloxetine hydrochloride capsules, 20 mg; Duloxetine hydrochloride pulvules; Duloxetine hydrochloride pulvules, 30 mg; Duloxetine hydrochloride pulvules, 60 mg; Pulvules duloxetine hydrochloride; Encapsulated Duloxetine, 30 mg; Duloxetine pellets; Duloxetine hydrochloride pulvules, 40 mg; Duloxetine hydrochloride pulvules, 20 mg; Duloxetine hydrochloride pellets; Duloxetine hydrochloride; Duloxetine; Duloxetine capsule mix; 246916 formulation

**Trademarks(s):** Cymbalta; AriClaim; Yentreve

**Lilly Item Code(s):** B02426; B02466; B02556; B02558; CK1079; CK1084; ND1068; ND1075; ND1078; ND1080; ND1109; PU3235; PU3236; PU3237; PU3240; PU3241; PU3242; PU3243; PU3244; PU3245; QA477P; QA511K; QD477P; UC5985; UC5986; UC5987; UC9542; UC9543; UC9544; UC9545; UC9564; UC9565; UC9566; UC9567; VF0344

See attached glossary for abbreviations.

## Section 2 - Composition / Information on Ingredients

<u>Ingredient</u>	<u>CAS</u>	<u>Concentration %</u>
Duloxetine Hydrochloride	136434-34-9	1.3 - 20
Excipients	NA	80 - 98

### Exposure Guidelines:

Duloxetine hydrochloride - LEG 25 micrograms/m<sup>3</sup> TWA for 12 hours. LEG 40 micrograms/m<sup>3</sup> TWA for 8 hours. Excursion Limit 300 micrograms/m<sup>3</sup> for no more than a total of 30 minutes.

## Section 3 - Hazards Identification

**Appearance:** Capsules containing pellets

**Physical State:** Solid

**Odor:** Odorless

## Emergency Overview



**Emergency Overview Effective Date:** 17-Aug-2004

**Lilly Laboratory Labeling Codes:**

**Health 3**

**Fire 1**

**Reactivity 0**

**Primary Physical and Health Hazards:** Not hazardous if intact. Corrosive (eyes). Nervous System and Liver Effects.

**Caution Statement:** Intact Duloxetine Hydrochloride Capsules are not considered to be a health hazard. The contents of Duloxetine Hydrochloride Capsules may cause burns or permanent tissue damage to the eyes. Effects of exposure may include dizziness, nausea, drowsiness, fatigue, and liver effects.

**Routes of Entry:** Inhalation and skin contact.

**Effects of Overexposure:** Capsules are intended for human consumption under guidance of a physician. Intact capsules are not considered hazardous under normal handling procedures. Adverse events commonly observed during therapeutic administration include nausea, dry mouth, constipation, decreased appetite, fatigue, dizziness, drowsiness, headache, insomnia, and increased sweating.

Duloxetine, the active ingredient, is harmful if swallowed, may cause burns or permanent tissue damage to the eyes, and may be slightly irritating to the skin. In animal studies, the major signs of overdose toxicity would be related to the central nervous (tremors, clonic convulsions, ataxia) and gastrointestinal (emesis, decreased appetite) systems. Liver effects have been reported in long-term animal studies at high doses.

**Medical Conditions Aggravated by Exposure:** None known.

**Carcinogenicity:**

Duloxetine hydrochloride - Not listed by IARC, NTP, ACGIH, or OSHA.

## 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:**

Duloxetine - No specific antidote is known. An airway should be established. Monitoring of cardiac and vital signs is recommended, along with appropriate symptomatic and supportive measures. Gastric lavage may be indicated if performed soon after ingestion or in symptomatic patients. Activated charcoal may be useful in limiting absorption. Duloxetine has a large volume of distribution and forced diuresis, hemoperfusion, and exchange perfusion are unlikely to be beneficial.

## 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

The following are recommended for manufacturing or other situations where exposure to the contents may occur.

**Spills:** 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. Wear protective equipment, including eye protection, to avoid exposure (see Section 8 for specific handling precautions).

## 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.

Intact capsules 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 contents 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:** Capsules containing pellets

**Odor:** Odorless

**Boiling Point:** Not applicable

**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:** 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

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

**Oral:**

Duloxetine hydrochloride - Rat, median lethal dose 491 mg/kg for males and 279 mg/kg for females, tremors, convulsions.

Dog, 100 mg/kg, no deaths, reduced activity, slow pupillary response, intermittent tremors, rigidity.

**Skin:**

Duloxetine hydrochloride - Rabbit, 1000 mg/kg, no deaths or toxicity.

**Inhalation:** No applicable information found.

**Skin Contact:**

Duloxetine hydrochloride - Rabbit, slight irritant

**Eye Contact:**

Duloxetine hydrochloride - Rabbit, corrosive

## Chronic Exposure

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

**Target Organ Effects:**

Duloxetine hydrochloride - Dilation of the pupil and slow pupillary light response reported in dogs administered 3, 10, and 30 mg/kg orally for 1 year. Slight increase in liver enzymes reported in the mid- and high-dose animals. Liver effects (tissue changes, enzyme induction) reported in rats administered up to 0.08% in diet (47 mg/kg/day) for 6 months.

**Reproduction:**

Duloxetine - Reproductive performance was not affected in male rats (45 mg/kg/day). In female rats (45 mg/kg/day), reproductive toxicity was demonstrated by a decrease in maternal food consumption and body weight, estrous cycle disruption, depressions in live birth indices and progeny survival, and progeny growth retardation. The no-observed-effect level (NOEL) for maternal toxicity, reproductive toxicity, and developmental toxicity in the female fertility study was 10 mg/kg/day. There was no evidence of teratogenicity in animal studies. Duloxetine and/or its metabolites are excreted into the milk of lactating rats.

**Sensitization:**

Duloxetine hydrochloride - Guinea pig, negative in active systemic anaphylaxis and passive cutaneous anaphylaxis tests.

**Mutagenicity:**

Duloxetine - Demonstrated no mutagenic potential in a battery of in vitro and in vivo genotoxicity tests.

**Carcinogenicity:**

Duloxetine - Administered in the diet to rats and mice for 2 years. In rats, did not cause any increase in incidence of expected or unusual neoplasms or decrease in the latency for any tumor type. In female mice, there was an increased incidence of hepatocellular adenomas and carcinomas at the high dose only (144 mg/kg/day), but these were considered to be secondary to hepatic enzyme induction with associated centrilobular hypertrophy and vacuolation.

## 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:**

Duloxetine

Rainbow trout 96-hour median lethal concentration: 1.3 mg/L

Daphnia magna 48-hour median effective concentration: 2.4 mg/L

Green algae (P. subcapitata) 72-hour median effective concentration (biomass) : 0.064 mg/L

Green algae (P. subcapitata) 72-hour no observable effect concentration (biomass) : 0.011 mg/L

Activated sludge respiration inhibition 3-hour median effective concentration (1.6 g solids/L): 36.5 mg/L

Daphnia magna 21-day no observable effect concentration: 0.011 mg/L

Earthworm 14-day median effective concentration: &gt;1000 mg/L

**Environmental Fate:**

Duloxetine hydrochloride

Log Kow: 0.78, 1.54, 3.35 (pH 4,7,9)

Bioconcentration factor (calculated): 324

pKa: 9.34

Sludge biodegradation: 91.3% to 62.1% at 8 hours

Sludge adsorption (Koc): 2893, 3150, 2970, 4296 (at 2500, 1250, 625, 313 mg solids/L)

Photolysis: 100% loss calculated over 1 month (pH 4, 7, 9)

Hydrolysis half-life (35 days at 30 C): 41.88, 100.62, 72.48 days (pH 4, 7, 9)

Hydrolysis half-life (35 days at 40 C): 15.73, 31.69, 22.64 days (pH 4, 7, 9)

**Environmental Summary:**

Duloxetine hydrochloride - Material is highly toxic to green algae and fish, moderately toxic to aquatic invertebrates and slightly toxic to activated sludge microorganisms. Measurable concentrations of material in atmosphere are not expected since it is a non-volatile solid. The solubility in water is high. After 24 hours in activated municipal sludge, the duloxetine concentration declined extensively (biodegradation and adsorption). Material is not expected to bioconcentrate in aquatic organisms.

**Lilly Aquatic Exposure Guideline (LAEG):**

Duloxetine hydrochloride

LAEG for Drinking Water: 20 micrograms/L

LAEG for Chronic Exposure of Aquatic Organisms: 1.7 micrograms/L

LAEG for Acute Exposure of Aquatic Organisms: 15 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

Duloxetine 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

Xi (Irritant)

#### Risk Phrases

R 41 - Risk of serious damage to eyes.

#### Safety Phrases

S 26 - In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

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).

## 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  
317-651-9533

**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)