Fluoxetine Hydrochloride Capsules and Tablets

Eli Lilly and Company
Material Safety Data Sheet

Effective Date: 30-Jun-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: Fluoxetine Hydrochloride Capsules and Tablets

Chemical Name: Benzenepropanamine, N-methyl-gamma-[4-(trifluoromethyl)phenoxy]-, hydrochloride
Chemical Name 2: (+-)-N-Methyl-3-phenyl-3-[(alpha,alpha,alpha-trifluoro-p-tolyl)oxy]propylamine hydrochloride
Synonym(s): Fluox; Prozac Delayed Release Pellets; Starter Kit Prozac (7-Pulvules and 7-Tablets); Fluoxetine HCl; Fluoxetine Hydrochloride; Fluoxetine; Fluoxetine Hydrochloride Capsules; Fluoxetine Hydrochloride Tablets; Fluoxetine Hydrochloride Capsule Mix; Fluoxetine Hydrochloride Tablet Mix; 110140 Formulation; 3105
Trademarks(s): Adzac; Alvenin; Branfluoxe; Debiton; Erotab; Fluctine; Fluoxeren; Fluctin; Profac; Prenu; Praxin; Nuzac; Lovan; Lonparin; Levilin; Ladose; Zolovan; Sertax; Sarazac; Sarafem; Prozyn; Prozac Weekly; Fonzac; Fontex; Foncin; Flutin; Erocap; Prozac
Lilly Item Code(s): CK0857; MS8320; ND0845; ND0966; ND0967; ND1008; ND1014; ND1015; ND1024; ND1058; ND1060; ND1066; ND1107; ND1108; PU3004; PU3103; PU3104; PU3105; PU3106; PU3107; PU3109; PU3120; PU3160; PU3161; PU3210; PU3220; QA512G; SA1031; SA1032; SA1035; SA1036; TA4006; TA4007; TA4169; TA4171; TA4400; UC5014; UC5015; UC5016; UC5370; UC5371; UC5905; UC8957; UC8963; UC8991; UC9526; UC9528; UC9551; UC9552; UC9559; VF0144; VF0145; VF0156; VF0236; VF0237; VF0268; VF0269; VF0270; VF0293; VF0299; VF0318; VF0319; VF0324; VF0326; VF0330; VF0332; VF0334; VF0339; VF0359

See attached glossary for abbreviations.

Section 2 - Composition / Information on Ingredients

Ingredient	CAS	Concentration %
Fluoxetine Hydrochloride	56296-78-7	4 - 20
Excipients	NA	80 - 94

Exposure Guidelines:
Fluoxetine hydrochloride - LEG 30 micrograms/m3 TWA for 12 hours. LEG 50 micrograms/m3 TWA

for 8 hours.

Section 3 - Hazards Identification

Appearance: White powder or pellets finished as capsules or coated tablets
Physical State: Solid
Odor: Odorless

Emergency Overview

Emergency Overview Effective Date: 30-Jun-2005

Lilly Laboratory Labeling Codes:
Health 3 **Fire** 1 **Reactivity** 0

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

Caution Statement: Intact Fluoxetine Hydrochloride Capsules and Tablets are not considered to be a health hazard. The contents of Fluoxetine Hydrochloride Capsules and Tablets may be irritating to the eyes and skin. Effects of exposure to the contents may include tremors, drowsiness, and liver tissue changes.

Routes of Entry: Inhalation and skin contact.

Effects of Overexposure: Capsules and tablets are intended for human consumption under guidance of a physician. Capsules and tablets are not considered hazardous under normal handling procedures. The most common adverse events reported with therapeutic administration include nausea, decreased appetite, anxiety, tremors, drowsiness, and sweating. The most common signs and symptoms associated with non-fatal overdosage were seizures, drowsiness, nausea, increased heart rate, and vomiting

Fluoxetine hydrochloride, the active ingredient, may cause burns or permanent tissue damage to the eyes. Contact dermatitis (rash) has been reported with occupational exposure to fluoxetine hydrochloride.

Medical Conditions Aggravated by Exposure: Acute overdose after sustained therapeutic exposure has resulted in seizures. The potential for aggravation of a seizure disorder has not been ruled out.

Carcinogenicity:
Fluoxetine hydrochloride - Not listed by IARC, NTP, ACGIH, or OSHA. The dietary administration to rats and mice for 2 years at doses of up to 10 and 12 mg/kg/day produced no evidence of carcinogenicity.

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:
Fluoxetine hydrochloride - Cardiac and vital signs monitoring is recommended, along with general symptomatic and supportive measures. No specific antidote is known. Forced diuresis, dialysis, haemoperfusion, and exchange transfusion are unlikely to be of benefit. In limited human overdose experience, seizures have been reported. Appropriate seizure precautions are advised for any patient regularly taking fluoxetine who has been exposed to an acute overdose. Based on experience in animals, which may not be relevant to humans, fluoxetine-induced seizures that fail to remit spontaneously may respond to diazepam.

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: 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.

Filled capsules or coated tablets are not considered hazardous under normal handling procedures. The following are 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: White powder or pellets finished as capsules or coated tablets
Odor: Odorless
Boiling Point: Not applicable
Melting Point: No applicable information found
Specific Gravity: Not applicable
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 active ingredient, fluoxetine hydrochloride, are reported.

Oral:
Fluoxetine hydrochloride - Rat, median lethal dose 451 mg/kg, reduced activity, tremors, convulsions, increased irritability, labored breathing, increased urine output.
Mouse, median lethal dose 248 mg/kg, increased irritability, tremors.
Monkey, 50 mg/kg, no deaths, vomiting.

Skin:
Fluoxetine hydrochloride - Rabbit, 500 mg/kg, no deaths or toxicity.

Inhalation: No applicable information found.

Skin Contact:
Fluoxetine hydrochloride - Rabbit, nonirritant

Eye Contact:
Fluoxetine hydrochloride - Rabbit, corrosive

Chronic Exposure

Data for active ingredient, fluoxetine hydrochloride, are reported.

Target Organ Effects:
Fluoxetine hydrochloride - Liver effects (reversible increases in serum enzymes, slight hepatic fat deposition, tissue changes).

Other Effects:
Fluoxetine hydrochloride - In a juvenile toxicology study in rats, where the exposure period corresponds to human childhood and adolescence, administration of 30 mg/kg resulted in skeletal muscle necrosis. Other findings in rats included necrosis of the testis and immaturity and inactivity of the female reproductive tract. Following an approximate 11-week recovery period, sperm assessments indicated an approximately 30% decrease in sperm concentrations without affecting sperm morphology or motility. Microscopic evaluation indicated that testicular degeneration was irreversible. Delays in sexual maturation occurred with administration of 10 or 30 mg/kg. The significance of these findings in humans is unknown. Femur lengths at 30 mg/kg increased to a lesser extent compared with control rats.

Reproduction:
Fluoxetine hydrochloride - Two fertility studies conducted in adult rats indicated no adverse effects on fertility. In embryo-fetal development studies in rats and rabbits, there was no evidence of teratogenicity. However, in rat reproduction studies, an increase in stillborn pups, a decrease in pup weight, and an increase in pup deaths during the first 7 days postpartum occurred following maternal exposure to 7.5 mg/kg/day during gestation and lactation. There was no evidence of developmental neurotoxicity in the surviving offspring of rats. The no effect dose for rat pup mortality was 5 mg/kg/day.

Data on a large number of exposed pregnancies in humans indicate no appearance of adverse effects on pregnancy or on the overall health of the fetus/newborn child. However, a few epidemiological studies

have noted that some women treated with fluoxetine and other SSRIs late in the third trimester have had newborns with increased complications that could be consistent with drug discontinuation syndrome (e.g. transient jitteriness, difficulty feeding, tachypnea and irritability) and required prolonged hospitalizations.

Sensitization: No applicable information found.

Mutagenicity:
Fluoxetine hydrochloride - No genotoxic effects based on the following assays: bacterial mutation assay, DNA repair assay in cultured rat hepatocytes, mouse lymphoma assay, and in vivo sister chromatid exchange assay in Chinese hamster bone marrow 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:
Fluoxetine hydrochloride
Rainbow trout 96-hour median lethal concentration: 1.57 mg/L
Daphnia magna 48-hour median effective concentration: 0.94 mg/L
Green algae (S. capricornutum) median effective concentration: 30.5 micrograms/L (average specific growth rate)
Microorganisms:
- fungus (Chaetomium globosum): MIC = 64 mg/L
- mold (Aspergillus flavus): MIC = 64 mg/L
- soil bacteria (Pseudomonas acidovorans): MIC = 1000 mg/L
- N-fixing bacteria (Azotobacter chroococcum): MIC = 64 mg/L
- blue-green algae (Nostoc sp.): MIC = 250 mg/L

Environmental Fate:
Fluoxetine hydrochloride
Dissociation constant (pKa): 8.7
Log Kow: 1.0, 1.8, 2.6 (pH 5, 7, 9)
Solubility (g/L): 15.0, 6.84, 5.47 (pH 5, 7, 9)
Light absorption (nm): none between 290 and 800
Hydrolysis rate (1/day): 0, 0, 0 (pH 5, 7, 9)
Aerobic biodegradation half-life (days): not measurable

Environmental Summary:
Fluoxetine hydrochloride - Moderately toxic to fish and highly toxic to invertebrates and green algae. No volatility expected. Low potential to bioaccumulate in aquatic organisms. Can be considered persistent due to low rates of biodegradation and hydrolysis.

Lilly Aquatic Exposure Guideline (LAEG):
Fluoxetine hydrochloride
LAEG for Drinking Water: 11.2 micrograms/L
LAEG for Chronic Exposure of Aquatic Organisms: 1.2 micrograms/L
LAEG for Acute Exposure of Aquatic Organisms: 30.5 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

Additional Information: This material is considered to be an Environmentally Hazardous Substance according to the criteria set forth in the European Agreement Concerning the International Carriage of Dangerous Goods by Road (ADR) and is regulated as a Hazard Class 9 (UN3077 or UN3082) when shipping under ADR.

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

Fluoxetine 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)
N (Dangerous for the Environment)

Risk Phrases
R 38 - Irritating to skin.
R 41 - Risk of serious damage to eyes.
R 51/53 - Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

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

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

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)