



Fluoxetine Hydrochloride Oral Solution

Eli Lilly and Company
Material Safety Data Sheet

Effective Date: 27-Aug-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 Oral Solution

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): Fluoxetine HCl; Fluoxetine Hydrochloride; Fluoxetine; 110140 Formulation

Trademarks(s): Adzac; Alvenin; Branfluoxe; Erocap; Fluctine; Fluoxeren; Fluctin; Foncin; Fonzac; Profac; Prenu; Praxin; Nuzac; Lovan; Lonparin; Levilin; Ladose; Zolovan; Sertax; Sarazac; Sarafem; Prozyn; Fontex; Flutin; Debiton; Prozac

Lilly Item Code(s): MS5120; UC5017; UC5932; UC5982; VF0271

See attached glossary for abbreviations.

Section 2 - Composition / Information on Ingredients

Ingredient	CAS	Concentration %
Fluoxetine Hydrochloride	56296-78-7	0.35
Sucrose	57-50-1	47
Glycerin	56-81-5	15
Ethyl Alcohol	64-17-5	0.23
N&A Mint 587.207/SE	NA	0.17
Benzoic Acid	65-85-0	0.04
Water	7732-18-5	36

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

Exposure Guidelines:

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

for 8 hours.

Sucrose - PEL 5 mg/m³ TWA (respirable) and 15 mg/m³ TWA (total). TLV 10 mg/m³ TWA.

UK - Exposure Standard 10 mg/m³ TWA, 20 mg/m³ STEL.

Ireland - Occupational Exposure Limit 10 mg/m³ TWA, 20 mg/m³ 15-minute STEL.

Italy - Occupational Exposure Limit 10 mg/m³ TWA.

France - Occupational Exposure Limit 10 mg/m³ (VME) TWA.

Spain - Occupational Exposure Limit 10 mg/m³ (VLA-ED) TWA.

Glycerin (mist) - PEL 5 mg/m³ TWA (respirable) and 15 mg/m³ TWA (total). TLV 10 mg/m³ TWA.

UK - Exposure Standard 10 mg/m³ TWA.

Ireland - Occupational Exposure Limit 10 mg/m³ TWA.

Italy - Occupational Exposure Limit 10 mg/m³ TWA.

France - Occupational Exposure Limit 10 mg/m³ (VME) TWA.

Spain - Occupational Exposure Limit 10 mg/m³ (VLA-ED) TWA.

Ethyl alcohol - PEL and TLV 1000 ppm (1900 mg/m³) TWA.

UK - Workplace Exposure Limit 1000 ppm (1920 mg/m³) TWA.

Ireland - Occupational Exposure Limit 1000 ppm (1900 mg/m³) TWA.

Italy - Occupational Exposure Limit 1000 ppm TWA.

France - Occupational Exposure Limit 1000 ppm (1900 mg/m³) (VME) TWA, 5000 ppm (9500 mg/m³) (VLE) STEL.

Spain - Occupational Exposure Limit 1000 ppm (1910 mg/m³) (VLA-ED) TWA.

Germany - TRGS 900 Limit Value 500 ppm (960 mg/m³), 15-minute limit not to exceed 4 times MAK.

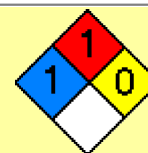
Section 3 - Hazards Identification

Appearance: Clear colorless solution

Physical State: Liquid

Odor: Mint-like

Emergency Overview



Emergency Overview Effective Date: 27-Aug-2005

Lilly Laboratory Labeling Codes:

Health 1

Fire 1

Reactivity 0

Primary Physical and Health Hazards: Nervous System and Liver Effects.

Caution Statement: Effects of exposure to Fluoxetine Hydrochloride Oral Solution may include tremors, drowsiness, and liver tissue changes.

Routes of Entry: Inhalation and skin contact.

Effects of Overexposure: Contact dermatitis (rash) has been reported with occupational exposure to fluoxetine hydrochloride. 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 overdose were seizures, drowsiness, nausea, increased heart rate, and vomiting.

Medical Conditions Aggravated by Exposure: Acute overdose after sustained therapeutic exposure to fluoxetine hydrochloride 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.

Remaining ingredients - Not listed by IARC, NTP, ACGIH, or OSHA.

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.

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: None known.

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). Prevent further migration into the environment. Use absorbent/adsorbent material to solidify liquids.

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.

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: Safety glasses.

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.

Section 9 - Physical and Chemical Properties

Appearance: Clear colorless solution

Odor: Mint-like

Boiling Point: No applicable information found

Melting Point: Not applicable

Specific Gravity: 1.20 to 1.30

pH: 2.5 to 4.5

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

Oral:

Fluoxetine hydrochloride oral solution - Rat, 625 mg/kg, no deaths or toxicity.

Skin:

Fluoxetine hydrochloride oral solution - Rabbit, 1250 mg/kg, no deaths or toxicity.

Inhalation: No applicable information found.

Skin Contact:

Fluoxetine hydrochloride oral solution - Rabbit, nonirritant

Eye Contact:

Fluoxetine hydrochloride oral solution - Rabbit, slight irritant

Chronic Exposure

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

Target Organ Effects:

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

Glycerin - Heart effects (increased weight), liver effects (increased weight), kidney effects (increased weight, 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:

Glycerin - Guinea pig, not a contact sensitizer.

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

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

Remaining Ingredients

TSCA - Yes

CERCLA - Not on this list

SARA 302 - Not on this list

SARA 313 - Not on this list
OSHA Substance Specific - No

EU Regulations

Risk Phrases

R 52/53 - Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Safety Phrases

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

Section 16 - Other Information

MSDS Sections Revised: Sections 3, 4, 11, 12 and 15.

Emergency Overview Sections Revised: Physical and health hazards and caution statement.

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)