SAFETY DATA SHEET

1. Identification

Product identifier **Symbyax®**

Other means of identification

Item Code B02079, B02081, ND1086, ND1087, ND1088, ND1089, PU3230, PU3231, PU3232, PU3233, PU3234, UC9560, UC9561, UC9562, UC9563

Synonyms 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- * Benzenepropanamine, N-methyl-gamma-[4-(trifluoromethyl)phenoxy]-, hydrochloride * 110140/170053 Formulation * LY900000 * OFC Capsules * Olanzapine Fluoxetine Capsule Mix

Recommended use Pharmaceutical

Recommended restrictions None known.

Manufacturer/Importer/Supplier/Distributor information

Manufacturer

Company name Eli Lilly and Company

Address Lilly Corporate Center
Indianapolis, IN 46285
United States

Telephone Phone: +1-317-276-2000

E-mail lilly_msds@lilly.com

Emergency phone number CHEMTREC: +1-800-424-9300

2. Hazard(s) identification

Physical hazards Not classified.

Health hazards

Acute toxicity, oral	Category 4
Acute toxicity, inhalation	Category 4
Skin corrosion/irritation	Category 2
Serious eye damage/eye irritation	Category 1
Sensitization, skin	Category 1
Specific target organ toxicity, single exposure	Category 3 narcotic effects
Specific target organ toxicity, repeated exposure	Category 2

OSHA defined hazards Not classified.

Label elements

Signal word Danger

Hazard statement

H302 Harmful if swallowed.
H315 Causes skin irritation.
H317 May cause an allergic skin reaction.
H318 Causes serious eye damage.
H332 Harmful if inhaled.
H336 May cause drowsiness or dizziness.
H373 May cause damage to organs (Liver, Blood) through prolonged or repeated exposure.

Precautionary statement

Prevention

P280 Wear protective gloves/protective clothing/eye protection/face protection.

Response

P305 + P351 + P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P302 + P352	IF ON SKIN: Wash with plenty of soap and water.
P304 + P340	IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing.
P310	Immediately call a POISON CENTER or doctor/physician.

Storage Not available.

Disposal Not available.

Hazard(s) not otherwise classified (HNOC) None known.

Supplemental information None.

3. Composition/information on ingredients

Mixtures

Chemical name	Common name and synonyms	CAS number	%
Fluoxetine Hydrochloride	(3S)-N-methyl-3-phenyl-3-[4-(trifluoromethyl) phenoxy]propan-1-amine hydrochloride	56296-78-7	12 - 19
Olanzapine	2-methyl-4-(4-methylpiperazin-1-yl)-10H-thieno[2,3-b][1,5]benzodiazepine 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-	132539-06-1	1 - 6

Composition comments Remaining components of this product are non-hazardous and/or are present at concentrations below reportable levels.

4. First-aid measures

Inhalation Move to fresh air. Oxygen or artificial respiration if needed. Get medical attention immediately.

Skin contact Immediately flush skin with plenty of water. Remove contaminated clothing and shoes. Get medical attention if irritation develops and persists. Wash contaminated clothing before reuse.

Eye contact In case of eye contact, remove contact lens and rinse immediately with plenty of water, also under the eyelids, for at least 15 minutes. Get medical attention immediately.

Ingestion Give several glasses of water. Never give anything by mouth to a victim who is unconscious or is having convulsions. Call a physician or poison control center immediately.

Most important symptoms/effects, acute and delayed Harmful if swallowed. Harmful if inhaled. Causes eye burns. May cause allergic skin reaction. May cause drowsiness or dizziness. Increased heart rate. Seizures. May cause damage to the liver. Risk of damage to blood system. 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.

Indication of immediate medical attention and special treatment needed Olanzapine fluoxetine combination - In managing overdose, consider the possibility of multiple drug involvement. 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 sympathomimetic agents with beta-agonist activity since beta stimulation may worsen hypotension .

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.

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.

5. Fire-fighting measures

Suitable extinguishing media Water. Carbon dioxide (CO2). Dry chemical.

Unsuitable extinguishing media	None known.
Specific hazards arising from the chemical	Hazardous decomposition products formed under fire conditions.
Special protective equipment and precautions for firefighters	Wear self-contained breathing apparatus and protective clothing.

6. Accidental release measures

Personal precautions, protective equipment and emergency procedures	Wear suitable protective clothing, gloves and eye/face protection. Do not breathe dust. See Section 8 of the SDS for Personal Protective Equipment.
Methods and materials for containment and cleaning up	The following are recommended for manufacturing or other situations where exposure to contents may occur. Do not sweep. Vacuum material with appropriate dust collection filter in place. If vacuum is not available, lightly mist/wet material and remove by mopping or wet wiping.
Environmental precautions	Prevent further leakage or spillage if safe to do so. Prevent spilled material from flowing onto adjacent land or into streams, ponds, or lakes.

7. Handling and storage

Precautions for safe handling	Do not get in eyes and avoid contact with skin and clothing. Do not breathe dust. Use only with adequate ventilation. Wear personal protective equipment. Wash hands thoroughly after handling. See Section 8 of the SDS for Personal Protective Equipment.
Conditions for safe storage, including any incompatibilities	Storage temperature: between 15 and 30 C (59 to 86 F).

8. Exposure controls/personal protection

Occupational exposure limits

Lilly (LEG)

Components	Type	Value
Fluoxetine Hydrochloride (CAS 56296-78-7)	TWA (12hrs)	30 ug/m3
	TWA (8hrs)	50 ug/m3
Olanzapine (CAS 132539-06-1)	STEG (15min)	114 ug/m3
	TWA (12hrs)	38 ug/m3
	TWA (8hrs)	50 ug/m3

Biological limit values	No biological exposure limits noted for the ingredient(s).
Appropriate engineering controls	Open handling is not recommended. Use appropriate control measures such as fume hood, ventilated enclosure, local exhaust ventilation, or down-draft booth. Intact capsules or 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 contents may occur.

Individual protection measures, such as personal protective equipment

Eye/face protection	Safety glasses with side shields recommended. If splash potential or dusty operations, wear goggles/faceshield.
Skin protection	
Hand protection	Chemical resistant gloves.
Other	Chemical-resistant gloves and impermeable body covering to minimize skin contact.
Respiratory protection	If the applicable occupational exposure level (OEL) is anticipated to be exceeded, wear an approved respirator with sufficient protection factor to control exposure below the OEL.
Thermal hazards	Not available.
General hygiene considerations	Engineering controls should be used as the primary means to control workplace exposures. Follow good workplace hygiene practices such as washing hands after handling this material.

9. Physical and chemical properties

Appearance	Capsules containing slightly yellow to yellow powder
Physical state	Solid.
Form	Capsules
Color	Yellow

Odor	Odorless
Odor threshold	Not available.
pH	Not available.
Melting point/freezing point	Not available.
Initial boiling point and boiling range	Not available.
Flash point	Not applicable.
Evaporation rate	Not available.
Flammability (solid, gas)	No test data available.
Upper/lower flammability or explosive limits	
Flammability limit - lower (%)	Not available.
Flammability limit - upper (%)	Not available.
Explosive limit - lower (%)	Not available.
Explosive limit - upper (%)	Not available.
Vapor pressure	Not available.
Vapor density	Not available.
Relative density	Not available.
Solubility(ies)	
Solubility (water)	Soluble in water.
Partition coefficient (n-octanol/water)	0.930 (pH 5)(Fluoxetine Hydrochoride) 1.780 (pH 7)(Fluoxetine Hydrochoride) 2.630 (pH 9)(Fluoxetine Hydrochoride)
Auto-ignition temperature	Not available.
Decomposition temperature	Not available.
Viscosity	Not available.
Other information	
Explosive properties	Not explosive
Oxidizing properties	No oxidizing properties.

10. Stability and reactivity

Reactivity	Not water reactive.
Chemical stability	Material is stable under normal conditions.
Possibility of hazardous reactions	Hazardous polymerization does not occur.
Conditions to avoid	None known.
Incompatible materials	Strong oxidizing agents.
Hazardous decomposition products	Hazardous decomposition products formed under fire conditions.

11. Toxicological information

Information on toxicological effects

Acute toxicity Harmful if swallowed. Harmful if inhaled.

Components	Species	Test Results
Fluoxetine Hydrochloride (CAS 56296-78-7)		
Acute		
Dermal		
LD50	Rabbit	> 500 mg/kg
Inhalation		
LC50	Rat	898 mg/m3, 1 h

Components	Species	Test Results
Oral		
LD50	Monkey	> 50 mg/kg
	Mouse	248 mg/kg
	Rat	451 mg/kg

Olanzapine (CAS 132539-06-1)

Acute		
Dermal		
LD	Rabbit	> 200 mg/kg
Inhalation		
LC0	Rat	> 880 mg/m3, 4 h
Oral		
LD	Monkey	> 100 mg/kg
LD50	Rat	177 mg/kg

Skin corrosion/irritation
Rabbit: No irritation (Olanzapine) (Fluoxetine hydrochloride)
Skin irritation has been reported with occupational exposure. (Fluoxetine hydrochloride)

Serious eye damage/eye irritation
Rabbit: Corrosive. (Fluoxetine hydrochloride)
Rabbit: Irritating. (Olanzapine)

Respiratory or skin sensitization

Respiratory sensitization
Due to lack of data the classification is not possible.

Skin sensitization
Did not cause sensitization on laboratory animals. 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%). (Olanzapine)

Germ cell mutagenicity
Result in genetic toxicity assays (in vitro and in vivo): Negative (Fluoxetine hydrochloride and Olanzapine)

Carcinogenicity
Animal testing did not show any carcinogenic effects. (Fluoxetine hydrochloride)
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. (Olanzapine)
Based on available data, the classification criteria are not met.

OSHA Specifically Regulated Substances (29 CFR 1910.1001-1050)

Not listed.

Reproductive toxicity
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.
There are no adequate and well-controlled clinical studies on the use of fluoxetine in pregnant women. Results of a number of published epidemiological studies assessing the risk of fluoxetine exposure during the first trimester of pregnancy have demonstrated inconsistent results. More than 10 studies failed to demonstrate an increased risk for congenital malformations. An epidemiological study reported an increased risk of cardiovascular malformations in infants born to women exposed to fluoxetine during the first trimester of pregnancy compared to women who were not exposed to fluoxetine. However, a causal relationship has not been established. (Fluoxetine hydrochloride)

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. (Olanzapine)

Based on available data, the classification criteria are not met.

Specific target organ toxicity - single exposure Narcotic effects. May cause drowsiness or dizziness. (Fluoxetine hydrochloride and Olanzapine)

Specific target organ toxicity - repeated exposure Liver effects (reversible increases in serum enzymes, slight hepatic fat deposition, tissue changes). (Fluoxetine hydrochloride)
Animal studies have reported the following effects: Central nervous system effects. Heart effects. Blood effects. (Olanzapine)

Aspiration hazard No aspiration toxicity classification

Further information Olanzapine fluoxetine combination - No new or unexpected toxicity resulting from co-administration of olanzapine and fluoxetine were reported in rats or dogs dosed orally for 3 months. In animals, exposure to olanzapine caused nervous system effects (sedation), increased heart rate, and decreased circulating blood cell counts. Liver effects such as reversible increases in serum enzymes and tissue changes were observed following exposure to fluoxetine.

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. (Fluoxetine hydrochloride)

12. Ecological information

Ecotoxicity Very toxic to aquatic life with long lasting effects.

Components		Species	Test Results
Fluoxetine Hydrochloride (CAS 56296-78-7)			
Other	NOEC	Selenastrum capricornutum (new name Pseudokirchnerella subca	1.2 µg/l
Acute			
	IC50		1000 mg/l Bacteria (Soil)
			250 mg/l Blue-green algae
			64 mg/l Mold
			64 mg/l Bacteria (n-fixing) (Azotobacter chroococcum)
			64 mg/l Fungus
Other	EC50	Selenastrum capricornutum (new name Pseudokirchnerella subca	30.5 µg/l (average specific growth rate)
Aquatic			
Acute			
Crustacea	IC50	Daphnia magna	0.94 mg/l, 48 h
Fish	LC50	Rainbow Trout	1.57 mg/l, 96 h
Olanzapine (CAS 132539-06-1)			
	NOEC		100 mg/l, 3 h Sewage microorganisms (highest concentration tested)
Other	NOEC	Pseudokirchnerella subcapitata	1.7 mg/l, 14 d (based on initial concentration)
			0.9 mg/l, 14 d (based on mean measured concentrations)
Acute			
	EC50		> 100 mg/l, 3 h Sewage microorganisms (Respiration inhibition)
	IC50		255 mg/l Isolated growth on agar (Microbial growth inhibition)
Other	EC50	Pseudokirchnerella subcapitata	> 14.1 mg/l, 14 d (average specific growth rate) (biomass)

Components		Species	Test Results
		Selenastrum capricornutum (new name Pseudokirchnerella subca	> 14.1 mg/l (average specific growth rate)
Aquatic			
Crustacea	NOEC	Daphnia magna	2.4 mg/l, 48 h
			0.027 mg/l, 21 d (chronic growth) (reproduction) (survival)
Fish	NOEC	Fathead minnow (Pimephales promelas)	0.011 mg/l
		Rainbow Trout	0.43 mg/l, 96 h
Acute			
Crustacea	EC50	Daphnia magna	8 mg/l, 48 h
Fish	LC50	Rainbow Trout	1.74 mg/l, 96 h

Persistence and degradability

Fluoxetine Hydrochloride:
Hydrolysis rate (1/day): 0,0, 0 (pH 5, 7, 9)
Aerobic biodegradation half-life (days): not measurable

Olanzapine:
Hydrolysis half-life at 25 C (days): 65, 76, 78 (pH 5, 7, 9)
Ready hydrolysis (% hydrolyzed after 28 days at 25 C): 31.15, 24.87, 61.85 (pH 5, 7, 9)
Biodegradation in sludge (28 days):
DT50: 7.4 days
1.45% CO_2 evolution
6.5% olanzapine remained
Degradation in aquatic sediment (100 days):
Aerobic systems:
4.3% CO_2 evolution
DT90 from overlying water: 2.6 days
Anaerobic systems:
0.3% CO_2 evolution
DT90 from overlying water: 14.6 to 17.2 days

Bioaccumulative potential log Kow: < 4.

Partition coefficient n-octanol / water (log Kow)

Fluoxetine Hydrochloride	0.93, (pH 5) 1.78, (pH 7) 2.63, (pH 9)
Olanzapine	0.3, (pH 5) 1.7, (pH 7) 2.1, (pH 9)

Mobility in soil No data available.

Other adverse effects Not available.

Ecotoxicological Properties

Drinking Water

Components	Test Results
Fluoxetine Hydrochloride	2.6 µg/l, (Lilly Aquatic Exposure Guideline)
Olanzapine	2.5 µg/l, (Lilly Aquatic Exposure Guideline)

Chronic Exposure of Aquatic Organisms

Components	Test Results
Fluoxetine Hydrochloride	0.33 µg/l, (Lilly Aquatic Exposure Guideline)
Olanzapine	7.4 µg/l, (Lilly Aquatic Exposure Guideline)

Acute Exposure of Aquatic Organisms

Components	Test Results
Fluoxetine Hydrochloride	2.1 µg/l, (Lilly Aquatic Exposure Guideline)
Olanzapine	67 µg/l, (Lilly Aquatic Exposure Guideline)

13. Disposal considerations

Disposal instructions Dispose of contents/container in accordance with local/regional/national/international regulations.

14. Transport information

DOT

Not regulated as dangerous goods.

IATA

UN number	UN3077
UN proper shipping name	Environmentally hazardous substance, solid, n.o.s. (Fluoxetine Hydrochloride, Olanzapine)
Transport hazard class(es)	
Class	9
Subsidiary risk	-
Packing group	III
Environmental hazards	Yes
ERG Code	9L
Special precautions for user	Not available.
Other information	
Passenger and cargo aircraft	Allowed.
Cargo aircraft only	Allowed.

IMDG

UN number	UN3077
UN proper shipping name	ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Fluoxetine Hydrochloride, Olanzapine)
Transport hazard class(es)	
Class	9
Subsidiary risk	-
Packing group	III
Environmental hazards	
Marine pollutant	Yes
EmS	F-A, S-F
Special precautions for user	Not available.
Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code	Not available.

IATA; IMDG

Marine pollutant

15. Regulatory information

US federal regulations

This product is a "Hazardous Chemical" as defined by the OSHA Hazard Communication Standard, 29 CFR 1910.1200.
CERCLA/SARA Hazardous Substances - Not applicable.

TSCA Section 12(b) Export Notification (40 CFR 707, Subpt. D)

Not regulated.

CERCLA Hazardous Substance List (40 CFR 302.4)

Not listed.

SARA 304 Emergency release notification

Not regulated.

OSHA Specifically Regulated Substances (29 CFR 1910.1001-1050)

Not listed.

Superfund Amendments and Reauthorization Act of 1986 (SARA)

Hazard categories

Immediate Hazard - Yes
Delayed Hazard - Yes
Fire Hazard - No
Pressure Hazard - No
Reactivity Hazard - No

SARA 313 (TRI reporting)

Not regulated.

Other federal regulations

Clean Air Act (CAA) Section 112 Hazardous Air Pollutants (HAPs) List

Not regulated.

Clean Air Act (CAA) Section 112(r) Accidental Release Prevention (40 CFR 68.130)

Not regulated.

Safe Drinking Water Act (SDWA) Not regulated.

US state regulations

US. California Controlled Substances. CA Department of Justice (California Health and Safety Code Section 11100)

Not listed.

US. Massachusetts RTK - Substance List

Not regulated.

US. New Jersey Worker and Community Right-to-Know Act

Not listed.

US. Pennsylvania Worker and Community Right-to-Know Law

Not listed.

US. Rhode Island RTK

Not regulated.

US. California Proposition 65

US - California Proposition 65 - CRT: Listed date/Developmental toxin

Olanzapine (CAS 132539-06-1) Listed: October 1, 1992

International Inventories

Country(s) or region	Inventory name	On inventory (yes/no)*
Canada	Domestic Substances List (DSL)	No
Canada	Non-Domestic Substances List (NDSL)	No
United States & Puerto Rico	Toxic Substances Control Act (TSCA) Inventory	No

*A "Yes" indicates that all components of this product comply with the inventory requirements administered by the governing country(s)
A "No" indicates that one or more components of the product are not listed or exempt from listing on the inventory administered by the governing country(s).

16. Other information, including date of preparation or last revision

Issue date 12-11-2014

Revision date 09-04-2015

Version # 02

Lilly Lab Code

Health: 3
Fire: 1
Reactivity: 0
Special 1: A

Disclaimer

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 MERCHANT ABILITY 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.

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Revision Information

Exposure controls/personal protection: General hygiene considerations
Physical & Chemical Properties: Multiple Properties
Ecological Information: Ecotox Property Data
Regulatory Information: Risk Phrases - Class.
GHS: Classification