LUPIN LIMITED

SAFETY DATA SHEET

Section 1: Identification

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Material	**Paroxetine Extended-Release Tablets, USP** **12.5 mg, 25mg and 37.5 mg**
Manufacturer	**Lupin Limited** Pithampur (M.P.) - 454 775 India
Distributor	Lupin Pharmaceuticals, Inc. 111 South Calvert Street, Harborplace Tower, 21st Floor, Baltimore, Maryland 21202 United States Tel. 001-410-576-2000 Fax. 001-410-576-2221

Section 2: Hazard(s) Identification

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GHS classification	Exempt from requirements - product regulated as a medicinal product
Label elements	Exempt from requirements - product regulated as a medicinal product
Health	The use of MAOIs intended to treat psychiatric disorders with paroxetine extended-release tablets or within 14 days of stopping treatment with paroxetine extended-release tablets is contraindicated because of an increased risk of serotonin syndrome. The use of paroxetine extended-release tablets within 14 days of stopping an MAOI intended to treat psychiatric disorders is also contraindicated. Starting paroxetine extended-release tablets in a patient who is being treated with MAOIs such as linezolid or intravenous methylene blue is also contraindicated because of an increased risk of serotonin syndrome. Concomitant use with thioridazine is contraindicated. Concomitant use in patients taking pimozide is contraindicated. Paroxetine extended-release tablets are contraindicated in patients with a hypersensitivity to paroxetine or to any of the inactive ingredients in paroxetine extended-release tablets.
Environment	No information is available about the potential of this product to produce adverse environmental effects.

Section 3: Composition/Information on Ingredients

Section 3, Composition/information on ingredients

Ingredients	CAS
Paroxetine USP	61869-08-7

Section 4: First-Aid Measures

Section 4, First-aid measures

Ingestion

If swallowed, rinse mouth with water (only if the person is conscious). If ingestion of a large amount does occur, call a poison control center immediately. Do not induce vomiting without advice from poison control center.

Inhalation

Move to fresh air. If breathing is difficult, trained personnel should give oxygen. Call a physician if symptoms develop or persist. Under normal conditions of intended use, this material is not expected to be an inhalation hazard.

Skin Contact

Immediately flush skin with plenty of water. Take off contaminated clothing and wash before reuse. Get medical attention if symptoms occur.

Eye Contact

Rinse thoroughly with plenty of water for at least 15 minutes and consult a physician.

NOTES TO HEALTH PROFESSIONALS

Medical Treatment

Treat according to locally accepted protocols. For additional guidance, refer to the current prescribing information or to the local poison control information center. Protect the patient's airway and support ventilation and perfusion. Meticulously monitor and maintain, within acceptable limits, the patient's vital signs, blood gases, serum electrolytes, etc.

No specific antidotes are recommended. Treat according to locally accepted protocols. For additional guidance, refer to the current prescribing information or to the local poison control information center.

OVERDOSAGE

Since the introduction of immediate-release paroxetine hydrochloride in the United States, 342 spontaneous cases of deliberate or accidental overdosage during paroxetine treatment have been reported worldwide (circa 1999). These include overdoses with paroxetine alone and in combination with other substances. Of these, 48 cases were fatal and of the fatalities, 17 appeared to involve paroxetine alone. Eight fatal cases that documented the amount of paroxetine ingested were generally on founded by the ingestion of other drugs or alcohol or the presence of significant comorbid conditions. Of 145 non-fatal cases with known outcome, most recovered without sequelae. The largest known ingestion involved 2,000 mg of paroxetine (33 times the maximum recommended daily dose) in a patient who recovered.

Commonly reported adverse events associated with paroxetine overdosage include somnolence, coma, nausea, tremor, tachycardia, confusion, vomiting, and dizziness. Other notable signs and symptoms observed with overdoses involving paroxetine (alone or with other substances) include mydriasis, convulsions (including status epilepticus),

ventricular dysrhythmias (including torsade de pointes), hypertension, aggressive reactions, syncope, hypotension, stupor, bradycardia, dystonia, rhabdomyolysis, symptoms of hepatic dysfunction (including hepatic failure, hepatic necrosis, jaundice, hepatitis, and hepatic steatosis), serotonin syndrome, manic reactions, myoclonus, acute renal failure, and urinary retention.

No specific antidotes for paroxetine are known. Treatment should consist of those general measures employed in the management of overdosage with any drugs effective in the treatment of major depressive disorder.

Ensure an adequate airway, oxygenation, and ventilation. Monitor cardiac rhythm and vital signs. General supportive and symptomatic measures are also recommended. Induction of emesis is not recommended. Due to the large volume of distribution of this drug, forced diuresis, dialysis, hemoperfusion, or exchange perfusion are unlikely to be of benefit.

A specific caution involves patients taking or recently having taken paroxetine who might ingest excessive quantities of a tricyclic antidepressant. In such a case, accumulation of the parent tricyclic and an active metabolite may increase the possibility of clinically significant sequelae and extend the time needed for close medical observation.

In managing overdosage, consider the possibility of multiple-drug involvement. The physician should consider contacting a poison control center for additional information on the treatment of any overdose. Telephone numbers for certified poison control centers are listed in the *Physicians' Desk Reference* (PDR).

Section 5: Fire-Fighting Measures

Section 5, Fire-fighting measures

Fire and Explosion Hazards	Toxic gases may be emitted from fires involving this product, therefore self-contained breathing apparatus and full protective equipment are recommended for fire fighters.
Extinguishing Media	Water. Foam. Dry chemical powder. Carbon dioxide (CO_2).
Special Firefighting Procedures	For single units (packages): No special requirements needed. For larger amounts (multiple packages/pallets) of product: Since toxic, corrosive or flammable vapors might be evolved from fires involving this product and associated packaging, self-contained breathing apparatus and full protective equipment are recommended for firefighters.

Section 6: Accidental Release Measures

Section 6, Accidental release measures

Personal Precautions	Keep unnecessary personnel away. Keep people away from and upwind of spill/leak. Wear appropriate protective equipment and clothing during clean-up. Do not touch damaged containers or spilled material unless wearing appropriate protective clothing. Ensure adequate ventilation.

	Local authorities should be advised if significant spillages cannot be contained.
Environmental Precautions	Avoid release to the environment. Prevent further leakage or spillage if safe to do so. Avoid discharge into drains, water courses or onto the ground. Inform appropriate managerial or supervisory personnel of all environmental releases.
Clean-up Methods	Collect and place it in a suitable, properly labeled container for recovery or disposal.

Section 7: Handling and Storage

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Handling	Do not get this material in contact with eyes. Avoid contact with eyes, skin, and clothing. Do not taste or swallow. When using, do not eat, drink or smoke. Avoid release to the environment. Avoid prolonged exposure. Wash hands thoroughly after handling.
Storage	Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

Section 8: Exposure Controls/Personal Protection

Section 8, Exposure controls/personal protection

Wear appropriate clothing to avoid skin contact. Wash hands and arms thoroughly after handling.

Section 9: Physical and Chemical Properties

Section 9, Physical and chemical properties

Physical Form	Paroxetine extended-release tablets USP, 12.5 mg are supplied as yellow colored, round shaped, biconvex, film coated tablets imprinted with “L067” on one side and plain on other side. They are available as follows: Bottle of 30 tablets (NDC 68180-647-06) Bottle of 100 tablets (NDC 68180-647-01) Bottle of 500 tablets (NDC 68180-647-02) Bottle of 1000 tablets (NDC 68180-647-03) Paroxetine extended-release tablets USP, 25 mg are supplied as pink colored, round shaped, biconvex, film coated tablets imprinted with “L068” on one side and plain on other side. They are available as follows: Bottle of 30 tablets (NDC 68180-646-06) Bottle of 100 tablets (NDC 68180-646-01) Bottle of 500 tablets (NDC 68180-646-02) Bottle of 1000 tablets (NDC 68180-646-03)

Paroxetine extended-release tablets USP, 37.5 mg are supplied as blue colored, round shaped, biconvex tablets imprinted with “L069” on one side and plain on other side. They are available as follows:

Bottle of 30 tablets (NDC 68180-645-06)
Bottle of 100 tablets (NDC 68180-645-01)
Bottle of 500 tablets (NDC 68180-645-02)

Section 10: Stability and Reactivity

Section 10, Stability and reactivity

Stable under recommended storage conditions.

Section 11: Toxicological Information

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Carcinogenesis, Mutagenesis, Impairment of Fertility

Two-year carcinogenicity studies were conducted in rodents given paroxetine in the diet at 1, 5, and 25 mg/kg/day (mice) and 1, 5, and 20 mg/kg/day (rats). These doses are up to approximately 2 (mouse) and 3 (rat) times the MRHD on a mg/m^2 basis. There was a significantly greater number of male rats in the high-dose group with reticulum cell sarcomas (1/100, 0/50, 0/50, and 4/50 for control, low-, middle-, and high-dose groups, respectively) and a significantly increased linear trend across dose groups for the occurrence of lymphoreticular tumors in male rats. Female rats were not affected. Although there was a dose-related increase in the number of tumors in mice, there was no drug-related increase in the number of mice with tumors. The relevance of these findings to humans is unknown.

Paroxetine produced no genotoxic effects in a battery of 5 *in vitro* and 2 *in vivo* assays that included the following: Bacterial mutation assay, mouse lymphoma mutation assay, unscheduled DNA synthesis assay, and tests for cytogenetic aberrations *in vivo* in mouse bone marrow and *in vitro* in human lymphocytes and in a dominant lethal test in rats.

Some clinical studies have shown that SSRIs (including paroxetine) may affect sperm quality during SSRI treatment, which may affect fertility in some men.

A reduced pregnancy rate was found in reproduction studies in rats at a dose of paroxetine of 15 mg/kg/day, which is approximately twice the MRHD on a mg/m^2 basis. Irreversible lesions occurred in the reproductive tract of male rats after dosing in toxicity studies for 2 to 52 weeks. These lesions consisted of vacuolation of epididymal tubular epithelium at 50 mg/kg/day and atrophic changes in the seminiferous tubules of the testes with arrested spermatogenesis at 25 mg/kg/day (approximately 8 and 4 times the MRHD on a mg/m^2 basis).

Section 12: Ecological Information

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No relevant studies identified.

Section 13: Disposal Considerations

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Incinerate in an approved facility. Follow all federal state and local environmental regulations.

Section 14: Transport Information

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IATA/ICAO - Not Regulated

IATA Proper shipping Name	:	N/A
IATA UN/ID No	:	N/A
IATA Hazard Class	:	N/A
IATA Packaging Group	:	N/A
IATA Label	:	N/A

IMDG - Not Regulated

IMDG Proper shipping Name	:	N/A
IMDG UN/ID No	:	N/A
IMDG Hazard Class	:	N/A
IMDG Flash Point	:	N/A
IMDG Label	:	N/A

DOT - Not Regulated

DOT Proper shipping Name	:	N/A
DOT UN/ID No	:	N/A
DOT Hazard Class	:	N/A
DOT Flash Point	:	N/A
DOT Packing Group	:	N/A
DOT Label	:	N/A

Section 15: Regulatory Information

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This Section Contains Information relevant to compliance with other Federal and/or state laws.

Section 16: Other Information

Section 16: Other information

The above information is believed to be correct but does not purport to be all-inclusive and shall be used only as a guide. Nothing herein shall be deemed to create any warranty, express or implied. It is the responsibility of the user to determine the applicability of this information and the suitability of the material or product for any particular purpose.

Lupin shall not be held liable for any damage resulting from handling or from contact with the above product. Lupin reserves the right to revise this SDS.