LUPIN LIMITED

SAFETY DATA SHEET

Section 1: Identification

Section 1, Identification

Material	**Quetiapine Fumarate Extended-Release Tablet** **50 mg, 150 mg, 200 mg, 300 mg and 400 mg**
Manufacturer	**Lupin Limited** Pithampur – 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

Section 2, Hazard(s) identification

Fire and Explosion	Expected to be non-combustible.
Health	Hypersensitivity to quetiapine or to any excipients in the quetiapine fumarate extended-release tablet formulation. Anaphylactic reactions have been reported in patients treated with quetiapine fumarate extended-release tablet.
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**
Quetiapine Fumarate	111974-72-2

Section 4: First-Aid Measures

Section 4, First-aid measures

Ingestion	If conscious, give water to drink and induce vomiting. Do not attempt to give any solid or liquid by mouth if the exposed subject is unconscious or semi-conscious. Wash out the mouth with water. Obtain medical attention.

Inhalation	Move individual to fresh air. Obtain medical attention if breathing difficulty occurs. If not breathing, provide artificial respiration assistance.
Skin Contact	Remove contaminated clothing and flush exposed area with large amounts of water. Wash all exposed areas of skin with plenty of soap and water. Obtain medical attention if skin reaction occurs.
Eye Contact	Flush eyes with plenty of water. Get medical attention.

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.
OVERDOSAGE	**Human Experience** In clinical trials, survival has been reported in acute overdoses of up to 30 grams of quetiapine. Most patients who overdosed experienced no adverse reactions or recovered fully from the reported events. Death has been reported in a clinical trial following an overdose of 13.6 grams of quetiapine alone. In general, reported signs and symptoms were those resulting from an exaggeration of the drug's known pharmacological effects, i.e., drowsiness and sedation, tachycardia and hypotension. Patients with pre-existing severe cardiovascular disease may be at an increased risk of the effects of overdose. One case, involving an estimated overdose of 9600 mg, was associated with hypokalemia and first degree heart block. In post-marketing experience, there were cases reported of QT prolongation with overdose. There were also very rare reports of overdose of quetiapine fumarate tablet alone resulting in death or coma. **Management of Overdosage** In case of acute overdosage, establish and maintain an airway and ensure adequate oxygenation and ventilation. Gastric lavage (after intubation, if patient is unconscious) and administration of activated charcoal together with a laxative should be considered. The possibility of obtundation, seizure or dystonic reaction of the head and neck following overdose may create a risk of aspiration with induced emesis. Cardiovascular monitoring should commence immediately and should include continuous electrocardiographic monitoring to detect possible arrhythmias. If antiarrhythmic therapy is administered, disopyramide, procainamide and quinidine carry a theoretical hazard of additive QT-prolonging effects when administered in patients with acute overdosage of quetiapine fumarate extended-release tablet. Similarly it is reasonable to expect that the α-adrenergic-blocking properties of bretylium might be additive to those of quetiapine, resulting in problematic hypotension. There is no specific antidote to quetiapine fumarate extended-release tablet. Therefore, appropriate supportive measures should be instituted. The possibility of multiple drug involvement should be considered. Hypotension and circulatory collapse should be treated with appropriate measures such as intravenous fluids and/or sympathomimetic agents (epinephrine and dopamine should not be used, since β stimulation may worsen hypotension in the setting of quetiapine-induced α blockade). In cases of severe extrapyramidal symptoms, anticholinergic medication should be administered. Close medical supervision and monitoring should continue until the patient recovers.

Section 5: Fire-Fighting Measures

Section 5, Fire-fighting measures

Fire and Explosion Hazards	Assume that this product is capable of sustaining combustion.
Extinguishing Media	Water spray, carbon dioxide, dry chemical powder or appropriate foam.
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.
Hazardous Combustion Products	Hazardous combustion or decomposition products are expected when the product is exposed to fire.

Section 6: Accidental Release Measures

Section 6, Accidental release measures

Personal Precautions	Wear protective clothing and equipment consistent with the degree of hazard.
Environmental Precautions	For large spills, take precautions to prevent entry into waterways, sewers, or surface drainage systems.
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	No special control measures required for the normal handling of this product. Normal room ventilation is expected to be adequate for routine handling of this product.
Storage	Store quetiapine fumarate extended-release tablets at 25ºC (77ºF); excursions permitted to 15 to 30ºC (59 to 86ºF) [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

How Supplied

50 mg Tablets are peach to red colored, capsule shaped, biconvex, film coated tablets debossed with “LU” on one side and “K71” on the other side
Bottle of 60 tablets (NDC 68180-612-07)
Bottle of 100 tablets (NDC 68180-612-01)

150 mg Tablets are white colored, capsule shaped, biconvex, film coated tablets debossed with “LU” on one side and “K72” on the other side
Bottle of 60 tablets (NDC 68180-613-07)
Bottle of 100 tablets (NDC 68180-613-01)

200 mg Tablets are yellow colored, capsule shaped, biconvex, film coated tablets debossed with “LU” on one side and “K73” on the other side
Bottle of 60 tablets (NDC 68180-614-07)
Bottle of 100 tablets (NDC 68180-614-01)

300 mg Tablets are pale yellow colored, capsule shaped, biconvex, film coated tablets debossed with “LU” on one side and “K74” on the other side
Bottle of 60 tablets (NDC 68180-615-07)
Bottle of 100 tablets (NDC 68180-615-01)

400 mg Tablets are white colored, capsule shaped, biconvex, film coated tablets debossed with “LU” on one side and “K75” on the other side
Bottle of 60 tablets (NDC 68180-616-07)
Bottle of 100 tablets (NDC 68180-616-01)

Section 10: Stability and Reactivity

Section 10, Stability and reactivity

Stable under recommended storage conditions.

Section 11: Toxicological Information

Section 11, Toxicological information

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies were conducted in C57BL mice and Wistar rats. Quetiapine was administered in the diet to mice at doses of 20, 75, 250, and 750 mg/kg and to rats by gavage at doses of 25, 75, and 250 mg/kg for two years. These doses are equivalent to 0.1, 0.5, 1.5, and 4.5 times the maximum human dose (MRHD) of 800 mg/day based on mg/m^2 body surface area (mice) or 0.3, 1, and 3 times the MRHD based on mg/m^2 body surface area (rats). There were statistically significant increases in thyroid gland follicular adenomas in male mice at doses 1.5 and 4.5 times the MRHD on mg/m^2 body surface area and in male rats at a dose of 3 times the MRHD on mg/m^2 body surface area. Mammary gland adenocarcinomas were statistically significantly increased in female rats at all doses tested (0.3, 1, and 3 times the MRHD on mg/m^2 body surface area).

Thyroid follicular cell adenomas may have resulted from chronic stimulation of the thyroid gland by thyroid stimulating hormone (TSH) resulting from enhanced metabolism and clearance of thyroxine by rodent liver. Changes in TSH, thyroxine, and thyroxine clearance consistent with this mechanism were observed in subchronic toxicity studies in rat and mouse and in a 1-year toxicity study in rat; however, the results of these studies were not definitive. The relevance of the increases in thyroid follicular cell adenomas to human risk, through whatever mechanism, is unknown.

Antipsychotic drugs have been shown to chronically elevate prolactin levels in rodents. Serum measurements in a 1-year toxicity study showed that quetiapine increased median serum prolactin levels a maximum of 32- and 13-fold in male and female rats, respectively. Increases in mammary neoplasms have been found in rodents after chronic administration of other antipsychotic drugs and are considered to be prolactin-mediated. The relevance of this increased incidence of prolactin-mediated mammary gland tumors in rats to human risk is unknown.

The mutagenic potential of quetiapine was tested in the *in vitro* Ames bacterial gene mutation assay and in the *in vitro* mammalian gene mutation assay in Chinese Hamster Ovary cells. The clastogenic potential of quetiapine was tested in the *in vitro* chromosomal aberration assay in cultured human lymphocytes and in the *in vivo* bone marrow micronucleus assay in rats up to 500 mg/kg which is 6 times the maximum recommended human dose on mg/m^2 body surface area. Based on weight of evidence quetiapine was not mutagenic or clastogenic in these tests.

Quetiapine decreased mating and fertility in male Sprague-Dawley rats at oral doses of 50 and 150 mg/kg or approximately 1 and 3 times the maximum human dose (MRHD) of 800 mg/day on mg/m^2 body surface area. Drug-related effects included increases in interval to mate and in the number of matings required for successful impregnation. These effects continued to be observed at 3 times the MRHD even after a two-week period without treatment. The no-effect dose for impaired mating and fertility in male rats was 25 mg/kg, or 0.3 times the MRHD dose on mg/m^2 body surface area. Quetiapine adversely affected mating and fertility in female Sprague-Dawley rats at an oral dose approximately 1 times the MRHD of 800 mg/day on mg/m^2 body surface area. Drug-related effects included decreases in matings and in matings resulting in pregnancy, and an increase in the interval to mate. An increase in irregular estrus cycles was observed at doses of 10 and 50 mg/kg, or approximately 0.1 and 1 times the MRHD of 800 mg/day on mg/m^2 body surface area. The no-effect dose in female rats was1 mg/kg or 0.01 times the MRHD of 800 mg/day on mg/m^2 body surface area.

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.