LUPIN LIMITED

SAFETY DATA SHEET

Section 1: Identification

Section 1, Identification

Material	**Zileuton Extended-Release Tablet 600 mg**
Manufacturer	**Lupin Limited** Nagpur 441 108 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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Fire and Explosion	Expected to be non-combustible.
Health	The use of Zileuton Extended-Release Tablets are contraindicated in patients with: • Active liver disease or persistent hepatic function enzyme elevations greater than or equal to 3 times the upper limit of normal (≥3×ULN). • A history of allergic reaction to zileuton or any of the ingredients of Zileuton Extended-Release Tablets (e.g., rash, eosinophilia, etc.).
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**
Zileuton	111406-87-2

Section 4: First-Aid Measures

Section 4, First-aid measures

Ingestion	Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.

Inhalation	Remove to fresh air and keep patient at rest. Seek medical attention immediately.
Skin Contact	Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.
Eye Contact	Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.

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 of acute overdose with zileuton is limited. A patient in a clinical study took between 6.6 and 9.0 grams of zileuton immediate-release tablets in a single dose. Vomiting was induced and the patient recovered without sequelae. Zileuton is not removed by dialysis. Should an overdose occur, the patient should be treated symptomatically and supportive measures instituted as required. If indicated, elimination of unabsorbed drug should be achieved by emesis or gastric lavage; usual precautions should be observed to maintain the airway. A Certified Poison Control Center should be consulted for up-to-date information on management of overdose with Zileuton Extended-Release Tablets.

Section 5: Fire-Fighting Measures

Section 5, Fire-fighting measures

Fire and Explosion Hazards	Fine particles (such as dust and mists) may fuel fires/explosions.
Extinguishing Media	Extinguish fires with CO_2, extinguishing powder, foam, or water.
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	Personnel involved in clean-up should wear appropriate personal protective equipment. Minimize exposure.
Environmental Precautions	Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.

Clean-up Methods	Contain the source of spill if it is safe to do so. Collect spilled material by a method that controls dust generation. A damp cloth or a filtered vacuum should be used to clean spills of dry solids. Clean spill area thoroughly.

Section 7: Handling and Storage

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Handling	If tablets or capsules are crushed and/or broken, avoid breathing dust and avoid contact with eyes, skin, and clothing. When handling, use appropriate personal protective equipment. Wash thoroughly after handling. Releases to the environment should be avoided.
Storage	Store at 20°C to 25°C (68°F to 77°F), excursions permitted between 15°C to 30°C (between 59°F to 86°F). [See USP controlled room temperature]. Protect from light.

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	Zileuton Extended-Release Tablets are white colored, oval shaped, film coated tablets, debossed with 'LU' on one side and 'R21' on other side; they are available in bottles of 60 tablets (NDC 68180-169-07), 120 tablets (NDC 68180-169-16) and 180 tablets (NDC 68180-169-26).

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

In 2-year carcinogenicity studies, increases in the incidence of liver, kidney, and vascular tumors in female mice and a trend toward an increase in the incidence of liver tumors in male mice were observed at 450 mg/kg/day (providing approximately 5 times [females] or 8 times [males] the systemic exposure [AUC=64 µg·hr/mL] achieved at the MRHD). No increase in the incidence of tumors was observed at 150 mg/kg/day (providing approximately 2 to 3 times the systemic exposure [AUC] achieved at the

MRHD). In rats, an increase in the incidence of kidney tumors was observed in both sexes at 170 mg/kg/day (providing approximately 8 times [males] or 16 times [females] the systemic exposure [AUC] achieved at the MRHD). No increased incidence of kidney tumors was seen at 80 mg/kg/day (providing approximately 4 times [males] or 7 times [females] the systemic exposure [AUC] achieved at the MRHD). Although a dose-related increased incidence of benign Leydig cell tumors was observed, Leydig cell tumorigenesis was prevented by supplementing male rats with testosterone.

Zileuton was negative in genotoxicity studies including bacterial reverse mutation (Ames) using *S. typhimurium* and *E. coli*, chromosome aberration in human lymphocytes, *in vitro* unscheduled DNA synthesis (UDS), in rat hepatocytes with or without zileuton pretreatment and in mouse and rat kidney cells with zileuton pretreatment, and mouse micronucleus assays. However, a dose- related increase in DNA adduct formation was reported in kidneys and livers of female mice treated with zileuton. Although some evidence of DNA damage was observed in a UDS assay in hepatocytes isolated from Aroclor-1254-treated rats, no such finding was noticed in hepatocytes isolated from monkeys, where the metabolic profile of zileuton is more similar to that of humans.

In reproductive performance/fertility studies, zileuton produced no effects on fertility in rats at oral doses up to 300 mg/kg/day (providing at least 10 times [male rats] and greater than 20 times [female rats] the systemic exposure [AUC] achieved at the MRHD). However, reduction in fetal implants was observed at oral doses of 150 mg/kg/day and higher (providing approximately 20 times the systemic exposure [AUC] achieved at the MRHD). Comparative systemic exposure (AUC) is based on measurements in male rats or nonpregnant female rats obtained from the comparable doses of 3-month or 1-year general toxicity study at similar dosages. Increases in gestation length, prolongation of estrus cycle, and increases in stillbirths were observed at oral doses of 75 mg/kg/day and higher (providing approximately 7 times the systemic exposure [AUC] achieved at the MRHD on an AUC basis with data obtained from the comparable doses of 2-year dietary carcinogenicity study). No adverse effects were observed at 15 mg/kg/day in the study at estimated exposure similar to that at the MRHD.

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.