LUPIN LIMITED

SAFETY DATA SHEET

Section 1: Identification

Section 1, Identification

Material	**Tramadol Hydrochloride Extended-Release Tablets USP C IV 100 mg, 200 mg & 300 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

Section 2, Hazard(s) identification

Fire and Explosion

This product is Non-Hazardous and is approved by the FDA. It is an aqueous solution and is not considered to constitute a Hazard.

Health

Tramadol hydrochloride extended-release tablets are contraindicated for:

- all children younger than 12 years of age.
- post-operative management in children younger than 18 years of age following tonsillectomy and/or adenoidectomy.

Tramadol hydrochloride extended-release tablets are also contraindicated in patients with:

- Significant respiratory depression.
- Acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment.
- Known or suspected gastrointestinal obstruction, including paralytic ileus.
- Hypersensitivity to tramadol (e.g., anaphylaxis).
- Concurrent use of monoamine oxidase inhibitors (MAOIs) or use within the last 14 days.

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**
Tramadol Hydrochloride USP	36282-47-0

Section 4: First-Aid Measures

Section 4, First-aid measures

Ingestion	Get medical attention. Do not induce vomiting unless directed by medical personnel. Never give anything by mouth to an unconscious person.
Inhalation	Remove to fresh air, If not breathing, give artificial respiration. Get medical attention.
Skin Contact	Wash off immediately with plenty of water. Continue to rinse for at least 15 minutes. Immediately take off all contaminated clothing. Get medical attention if irritation develops and persists.
Eye Contact	Immediately flush eyes with water for at least 15 minutes. If irritation occurs or persist, 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	Acute overdosage with tramadol hydrochloride extended-release tablets can be manifested by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted pupils, and, in some cases, pulmonary edema, bradycardia, QT prolongation, hypotension, partial or complete airway obstruction, atypical snoring, and death. Marked mydriasis rather than miosis may be seen with hypoxia in overdose situations. In case of overdose, priorities are the reestablishment of a patent and protected airway and institution of assisted or controlled ventilation, if needed. Employ other supportive measures (including oxygen and vasopressors) in the management of circulatory shock and pulmonary edema as indicated. Cardiac arrest or arrhythmias will require advanced life-support techniques. Opioid antagonists, such as naloxone,, are specific antidotes to respiratory depression resulting from opioid overdose. For clinically significant respiratory or circulatory depression secondary to opioid overdose, administer an opioid antagonist. While naloxone will reverse some, but not all, symptoms caused by overdosage with tramadol, the risk of seizures is also increased with naloxone administration. In animals, convulsions following the administration of toxic doses of tramadol hydrochloride extended-release tablets could be suppressed with barbiturates or benzodiazepines but were increased with naloxone. Naloxone administration did not change the lethality of an overdose in mice. Hemodialysis is not expected to be helpful in an overdose because it removes less than 7% of the administered dose in a 4-hour dialysis period. Because the duration of opioid reversal is expected to be less than the duration of action of tramadol in tramadol hydrochloride extended-release tablets, carefully monitor the patient until spontaneous respiration is reliably reestablished. Tramadol hydrochloride extended-release tablets will

continue to release tramadol and add to the tramadol load for 24 to 48 hours or longer following ingestion, necessitating prolonged monitoring. If the response to an opioid antagonist is suboptimal or only brief in nature, administer additional antagonist as directed by the product's prescribing information.

In an individual physically dependent on opioids, administration of the recommended usual dosage of the antagonist will precipitate an acute withdrawal syndrome. The severity of the withdrawal symptoms experienced will depend on the degree of physical dependence and the dose of the antagonist administered. If a decision is made to treat serious respiratory depression in the physically dependent patient, administration of the antagonist should be initiated with care and by titration with smaller than usual doses of the antagonist.

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 suitable protective clothing, gloves and eye/face protection.
Environmental Precautions	Avoid release to the environment.
Clean-up Methods	Collect and place it in a suitable, properly labeled container for recovery or disposal.

Section 7: Handling and Storage

Section 7, Handling and storage

Handling	Minimize dust generation and accumulation. 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 hands and any exposed skin.
Storage	Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature]. Store tramadol hydrochloride extended-release tablets securely and dispose of properly.

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

HOW SUPPLIED
Tramadol hydrochloride extended-release tablets USP are supplied in the following package and dose strength forms:

100 mg tablets (white to off-white circular, biconvex, beveled edge, coated) imprinted with 'L010' on one side and plain on the other side.

Bottles of 30 tablets	NDC 68180-697-06
Bottles of 100 tablets	NDC 68180-697-01
Bottles of 500 tablets	NDC 68180-697-02

200 mg tablets (white to off-white circular, biconvex, beveled edge, coated) imprinted with 'L011' on one side and plain on the other side.

Bottles of 30 tablets	NDC 68180-698-06
Bottles of 100 tablets	NDC 68180-698-01
Bottles of 500 tablets	NDC 68180-698-02

300 mg tablets (white to off-white circular, biconvex, beveled edge, coated) imprinted with 'L012' on one side and plain on the other side

Bottles of 30 tablets	NDC 68180-699-06
Bottles of 100 tablets	NDC 68180-699-01

Section 10: Stability and Reactivity

Section 10, Stability and reactivity

The product is stable and non-reactive under normal conditions of use, storage and transport.

Section 11: Toxicological Information

Section 11, Toxicological information

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity assessment has been conducted in mice, rats and p53(+/-) heterozygous mice. A slight but statistically significant increase in two common murine tumors, pulmonary and hepatic, was observed in an NMRI mouse carcinogenicity study, particularly in aged mice. Mice were dosed orally up to 30 mg/kg in the drinking water (0.5 times the maximum recommended daily human dosage or MRHD) for approximately two years, although the study was not done with the Maximum Tolerated Dose. This finding is not believed to suggest risk in humans.

No evidence of carcinogenicity was noted in a rat 2-year carcinogenicity study testing oral doses of up to 30 mg/kg in the drinking water (1 times the MRHD). In a second rat study, no evidence of carcinogenicity was noted in rats at oral doses up to 75 mg/kg/day for males and 100 mg/kg/day for

females (approximately 2-fold the maximum recommended human daily dose MRHD) for two years. However, the excessive decrease in body weight gain observed in the rat study might have reduced their sensitivity to any potential carcinogenic effect of the drug. No carcinogenic effect of tramadol was observed in p53(+/–)-heterozygous mice at oral doses up to 150 mg/kg/day for 26 weeks.

Tramadol was mutagenic in the presence of metabolic activation in the mouse lymphoma assay. Tramadol was not mutagenic in the *in vitro* bacterial reverse mutation assay using *Salmonella* and *E. coli* (Ames), the mouse lymphoma assay in the absence of metabolic activation, the *in vitro* chromosomal aberration assay, or the *in vivo* micronucleus assay in bone marrow.

No effects on fertility were observed for tramadol at oral dose levels up to 50 mg/kg in male rats and 75 mg/kg in female rats. These dosages are 1.2 and 1.8 times the maximum recommended human daily dose based on body surface area, respectively.

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.