MATERIAL SAFETY DATA SHEET

1. IDENTIFICATION OF THE SUBSTANCE AND THE COMPANY

Material **Trandolapril Tablets**
1 mg, 2 mg & 4 mg Tablets

Manufacturer Lupin Limited
Mumbai 400 098 INDIA

Distributor Lupin Pharmaceuticals, Inc.
Harborplace Tower, 21st Floor
111, South Calvert Street
Baltimore, MD 21202
United States
Tel. 001-410-576-2000
Fax. 001-410-576-2221

2. COMPOSITION / INFORMATION ON INGREDIENTS

Ingredients	CAS	Quantity
Trandolapril	87679-37-6	1 mg, 2 mg or 4 mg/Tablets
Non-hazardous ingredients	----------	q.s.

3. HAZARD IDENTIFICATION

Fire and Explosion Assume that this product is capable of sustaining combustion.

Health Exposure might occur via skin; eyes; ingestion; inhalation.
May cause sensitization by inhalation or skin contact.

Environment No information is available about the potential of this product to produce adverse environmental effects.

4. FIRST AID MEASURES

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.

Drug Interactions

Concomitant diuretic therapy:

As with other ACE inhibitors, patients on diuretics, especially those on recently instituted diuretic therapy, may experience an excessive reduction of blood pressure after initiation of therapy with trandolapril. The possibility of exacerbation of hypotensive effects with trandolapril may be minimized by either discontinuing the diuretic or cautiously increasing salt intake prior to initiation of treatment with trandolapril. If it is not possible to discontinue the diuretic, the starting dose of trandolapril should be reduced.

Agents increasing serum potassium:

Trandolapril can attenuate potassium loss caused by thiazide diuretics and increase serum potassium when used alone. Use of potassium-sparing diuretics (spironolactone, triamterene, or amiloride), potassium supplements, or potassium-containing salt substitutes concomitantly with ACE inhibitors can increase the risk of hyperkalemia. If concomitant use of such agents is indicated, they should be used with caution and with appropriate monitoring of serum potassium.

Lithium:

Increased serum lithium levels and symptoms of lithium toxicity have been reported in patients receiving concomitant lithium and ACE inhibitor therapy. These drugs should be coadministered with caution, and frequent monitoring of serum lithium levels is recommended. If a diuretic is also used, the risk of lithium toxicity may be increased.

Other:

No clinically significant interaction has been found between trandolaprilat and food, cimetidine, digoxin, or furosemide. The anticoagulant effect of warfarin was not significantly changed by trandolapril.

Antidotes

No specific antidote exists.

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.

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.

7. HANDLING AND STORAGE

Handling	No special precautions are necessary when handling packed product. In case of accident, avoid breathing dust from crushed tablets. Avoid contact with skin and eyes. Wash hands after use.
Storage	Store at 20° - 25°C (68° - 77°F). [See USP Controlled Room Temperature].

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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

9. PHYSICAL AND CHEMICALS PROPERTIES

Physical Form	Tablets
Appearance	1 mg – Pink, round, biconvex tablets. 2 mg – Yellow, round, biconvex tablets. 4 mg – Brick red, round, biconvex tablets.

10. STABILITY AND REACTIVITY

Stable under recommended storage conditions.

11. TOXICOLOGICAL INFORMATION

Oral Toxicity	Not expected to be toxic following ingestion of recommended maximum daily dose.
Inhalation Toxicity	Can produce respiratory irritation. Adverse effects might occur following inhalation.
Skin Effects	Irritation might occur following direct contact.
Eye Effects	Irritation might occur following direct contact with eyes.
Gastrointestinal Reactions	abdominal distention, abdominal pain/cramps, constipation, dyspepsia, diarrhea, vomiting, pancreatitis.
Anaphylactoid and Possibly Related Reactions	Presumably because angiotensin converting enzyme inhibitors affect the metabolism of eicosanoids and polypeptides, including endogenous bradykinin, patients receiving ACE inhibitors, including trandolapril, may be subject to a variety of adverse reactions, some of them serious.
Carcinogenesis, Mutagenesis, Impairment of Fertiliy	Long-term studies were conducted with oral trandolapril administered by gavage to mice (78 weeks) and rats (104 and 106 weeks). No evidence of carcinogenic potential was seen in mice dosed up to 25 mg/kg/day (85 mg/m^2/day) or rats dosed up to 8 mg/kg/day (60 mg/m^2/day). These doses are 313 and 32 times (mice), and 100 and 23 times (rats) the maximum recommended human daily dose (MRHDD) of 4 mg based on body-weight and body-surface-area, respectively assuming a 50 kg individual. The genotoxic potential of trandolapril was

evaluated in the microbial mutagenicity (Ames) test, the point mutation and chromosome aberration assays in Chinese hamster V79 cells, and the micronucleus test in mice. There was no evidence of mutagenic or clastogenic potential in these *in vitro* and *in vivo* assays.

Reproduction studies in rats did not show any impairment of fertility at doses up to 100 mg/kg/day (710 mg/m^2/day) of trandolapril, or 1250 and 260 times the MRHDD on the basis of body-weight and body-surface-area, respectively.

Pregnancy

Pregnancy Categories C (first trimester) and D (second and third trimesters.

Nursing Mothers

Radiolabeled trandolapril or its metabolites are secreted in rat milk. Trandolapril should not be administered to nursing mothers.

Overdose

No data are available with respect to overdosage in humans. The oral LD_{50} of trandolapril in mice was 4875 mg/Kg in males and 3990 mg/Kg in females. In rats, an oral dose of 5000 mg/Kg caused low mortality (1 male out of 5; 0 females). In dogs, an oral dose of 1000 mg/Kg did not cause mortality and abnormal clinical signs were not observed. In humans the most likely clinical manifestation would be symptoms attributable to severe hypotension.

Laboratory determinations of serum levels of trandolapril and its metabolites are not widely available, and such determinations have, in any event, no established role in the management of trandolapril overdose. No data are available to suggest that physiological maneuvers (e.g., maneuvers to change the pH of the urine) might accelerate elimination of trandolapril and its metabolites. Trandolaprilat is removed by hemodialysis. Angiotensin II could presumably serve as a specific antagonist antidote in the setting of trandolapril overdose, but angiotensin II is essentially unavailable outside of scattered research facilities. Because the hypotensive effect of trandolapril is achieved through vasodilation and effective hypovolemia, it is reasonable to treat trandolapril overdose by infusion of normal saline solution.

12. ECOLOGICAL INFORMATION

No information available.

13. DISPOSAL CONSIDERATION

Waste Disposal Method

Dispose of by incineration in accordance with applicable international, national, state, and/or local waste disposal regulations.

14. TRANSPORT INFORMATION

The Material Safety Data Sheet (MSDS) should accompany all shipments for reference in the event of spillage or accidental release. Transportation and shipping of this product is not restricted. It has no known, significant hazards requiring special packaging or labeling for air, maritime, or ground transport purposes.

15. REGULATORY INFORMATION

No information available.

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 MSDS.