MATERIAL SAFETY DATA SHEET

1. IDENTIFICATION OF THE SUBSTANCE AND THE COMPANY

Material **Losartan Potassium and Hydrochlorothiazide Tablets 50 mg/12.5 mg, 100 mg/12.5 mg & 100 mg/25 mg**

Manufacturer
Lupin Limited
Goa 403 722
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
Losartan Potassium	124750-99-8	50 mg/tablet,100 mg/tablet
Hydrochlorothiazide	00058-93-5	12.5 mg/tablet, 25 mg/tablet
Non-hazardous ingredients	----------	q.s.

3. HAZARDOUS IDENTIFICATION

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

Health Losartan and hydrochlorothiazide is contraindicated in patients who are hypersensitive to any component of this product. Because of the hydrochlorothiazide component, this product is contraindicated in patients with anuria or hypersensitivity to other sulfonamide-derived drugs.

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

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

Losartan Potassium

Significant lethality was observed in mice and rats after oral administration of 1000 mg/kg and 2000 mg/kg, respectively, about 44 and 170 times the maximum recommended human dose on a mg/m^2 basis.

Limited data are available in regard to overdosage in humans. The most likely manifestation of overdosage would be hypotension and tachycardia; bradycardia could occur from parasympathetic (vagal) stimulation. If symptomatic hypotension should occur, supportive treatment should be instituted.
Neither losartan nor its active metabolite can be removed by hemodialysis.

Hydrochlorothiazide

The oral LD_{50} of hydrochlorothiazide is greater than 10 g/kg in both mice and rats. The most common signs and symptoms observed are those caused by electrolyte depletion (hypokalemia, hypochloremia, hyponatremia) and dehydration resulting from excessive diuresis. If digitalis has also been administered, hypokalemia may accentuate cardiac arrhythmias. The degree to which hydrochlorothiazide is removed by hemodialysis has not been established.

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.

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 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 at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

Keep container tightly closed. Protect from light.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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

9. PHYSICAL & CHEMICAL PROPERTIES

Physical Form Losartan and hydrochlorothiazide tablets 50 mg/12.5 mg are supplied as yellow, capsule shaped, biconvex, film-coated tablets, debossed with ‘LU’ on one side and ‘M41’ on the other side.

NDC 68180-215-06: Bottles of 30 Tablets
NDC 68180-215-09: Bottles of 90 Tablets
NDC 68180-215-01: Bottles of 100 Tablets
NDC 68180-215-03 Bottle of 1000 Tablets

Losartan and hydrochlorothiazide tablets 100 mg/12.5 mg are supplied as white, oval shaped, biconvex, film-coated tablets, debossed with 'LU' on one side and 'M42' on the other side.

NDC 68180-216-06: Bottles of 30 Tablets
NDC 68180-216-09: Bottles of 90 Tablets
NDC 68180-216-01: Bottles of 100 Tablets
NDC 68180-216-03 Bottle of 1000 Tablets

Losartan and hydrochlorothiazide tablets 100 mg/25 mg are supplied as yellow, tear drop shaped, biconvex, film-coated tablets, debossed with 'LU' on one side and 'M43' on the other side.

NDC 68180-217-06: Bottles of 30 Tablets
NDC 68180-217-09: Bottles of 90 Tablets
NDC 68180-217-01: Bottles of 100 Tablets
NDC 68180-217-03 Bottle of 1000 Tablets

10. STABILITY AND REACTIVITY

Stable under recommended storage conditions.

11. TOXICOLOGICAL INFORMATION

Carcinogenesis, Mutagenesis, Impairment of Fertility:

No carcinogenicity studies have been conducted with the losartan potassium-hydrochlorothiazide combination.

Losartan potassium-hydrochlorothiazide when tested at a weight ratio of 4:1, was negative in the Ames microbial mutagenesis assay and the V-79 Chinese hamster lung cell mutagenesis assay. In addition, there was no evidence of direct genotoxicity in the *in vitro* alkaline elution assay in rat hepatocytes and *in vitro* chromosomal aberration assay in Chinese hamster ovary cells at noncytotoxic concentrations.

Losartan potassium, coadministered with hydrochlorothiazide, had no effect on the fertility or mating behavior of male rats at dosages up to 135 mg/kg/day of losartan and 33.75 mg/kg/day of hydrochlorothiazide. These dosages have been shown to provide respective systemic exposures (AUCs) for losartan, its active metabolite and hydrochlorothiazide that are approximately 60, 60 and 30 times greater than those achieved in humans with 100 mg of losartan potassium in combination with 25 mg of hydrochlorothiazide. In female rats, however, the coadministration of doses as low as 10 mg/kg/day of losartan and 2.5 mg/kg/day of hydrochlorothiazide was associated with slight but statistically significant decreases in fecundity and fertility indices. AUC values for losartan, its active metabolite and hydrochlorothiazide, extrapolated from data obtained with losartan administered to rats at a dose of 50 mg/kg/day in combination with 12.5 mg/kg/day of hydrochlorothiazide, were approximately 6, 2, and 2 times greater than

those achieved in humans with 100 mg of losartan in combination with 25 mg of hydrochlorothiazide.

12. ECOLOGICAL INFORMATION

No relevant studies identified.

13. DISPOSAL CONSIDERATION

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

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.