MATERIAL SAFETY DATA SHEET

1. IDENTIFICATION OF THE SUBSTANCE AND THE COMPANY

Material **Amlodipine Besylate and Benazepril Hydrochloride Capsules 2.5 mg/10 mg, 5 mg/10 mg, 5 mg/20 mg and 10 mg/20 mg**

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
Amlodipine Besylate USP and	111470-99-6	2.5 mg or 5 mg or 10 mg
Benazepril Hydrochloride USP	86541-74-4	10 mg or 20 mg

3. HAZARD IDENTIFICATION

Fire and Explosion Expected to be non-combustible

Health Amlodipine besylate and benazepril hydrochloride are contraindicated in patients who are hypersensitive to benazepril, to any other ACE inhibitor, or to amlodipine

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

4. FIRST AID MEASURE

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 — Only a few cases of human overdose with amlodipine have been reported. One patient was asymptomatic after 250 mg ingestion; another, who combined 70 mg of amlodipine with an unknown large quantity of a benzodiazepine, developed refractory shock and died.

Human overdoses with any combination of amlodipine and benazepril have not been reported. In scattered reports of human overdoses with benazepril and other ACE inhibitors, there are no reports of death.

When mice were given single oral doses of benazepril/amlodipine, mortality was 20% at 50:25 mg/kg, 10% at 100:50 mg/kg, and 100% at 500:250 mg/kg. In rats, mortality was 25% (pooling two studies) at 500:250 mg/kg and 100% at 900:450 mg/kg.

5. FIRE FIGHTING MEASURE

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 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.]

Protect from moisture. Dispense in a tight container (USP).

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical Form

Amlodipine besylate and benazepril hydrochloride 2.5/10 mg capsules are size '2' capsules with white opaque cap and white opaque body, imprinted with 'LU' (in black ink) on cap and 'E11' (in black ink) on body, containing white to off-white powder and white to off-white, circular tablet debossed with '1' on one side and plain on the other side.

NDC 68180-755-01 Bottles of 100 capsules.

Amlodipine besylate and benazepril hydrochloride 5/10 mg capsules are size '2' capsule with light brown opaque cap and light brown opaque body, imprinted with 'LU' (in black ink) on cap and 'E12' (in black ink) on body, containing white to off-white powder and white to off-white, circular tablet debossed with '1' on one side and plain on the other side.

NDC 68180-756-01 Bottles of 100 capsules.
NDC 68180-756-02 Bottles of 500 capsules.

Amlodipine besylate and benazepril hydrochloride 5/20 mg capsules are size '2' capsule with flesh opaque cap and flesh opaque body, imprinted with 'LU' (in black ink) on cap and 'E13' (in black ink) on body, containing white to off-white powder and white to off-white, circular tablet debossed with '2' on one side and plain on the other side.

NDC 68180-757-01 Bottles of 100 capsules.
NDC 68180-757-02 Bottles of 500 capsules.

Amlodipine besylate and benazepril hydrochloride 10/20 mg capsules are size '2' capsule with purple cap and purple body, imprinted with 'LU' (in black ink) on cap and 'E14' (in black ink) on body, containing white to off-white powder and white to off-white, circular tablet debossed with '2' on one side and plain on the other side.

NDC 68180-758-01 Bottles of 100 capsules.
NDC 68180-758-02 Bottles of 500 capsules.

10. STABILITY AND REACTIVITY

Stable under recommended storage conditions.

11. TOXICOLOGICAL INFORMATION

Carcinogenesis, Mutagenesis Impairment of Fertility

No evidence of carcinogenicity was found when benazepril was given, via dietary administration, to rats and mice for 104 weeks at doses up to 150 mg/kg/day. On a body-weight basis, this dose is over 100 times the maximum

recommended human dose; on a body-surface-area basis, this dose is 18 times (rats) and 9 times (mice) the maximum recommended human dose.

No mutagenic activity was detected in the Ames test in bacteria, in an *in vitro* test for forward mutations in cultured mammalian cells, or in a nucleus anomaly test. At doses of 50-500 mg/kg/day (38-375 times the maximum recommended human dose on a body-weight basis; 6-61 times the maximum recommended dose on a body-surface-area basis), benazepril had no adverse effect on the reproductive performance of male and female rats.

Rats and mice treated with amlodipine in the diet for 2 years, at concentrations calculated to provide daily dosage levels of 0.5, 1.25, and 2.5 mg/kg/day, showed no evidence of carcinogenicity. For mice, but not for rats, the highest dose was close to the maximum tolerated dose. On a mg/m^2 basis, this dose given to mice was approximately equal to the maximum recommended clinical dose. On the same basis, the same dose given to rats was approximately twice the maximum recommended clinical dose.

Mutagenicity studies with amlodipine revealed no drug-related effects at either the gene or chromosome levels.
There was no effect on the fertility of rats treated with amlodipine (males for 64 days and females for 14 days prior to mating) at doses up to 10 mg/kg/day (8 times the maximum recommended human dose of 10 mg on a mg/m^2 basis, assuming a 50 kg person).

No adverse effects on fertility occurred when the benazepril:amlodipine combination was given orally to rats of either sex at dose ratios up to 15:7.5 mg/kg/day (benazepril:amlodipine), prior to mating and throughout gestation.

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.