

# LUPIN LIMITED

## SAFETY DATA SHEET

### Section 1: Identification

#### Section 1, Identification

<b>Material</b>	<b>Amlodipine Besylate and Benazepril Hydrochloride Capsules 2.5 mg/10 mg, 5 mg/10 mg, 5 mg/20 mg, 5 mg/40 mg, 10 mg/20 mg and 10 mg/40 mg</b>
<b>Manufacturer</b>	<b>Lupin Limited, India</b>
<b>Distributor</b>	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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<b>Fire and Explosion</b>	Expected to be non-combustible.
<b>Health</b>	Do not co-administer aliskiren with angiotensin receptor blockers, ACE inhibitors, including amlodipine besylate and benazepril hydrochloride in patients with diabetes.  Amlodipine besylate and benazepril hydrochloride is contraindicated in patients with a history of angioedema, with or without previous ACE inhibitor treatment, or patients who are hypersensitive to benazepril, to any other ACE inhibitor, to amlodipine, or to any of the excipients of amlodipine besylate and benazepril hydrochloride.
<b>Environment</b>	No information is available about the potential of this product to produce adverse environmental effects.

### Section 3: Composition/Information on Ingredients

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<b>Ingredients</b>	<b>CAS</b>
Amlodipine Besylate USP	111470-99-6
Benazepril Hydrochloride USP	86541-74-4

## Section 4: First-Aid Measures

### Section 4, First-aid measures

<b>Ingestion</b>	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.
<b>Inhalation</b>	Move individual to fresh air. Obtain medical attention if breathing difficulty occurs. If not breathing, provide artificial respiration assistance.
<b>Skin Contact</b>	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.
<b>Eye Contact</b>	Flush eyes with plenty of water. Get medical attention.

### NOTES TO HEALTH PROFESSIONALS

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

#### **Treatment**

Patients should be admitted to hospital and, generally, should be managed in an intensive care setting, with continuous monitoring of cardiac function, blood gases, and blood biochemistry. Emergency supportive measures such as artificial ventilation or cardiac pacing should be instituted if appropriate.

In the event of a potentially life-threatening oral overdose, use induction of vomiting or gastric lavage and/or activated charcoal to remove the drug from the gastrointestinal tract (only if presented within 1 hour after ingestion of amlodipine and benazepril hydrochloride).

Other clinical manifestations of overdose should be managed symptomatically based on modern methods of intensive care.

To obtain up-to-date information about the treatment of overdose, a good resource is your certified Regional Poison-Control Center. Telephone numbers of certified poison-control centers are listed in the Physicians' Desk Reference (PDR). In managing overdose, consider the possibilities of multiple-drug overdoses, drug-drug interactions, and unusual drug kinetics in your patient.

The most likely effect of overdose with amlodipine and benazepril hydrochloride capsule is vasodilation, with consequent hypotension and tachycardia. Simple repletion of central fluid volume (Trendelenburg positioning, infusion of crystalloids) may be sufficient therapy, but pressor agents (norepinephrine or high-dose dopamine) may be required. With abrupt return of peripheral vascular tone, overdoses of other dihydropyridine calcium channel blockers have sometimes progressed to pulmonary edema, and patients must be monitored for this complication.

Analyses of bodily fluids for concentrations of amlodipine, benazepril, or their metabolites are not widely available. Such analyses are, in any event, not known to be of value in therapy or prognosis.

No data are available to suggest physiologic maneuvers (e.g., maneuvers to change the pH of the urine) that might accelerate elimination of amlodipine, benazepril, or their metabolites. Benazeprilat is only slightly dialyzable; attempted clearance of amlodipine by hemodialysis or hemo-perfusion has not been reported, but amlodipine's high protein binding makes it unlikely that these interventions will be of value.

Angiotensin II could presumably serve as a specific antagonist-antidote to benazepril, but angiotensin II is essentially unavailable outside of scattered research laboratories.

## 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

<b>Personal Precautions</b>	Wear protective clothing and equipment consistent with the degree of hazard.
<b>Environmental Precautions</b>	For large spills, take precautions to prevent entry into waterways sewers, or surface drainage systems.
<b>Clean-up Methods</b>	Collect and place it in a suitable, properly labeled container for recovery or disposal.

## Section 7: Handling and Storage

### Section 7, Handling and storage

<b>Handling</b>	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.
<b>Storage</b>	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 tight container (USP).

## 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

<b>Physical Form</b>	<b>How Supplied</b>
	Amlodipine and benazepril hydrochloride capsules USP are available as capsules containing amlodipine besylate equivalent to 2.5 mg, 5 mg or 10 mg of amlodipine, with 10 mg, 20 mg or 40 mg of benazepril hydrochloride providing for the following available combinations: 2.5 mg/10 mg, 5 mg/10 mg, 5 mg/20 mg, 5 mg/40 mg, 10 mg/20 mg and 10 mg/40 mg.
	Amlodipine and benazepril hydrochloride capsules USP, 2.5 mg/10 mg 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 tablets, debossed with '1' on one side and plain on the other side.

NDC 68180-755-01      Bottles of 100 capsules  
NDC 68180-755-02      Bottles of 500 capsules  
NDC 68180-755-03      Bottles of 1000 capsules

Amlodipine and benazepril hydrochloride capsules USP, 5 mg/10 mg are size '2' capsules 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 tablets, 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  
NDC 68180-756-03      Bottles of 1000 capsules

Amlodipine and benazepril hydrochloride capsules USP, 5 mg/20 mg are size '2' capsules 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 tablets, 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  
NDC 68180-757-03      Bottles of 1000 capsules

Amlodipine and benazepril hydrochloride capsules USP, 5 mg/40 mg are size '2' capsules with dark green cap and white body, imprinted with 'LU' (in black ink) on cap and 'E15' (in black ink) on body, containing white to off-white powder and two white to off-white, circular tablets, debossed with '2' on one side and plain on the other side.

NDC 68180-759-01      Bottles of 100 capsules  
NDC 68180-759-02      Bottles of 500 capsules  
NDC 68180-759-03      Bottles of 1000 capsules

Amlodipine and benazepril hydrochloride capsules USP, 10 mg/20 mg are size '2' capsules 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 tablets, 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  
NDC 68180-758-03      Bottles of 1000 capsules

Amlodipine and benazepril hydrochloride capsules USP, 10 mg/40 mg are size '2' capsules with dark blue cap and white body, imprinted with 'LU' (in black ink) on cap and 'E16' (in black ink) on body, containing white to off-white powder and two white to off-white, circular tablets, debossed with '2' on one side and plain on the other side.

NDC 68180-760-01      Bottles of 100 capsules  
NDC 68180-760-02      Bottles of 500 capsules  
NDC 68180-760-03      Bottles of 1000 capsules

## 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

Carcinogenicity and mutagenicity studies have not been conducted with this combination. However, these studies have been conducted with amlodipine and benazepril alone (see below). No adverse effects on fertility occurred when the benazepril:amlodipine combination was given orally to rats of either sex at doses up to 15:7.5 mg (benazepril:amlodipine)/kg/day, prior to mating and throughout gestation.

#### **Benazepril**

No evidence of carcinogenicity was found when benazepril was administered to rats and mice for up to 2 years at doses of up to 150 mg/kg/day. When compared on the basis of body surface area, this dose is 18 and 9 times (rats and mice, respectively) the maximum recommended human dose (MRHD) (calculations assume a patient weight of 60 kg). 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 to 500 mg/kg/day (6 to 60 times the MRHD on a body surface area basis), benazepril had no adverse effect on the reproductive performance of male and female rats.

#### **Amlodipine**

Rats and mice treated with amlodipine maleate in the diet for up to two years, at concentrations calculated to provide daily dosage levels of 0.5, 1.25, and 2.5 mg amlodipine/kg/day, showed no evidence of a carcinogenic effect of the drug. For the mouse, the highest dose was, on a body surface area basis, similar to the MRHD of 10 mg amlodipine/day. For the rat, the highest dose was, on a body surface area basis, about two and a half times the MRHD. (Calculations based on a 60 kg patient.) Mutagenicity studies conducted with amlodipine maleate revealed no drug-related effects at either the gene or chromosome level. There was no effect on the fertility of rats treated orally with amlodipine maleate (males for 64 days and females for 14 days prior to mating) at doses of up to 10 mg amlodipine/kg/day (about 10 times the MRHD of 10 mg/day on a body surface area basis).

## Section 12: Ecological Information

### Section 12: Ecological Information

No relevant studies identified.

## Section 13: Disposal Considerations

### Section 13: Disposal Considerations

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

## Section 14: Transport Information

### Section 14: Transport Information

#### 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

### Section 15: Regulatory Information

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 MSDS.