LUPIN LIMITED

SAFETY DATA SHEET

Section 1: Identification

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Material	**Amlodipine and Valsartan Tablets USP** **5/160 mg, 10/160 mg, 5/320 mg and 10/320 mg**
Manufacturer	**Lupin Limited** Goa 403 722 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	Expected to be non-combustible.
Health	Do not use in patients with known hypersensitivity to any component. Do not coadminister aliskiren with amlodipine and valsartan in patients with diabetes.
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**
Amlodipine Besylate USP	111470-99-6
Valsartan USP	137862-53-4

Section 4: First-Aid Measures

Section 4, First-aid measures

Ingestion	After unintentional swallowing, induce vomiting only if fully conscious. Rinse out mouth and give plenty of water to drink. Seek medical advice

Inhalation	Not required under normal conditions.
Skin Contact	In case of contact with skin wash off immediately with soap and water Consult a doctor if skin irritation persist.
Eye Contact	Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If irritation persists: Get medical advice/attention.
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	**Amlodipine** Single oral doses of amlodipine maleate equivalent to 40 mg/kg and 100 mg/kg amlodipine in mice and rats, respectively, caused deaths. Single oral doses equivalent to 4 or more mg/kg amlodipine in dogs (11 or more times the maximum recommended human dose on a mg/m^2 basis) caused a marked peripheral vasodilation and hypotension. Overdosage might be expected to cause excessive peripheral vasodilation with marked hypotension. In humans, experience with intentional overdosage of amlodipine is limited. Marked and potentially prolonged systemic hypotension up to and including shock with fatal outcome have been reported. If massive overdose should occur, initiate active cardiac and respiratory monitoring. Frequent blood pressure measurements are essential. Should hypotension occur, cardiovascular support including elevation of the extremities and the judicious administration of fluids should be initiated. If hypotension remains unresponsive to these conservative measures, consider administration of vasopressors (such as phenylephrine) with attention to circulating volume and urine output. As amlodipine is highly protein bound, hemodialysis is not likely to be of benefit. Administration of activated charcoal to healthy volunteers immediately or up to two hours after ingestion of amlodipine has been shown to significantly decrease amlodipine absorption. **Valsartan** Limited data are available related to overdosage in humans. The most likely effect of overdose with valsartan would be peripheral vasodilation, hypotension, and tachycardia; bradycardia could occur from parasympathetic (vagal) stimulation. Depressed level of consciousness, circulatory collapse, and shock have been reported. If symptomatic hypotension should occur, supportive treatment should be instituted. Valsartan is not removed from the plasma by hemodialysis. Valsartan was without grossly observable adverse effects at single oral doses up to 2000 mg/kg in rats and up to 1000 mg/kg in marmosets, except for the salivation and diarrhea in the rat and vomiting in the marmoset at the highest dose (60 and 37 times, respectively, the maximum recommended human dose (MRHD) on a mg/m^2 basis). (Calculations assume an oral dose of 320 mg/day and a 60 kg patient.)

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	All extinguishing media are suitable but method must take into account the surrounding area to minimize dispersion.
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.

Section 6: Accidental Release Measures

Section 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.

Section 7: Handling and Storage

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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 after removal of PPE. Releases to the environment should be avoided. Review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure or environmental releases. Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls.
Storage	Store at 25ºC (77ºF); excursions permitted to 15 to 30ºC (59 to 86ºF). [See USP Controlled Room Temperature.] Protect from moisture.

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

Physical Form

HOW SUPPLIED

Amlodipine and Valsartan is available as tablets containing amlodipine besylate equivalent to 5 mg, or 10 mg of amlodipine free-base with valsartan 160 mg or 320 mg, providing for the following available combinations: 5/160 mg, 10/160 mg, 5/320 mg, and 10/320 mg.

All strengths are packaged in bottles of 30, 90 and 500 count, and unit dose blister packages.

5/160 mg Tablets - Mustard coloured, capsule shaped, film coated, biconvex tablets debossed 'LU' on one side and 'Q12' on the other side.

Bottles of 30 NDC # 68180-764-06
Bottles of 90 NDC # 68180-764-09
Bottles of 500 NDC # 68180-764-02
Unit Dose 100 tablets (10 X 10 tablets blister cards) NDC # 68180-764-13

10/160 mg Tablets - Yellow, capsule shaped, film coated, biconvex tablets debossed 'LU' on one side and 'Q14' on the other side.
Bottles of 30 NDC # 68180-765-06
Bottles of 90 NDC # 68180-765-09
Bottles of 500 NDC # 68180-765-02
Unit Dose 100 tablets (10 X 10 tablets blister cards) NDC # 68180-765-13

5/320 mg Tablets - Mustard coloured, capsule shaped, film coated, biconvex tablets debossed 'LU' on one side and 'Q13' on the other side.
Bottles of 30 NDC # 68180-766-06
Bottles of 90 NDC # 68180-766-09
Bottles of 500 NDC # 68180-766-02
Unit Dose 100 tablets (10 X 10 tablets blister cards) NDC # 68180-766-13

10/320 mg Tablets - Yellow, capsule shaped, film coated, biconvex tablets debossed 'LU' on one side and 'Q15' on the other side
Bottles of 30 NDC # 68180-767-06
Bottles of 90 NDC # 68180-767-09
Bottles of 500 NDC # 68180-767-02
Unit Dose 100 tablets (10 X 10 tablets blister cards) NDC # 68180-767-13

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

Amlodipine
Rats and mice treated with amlodipine maleate in the diet for up to 2 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 mg/m^2 basis, similar to the MRHD of 10 mg amlodipine/day. For the rat, the highest dose was, on a mg/m^2 basis, about 2.5 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 mg/m^2 basis).

Valsartan
There was no evidence of carcinogenicity when valsartan was administered in the diet to mice and rats for up to 2 years at concentrations calculated to provide doses of up to 160 and 200 mg/kg/day, respectively. These doses in mice and rats are about 2.4 and 6 times, respectively, the MRHD of 320 mg/day on a mg/m^2 basis. (Calculations based on a 60 kg patient.)

Mutagenicity assays did not reveal any valsartan-related effects at either the gene or chromosome level. These assays included bacterial mutagenicity tests with *Salmonella* and *E. coli*, a gene mutation test with Chinese hamster V79 cells, a cytogenetic test with Chinese hamster ovary cells, and a rat micronucleus test.

Valsartan had no adverse effects on the reproductive performance of male or female rats at oral doses of up to 200 mg/kg/day. This dose is about 6 times the MRHD on a mg/m^2 basis.

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.