1. IDENTIFICATION OF THE SUBSTANCE AND THE COMPANY

Material: Valsartan and Hydrochlorothiazide Tablet USP
80 mg/12.5 mg, 160 mg/12.5 mg, 160 mg/25 mg, 320 mg/12.5 mg,
320 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

<table>
<thead>
<tr>
<th>Ingredients</th>
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<tr>
<td>Valsartan USP</td>
<td>137862-53-4</td>
<td>80 mg/12.5 mg, 160mg/12.5 mg, 160mg/25 mg,</td>
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<td></td>
<td>320 mg/12.5 mg, 320 mg/25 mg</td>
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<tr>
<td>Hydrochlorothiazide USP</td>
<td>00058-93-5</td>
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3. HAZARD IDENTIFICATION

Fire and Explosion
Expected to be non-combustible

Health
Valsartan and hydrochlorothiazide tablets are 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.

Do not co-administer aliskiren with valsartan and hydrochlorothiazide tablets in patients with diabetes.
4. FIRST AID MEASURE

Environment

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

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

Limited data are available related to overdosage in humans. The most likely manifestations of overdosage would be 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 dialysis.

The degree to which hydrochlorothiazide is removed by hemodialysis has not been established. The most common signs and symptoms observed in patients 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.
In rats and marmosets, single oral doses of valsartan up to 1524 and 762 mg/kg in combination with hydrochlorothiazide at doses up to 476 and 238 mg/kg, respectively, were very well tolerated without any treatment-related effects. These no adverse effect doses in rats and marmosets, respectively, represent 46.5 and 23 times the maximum recommended human dose (MRHD) of valsartan and 188 and 113 times the MRHD of hydrochlorothiazide on a mg/m² basis. (Calculations assume an oral dose of 320 mg/day valsartan in combination with 25 mg/day hydrochlorothiazide and a 60-kg patient.)

Valsartan

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 salivation and diarrhea in the rat and vomiting in the marmoset at the highest dose (60 and 31 times, respectively, the maximum recommended human dose on a mg/m² basis). (Calculations assume an oral dose of 320 mg/day valsartan and a 60-kg patient.)

Hydrochlorothiazide

The oral LD₅₀ of hydrochlorothiazide is greater than 10 g/kg in both mice and rats, which represents 2027 and 4054 times, respectively, the maximum recommended human dose on a mg/m² basis. (Calculations assume an oral dose of 25 mg/day and a 60-kg patient.)

### 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.
Dispense in tight container (USP).

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.

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
Valsartan and hydrochlorothiazide tablets USP are available as non-scored tablets containing valsartan/hydrochlorothiazide 80 mg/12.5 mg, 160 mg/12.5 mg, 160 mg/25 mg, 320 mg/12.5 mg and 320 mg/25 mg. Strengths are available as follows.

80 mg/12.5 mg Tablet - Light pink colored, capsule shaped, film-coated, biconvex tablets, debossed with "LU" on one side and "P11" on the other side.

| Bottles of 90 | NDC 68180-103-09 |
| Bottles of 500 | NDC 68180-103-02 |
| Bottles of 1000 | NDC 68180-103-03 |
| 10 X 10' Blister Pack | NDC 68180-103-13 |

160 mg/12.5 mg Tablet - Reddish brown colored, capsule shaped, film-coated, biconvex tablets, debossed with "LU" on one side and "P12" on the other side.

| Bottles of 90 | NDC 68180-104-09 |
| Bottles of 500 | NDC 68180-104-02 |
| Bottles of 1000 | NDC 68180-104-03 |
| 10 X 10' Blister Pack | NDC 68180-104-13 |
11. TOXICOLOGICAL INFORMATION

Carcinogenesis, Mutagenesis, Impairment of Fertility

Valsartan-Hydrochlorothiazide

No carcinogenicity, mutagenicity or fertility studies have been conducted with the combination of valsartan and hydrochlorothiazide. However, these studies have been conducted for valsartan as well as hydrochlorothiazide alone. Based on the preclinical safety and human pharmacokinetic studies, there is no indication of any adverse interaction between valsartan and hydrochlorothiazide.

Valsartan

There was no evidence of carcinogenicity when valsartan was administered in the diet to mice and rats for up to 2 years at doses up to 160 and 200 mg/kg/day, respectively. These doses in mice and rats are about 2.6 and 6 times, respectively, the maximum recommended human dose on a mg/m² basis. (Calculations assume an oral dose of 320 mg/day and 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* (Ames) 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 up to 200 mg/kg/day. This dose is about 6 times the maximum recommended human dose on a mg/m² basis. (Calculations assume an oral dose of 320 mg/day and a 60-kg patient.)

**Hydrochlorothiazide**

Two-year feeding studies in mice and rats conducted under the auspices of the National Toxicology Program (NTP) uncovered no evidence of a carcinogenic potential of hydrochlorothiazide in female mice (at doses of up to approximately 600 mg/kg/day) or in male and female rats (at doses of up to approximately 100 mg/kg/day). The NTP, however, found equivocal evidence for hepatocarcinogenicity in male mice.

Hydrochlorothiazide was not genotoxic in vitro in the Ames mutagenicity assay of *Salmonella Typhimurium* strains TA 98, TA 100, TA 1535, TA 1537, and TA 1538 and in the Chinese Hamster Ovary (CHO) test for chromosomal aberrations, or in vivo in assays using mouse germinal cell chromosomes, Chinese hamster bone marrow chromosomes, and the *Drosophila* sex-linked recessive lethal trait gene. Positive test results were obtained only in the in vitro CHO Sister Chromatid Exchange (clastogenicity) and in the Mouse Lymphoma Cell (mutagenicity) assays, using concentrations of hydrochlorothiazide from 43 to 1300 mcg/mL, and in the *Aspergillus Nidulans* non-disjunction assay at an unspecified concentration.

Hydrochlorothiazide had no adverse effects on the fertility of mice and rats of either sex in studies wherein these species were exposed, via their diet, to doses of up to 100 and 4 mg/kg, respectively, prior to mating and throughout gestation. These doses of hydrochlorothiazide in mice and rats represent 19 and 1.5 times, respectively, the maximum recommended human dose on a mg/m² basis. (Calculations assume an oral dose of 25 mg/day and a 60-kg patient.)

**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

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15. REGULATORY INFORMATION

This Section Contains Information relevant to compliance with other Federal and/or state laws.

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.