1. IDENTIFICATION OF THE SUBSTANCE AND THE COMPANY

Material: Irbesartan and hydrochlorothiazide Tablets USP 150 mg/12.5 mg, 300 mg/12.5 mg and 300 mg/25 mg

Manufacturer: Lupin Limited
Pithampur (M.P.) - 454 775
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>
<th>CAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irbesartan</td>
<td>138402-11-6</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>00058-93-5</td>
</tr>
</tbody>
</table>

3. HAZARD IDENTIFICATION

Fire and Explosion: Expected to be non-combustible.

Health: Irbesartan-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 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**

**Irbesartan**
No data are available in regard to overdosage in humans. However, daily doses of 900 mg for 8 weeks were well tolerated. The most likely manifestations of overdosage are expected to be hypotension and tachycardia; bradycardia might also occur from overdose. Irbesartan is not removed by hemodialysis.

To obtain up-to-date information about the treatment of overdosage, a good resource is a 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 interactions, drug-drug interactions, and unusual drug kinetics in the patient.

Laboratory determinations of serum levels of irbesartan are not widely available, and such determinations have, in any event, no established role in the management of irbesartan overdose.

Acute oral toxicity studies with irbesartan in mice and rats indicated acute lethal doses were in excess of 2000 mg/kg, about 25- and 50-fold the MRHD (300 mg) on a mg/m² basis, respectively.

**Hydrochlorothiazide**
The most common signs and symptoms of overdose observed in humans 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. The oral LD₅₀ of hydrochlorothiazide is greater than 10 g/kg in both mice and rats.

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.

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

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

Irbesartan and Hydrochlorothiazide Tablets USP are film-coated tablets, have markings on one side and available in the strengths and packages listed in the following table:

<table>
<thead>
<tr>
<th>Tablet Strength (irbesartan and hydrochlorothiazide)</th>
<th>Film-Coated Tablet Color/Shape</th>
<th>Tablet Markings</th>
<th>Package Size</th>
<th>NDC Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>150 mg/12.5 mg</td>
<td>light peach, biconvex, oval shaped</td>
<td>Imprinted with “L058” on one side and plain on other side</td>
<td>Bottles of 30 Bottles of 90</td>
<td>68180-413-06 68180-413-09</td>
</tr>
<tr>
<td>300 mg/12.5 mg</td>
<td>light peach, biconvex, oval shaped</td>
<td>Imprinted with “L059” on one side and plain on other side</td>
<td>Bottles of 30 Bottles of 90</td>
<td>68180-414-06 68180-414-09</td>
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<tr>
<td>300 mg/25 mg</td>
<td>tan, biconvex, oval-shaped</td>
<td>Imprinted with “L060” on one side and plain on other side</td>
<td>Bottles of 30 Bottles of 90</td>
<td>68180-415-06 68180-415-09</td>
</tr>
</tbody>
</table>

10. STABILITY AND REACTIVITY

Stable under recommended storage conditions.

11. TOXICOLOGICAL INFORMATION

Carcinogenesis Mutagenesis, Impairment of Fertility

Irbesartan-Hydrochlorothiazide

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

Irbesartan-hydrochlorothiazide was not mutagenic in standard in vitro tests (Ames microbial test and Chinese hamster mammalian-cell forward gene-mutation assay). Irbesartan-hydrochlorothiazide was negative in tests for induction of chromosomal aberrations (in vitro-human lymphocyte assay; in vivo-mouse micronucleus study).

The combination of irbesartan and hydrochlorothiazide has not been evaluated in definitive studies of fertility.

Irbesartan

No evidence of carcinogenicity was observed when irbesartan was administered at doses of up to 500/1000 mg/kg/day (males/ females, respectively) in rats and 1000 mg/kg/day in mice for up to 2 years. For
male and female rats, 500 mg/kg/day provided an average systemic exposure to irbesartan (AUC$_{0-24}$ hours, bound plus unbound) about 3 and 11 times, respectively, the average systemic exposure in humans receiving the maximum recommended dose (MRD) of 300 mg irbesartan/day, whereas 1000 mg/kg/day (administered to females only) provided an average systemic exposure about 21 times that reported for humans at the MRD. For male and female mice, 1000 mg/kg/day provided an exposure to irbesartan about 3 and 5 times, respectively, the human exposure at 300 mg/day.

Irbesartan was not mutagenic in a battery of in vitro tests (Ames microbial test, rat hepatocyte DNA repair test, V79 mammalian-cell forward gene-mutation assay). Irbesartan was negative in several tests for induction of chromosomal aberrations (in vitro-human lymphocyte assay; in vivo-mouse micronucleus study).

Irbesartan had no adverse effects on fertility or mating of male or female rats at oral doses ≤650 mg/kg/day, the highest dose providing a systemic exposure to irbesartan (AUC$_{0-24}$ hours, bound plus unbound) about 5 times that found in humans receiving the MRD of 300 mg/day.

**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.

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**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.