MATERIAL SAFETY DATA SHEET

1. IDENTIFICATION OF THE SUBSTANCE AND THE COMPANY

Material **Simvastatin Tablets, USP**
5 mg, 10 mg, 20 mg, 40 mg and 80 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
Simvastatin	79902-63-9	5 mg/Tablet ; 10 mg /Tablet; 20 mg/Tablet; 40 mg/Tablet and 80 mg/Tablet
Non-hazardous ingredients	----------	q.s.

3. HAZARDOUS IDENTIFICATION

As a result of the physical presentation of the product, the risk to health in the normal handling of the product is expected to be low.

4. FIRST AID MEASURES

Ingestion Get medical attention to determine whether vomiting or evacuation of stomach is necessary. Do not give anything by mouth to an unconscious or convulsing person.

.

Inhalation Remove from area to fresh air. Seek medical attention if respiratory irritation develops or if breathing becomes difficult.

Skin Contact	Remove contaminated clothing. Wash affected areas with plenty of water and soap if available, for several minutes. Seek medical attention if irritation or rash develops and persists.
Eye Contact	Flush eyes with large amounts of running water for 15 minutes. Hold eyelids open. Get immediate medical attention
Antidotes	No specific antidote exists.

5. FIRE-FIGHTING MEASURES

Fire and Explosion Hazards	Not expected for the product, although the packaging is combustible.
Extinguishing Media	Water, carbon dioxide, or dry chemical.
Fire Fighting Protective Equipment	A self-contained breathing apparatus and suitable protective clothing should be worn in fire conditions.

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.
Decontamination Procedure	No specific decontamination or detoxification procedures have been identified for this product. Water can be used for clean-up and decontamination operations.

7. HANDLING AND STORAGE

Precautions for Safe Handling and Use

Avoid generating dust or mist and contact with skin, eyes and clothing. Use with adequate ventilation. Wash thoroughly after handling. Launder contaminated clothing before reuse. Do not get in eyes, on skin or clothing. Avoid breathing dust or mist. Use adequate dust/vapor control

Storage

Store at 20° - 25°C (68° - 77° F) [See USP Controlled Room Temperature]. Preserve in tight container as defined in USP.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

PERSONAL PROTECTIVE EQUIPMENT

Eye Protection

Safety glasses with side.

Respirators

In operations where mists or aerosols are generated, wear a NIOSH approved respirator that has been selected by a technically qualified person for the specific conditions.

Other Equipment or Procedures

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

Work/Hygienic Practices

Do not permit eating, drinking or smoking near this material.

9. PHYSICAL & CHEMICAL PROPERTIES

Physical Form

Tablet.

Appearance

5 mg Tablets : Tan, Round, Biconvex Tablets.
10 mg Tablets : Peach, Oval, Biconvex Tablets
20 mg Tablets : Tan, Oval, Biconvex Tablets.
40 mg Tablets : Brick Red, Oval, Biconvex Tablets.
80 mg Tablets : Brick Red, Capsule Shaped, Biconvex Tablets.

10. STABILITY AND REACTIVITY

Stable under recommended storage conditions.

11. TOXICOLOGICAL INFORMATION

Oral Toxicity (RAT)

At maximally tolerated doses in both the rat and the rabbit, simvastatin produced no foetal malformations and had no effects on fertility, reproductive function or neonatal development. However, in rats, an oral dose of 60 mg/kg/day of the hydroxy acid, pharmacologically active metabolite of simvastatin resulted in decreased maternal body weight and an increased incidence of foetal resorptions and skeletal malformations compared with controls. Subsequent studies conducted at dosages of up to 60 mg/kg/day with this metabolite showed that these resorptions and skeletal malformations were consequences of maternal toxicity (forestomach lesions associated with maternal weight loss) specific to rodents and are highly unlikely to be due to a direct effect on the developing foetus. Although no studies have been conducted with simvastatin, maternal treatment of pregnant rats with a closely related HMG-CoA reductase inhibitor at dosages of 80 and 400 mg/kg/day (10- and 52-fold the maximum recommended therapeutic dose based on mg/m^2 body surface area) has been shown to reduce the foetal plasma levels of mevalonate.

Genetic Toxicology and Carcinogenicity

An extensive battery of *in vitro* and *in vivo* genetic toxicity tests have been conducted on both simvastatin and its corresponding open acid L-654,969. These include assays for microbial mutagenesis, mammalian cell mutagenesis, single stranded DNA breakage and tests for chromosome aberrations. The results of these studies provided no evidence of an interaction between simvastatin or L-654,969 with genetic material at the highest soluble noncytotoxic concentrations tested in *in vitro* assay systems or at maximally tolerated doses tested *in vivo*. Initial carcinogenicity studies conducted in rats and mice with simvastatin employed doses ranging from 1 mg/kg/day to 25 mg/kg/day. No evidence of a treatment-related incidence of tumour types was found in mice in any tissue. A statistically significant ($p \leq 0.05$) increase in the incidence of thyroid follicular cell adenomas was observed in female rats receiving 25 mg/kg of simvastatin per day (more than an order of magnitude greater than the maximum human dose). This benign tumour type was limited to female rats; no similar changes were seen in male rats or in female rats at lower dosages (up to 5 mg/kg/day). These tumours are a secondary effect reflective of a simvastatin-mediated enhancement of thyroid hormone clearance in the female rat. No other statistically significant increased evidence of tumour types was identified in any tissues in rats receiving simvastatin. Data from both of these studies indicated that squamous epithelial hyperplasia of the forestomach occurred at all dosage levels. These gastric changes are confined to an anatomical structure which is not found in humans. Moreover, identical cells found in other locations (e.g. oesophagus and anorectal junction of the rat, mouse and dog) are unaffected.

12. ECOLOGICAL INFORMATION

No information available

13. DISPOSAL CONSIDERATION

Waste Disposal Method

Dispose of by incineration in accordance with applicable international, national, state, and/or local waste disposal regulations.

14. TRANSPORT INFORMATION

Not regulated for transportation by the United States Department of Transportation (DOT), International Maritime Organization (IMO), or International Air Transport Association (IATA). May be subject to state and/or local transportation requirements.

15. REGULATORY INFORMATION

No information available.

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.