NATCO PHARMA LIMITED

SAFETY DATA SHEET

Section 1: Identification

Section 1, Identification

Material	**Imatinib Mesylate Tablets 100 mg and 400 mg**
Manufacturer	**NATCO Pharma Limited** Kothur- 509 228, Telangana, 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	None.
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**
Imatinib Mesylate	220127-27-1

Section 4: First-Aid Measures

Section 4, First-aid measures

Ingestion	Flush out mouth with water, consult a physician immediately.

Inhalation	In case of inhalation remove to fresh air and seek medical aid.
Skin Contact	Remove immediately contaminated clothes, wash affected skin with plenty of water.
Eye Contact	In case of contact with eyes rinse thoroughly with plenty of water and get medical advice.

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	Experience with doses greater than 800 mg is limited. Isolated cases of Imatinib mesylate overdose have been reported. In the event of overdosage, observe the patient and give appropriate supportive treatment.

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	Use extinguishing media appropriate to surrounding fire conditions, such as water, fog, spray, dry chemical, regular foam, carbon dioxide.
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

Personal Precautions	Avoid excessive contact and contact with eyes. Wear safety goggles or shield.
Environmental Precautions	For large spills, take precautions to prevent entry into waterways, sewers, or surface drainage systems.
Clean-up Methods	This material is not known to possess additional hazards when spilled beyond those of other non-hazardous solids.

Section 7: Handling and Storage

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Handling	No special control measures required for the normal handling of this product. Do not crush Imatinib mesylate tablets. Avoid direct contact of crushed tablets with the skin or mucous membranes. If such contact occurs, wash thoroughly as outlined in the references. Avoid exposure to crushed tablets.
Storage	Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F) [See USP Controlled Room Temperature]. Protect from moisture. Dispense in a 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

Physical Form	Each film-coated tablet contains 100 mg or 400 mg of imatinib free base. **100 mg Tablets** Brownish, round, biconvex, film-coated tablets debossed with “100” on one side and score line on other side with “N” on one side of the score line and “I” on other side of score line. Bottle of 90 tablets ……NDC 68180-390-09 Carton of 30 tablets (3 X 10 unit-dose)…… NDC 68180-390-13 **400 mg Tablets** Brownish, oval, biconvex, film-coated tablets debossed with “400” on one side and score line on other side with “N” on one side of the score line and “I” on other side of score line. Bottle of 30 tablets ……NDC 68180-391-06 Carton of 30 tablets (3 X 10 unit-dose)…… NDC 68180-391-13

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

In the 2-year rat carcinogenicity study administration of imatinib at 15, 30, and 60 mg/kg/day resulted in a statistically significant reduction in the longevity of males at 60 mg/kg/day and females at greater than or equal to 30 mg/kg/day. Target organs for neoplastic changes were the kidneys (renal tubule and renal pelvis), urinary bladder, urethra, preputial and clitoral gland, small intestine, parathyroid glands, adrenal glands and non-glandular stomach. Neoplastic lesions were not seen at: 30 mg/kg/day for the kidneys, urinary bladder, urethra, small intestine, parathyroid glands, adrenal glands and non-glandular stomach, and 15 mg/kg/day for the preputial and clitoral gland. The papilloma/carcinoma of the preputial/clitoral gland were noted at 30 and 60 mg/kg/day, representing approximately 0.5 to 4 or 0.3 to 2.4 times the human daily exposure (based on AUC) at 400 mg/day or 800 mg/day, respectively, and 0.4 to 3.0 times the daily exposure in children (based on AUC) at 340 mg/m^2. The renal tubule adenoma/carcinoma, renal pelvis transitional cell neoplasms, the urinary bladder and urethra transitional cell papillomas, the small intestine adenocarcinomas, the parathyroid glands adenomas, the benign and malignant medullary tumors of the adrenal glands and the non-glandular stomach papillomas/carcinomas were noted at 60 mg/kg/day. The relevance of these findings in the rat carcinogenicity study for humans is not known. Positive genotoxic effects were obtained for imatinib in an *in vitro* mammalian cell assay (Chinese hamster ovary) for clastogenicity (chromosome aberrations) in the presence of metabolic activation. Two intermediates of the manufacturing process, which are also present in the final product, are positive for mutagenesis in the Ames assay. One of these intermediates was also positive in the mouse lymphoma assay. Imatinib was not genotoxic when tested in an *in vitro* bacterial cell assay (Ames test), an *in vitro* mammalian cell assay (mouse lymphoma) and an *in vivo* rat micronucleus assay.

In a study of fertility, male rats were dosed for 70 days prior to mating and female rats were dosed 14 days prior to mating and through to gestational Day 6. Testicular and epididymal weights and percent motile sperm were decreased at 60 mg/kg, approximately three-fourths the maximum clinical dose of 800 mg/day based on body surface area. This was not seen at doses less than or equal to 20 mg/kg (one-fourth the maximum human dose of 800mg). The fertility of male and female rats was not affected.

Fertility was not affected in the preclinical fertility and early embryonic development study although lower testes and epididymal weights as well as a reduced number of motile sperm were observed in the high dose males rats. In the preclinical pre- and postnatal study in rats, fertility in the first generation offspring was also not affected by imatinib mesylate.

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.

NATCO shall not be held liable for any damage resulting from handling or from contact with the above product. NATCO reserves the right to revise this SDS.