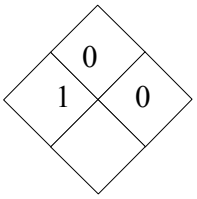
NOVARTIS



MATERIAL SAFETY DATA SHEET
NOVARTIS PHARMACEUTICALS CORPORATION
One Health Plaza
East Hanover, NJ 07936

24-Hour Emergency Telephone Number: 1-862-778-7000
Customer Interaction Center (MSDS requests): 1-888-669-6682
For Technical Information: 1-862-778-3680 (9:00 AM – 5:00 PM E.S.T.)

SECTION 1. PRODUCT IDENTIFICATION

PRODUCT NAME:	**Gleevec™ Tablets, 100 and 400mg**
SYNONYMS:	STI571
THERAPEUTIC CATEGORY:	Antitumor agent (tyrosine protein kinase inhibitor)
GENERIC NAME:	Imatinib mesylate
CHEMICAL NAME:	4-[(4-Methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-phenyl]benzamide methanesulfonate
CHEMICAL FORMULA:	$C_{29}H_{31}N_7O \cdot CH_4SO_3$
MOLECULAR WEIGHT:	589.7

SECTION 2. COMPOSITION/INFORMATION ON INGREDIENTS

COMPOSITION	CAS#	CONCENTRATION (% by wt.)
Active Ingredients		
Gleevec Active Ingredient	220127-57-1	60 - 62
Inactive Ingredients		
Microcrystalline cellulose	9004-34-6	17 - 18
Crospovidone	9003-39-8	14 - 15
Hydroxypropyl methylcellulose	9004-65-3	~1

SECTION 3. HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW

****

FINISHED PHARMACEUTICAL PRODUCT
REFER TO PHYSICIANS' DESK REFERENCE OR PACKAGE INSERT
MAY CAUSE NAUSEA, VOMITING AND DIARRHEA
MAY CAUSE FLUID RETENTION
MAY ADVERSELY AFFECT THE DEVELOPING FETUS

****

PRIMARY ROUTE(S) OF ENTRY:	Oral
EFFECTS OF OVEREXPOSURE:	Finished pharmaceutical product. Potential for exposure is reduced in this form.
Skin:	No hazard is expected from normal clinical use.
Eye:	No hazard is expected from normal clinical use.
Inhalation:	No hazard is expected from normal clinical use.
Ingestion:	No hazard is expected from normal clinical use.
THERAPEUTIC SIDE EFFECTS:	Nausea, vomiting, diarrhea, fluid retention, muscle cramps, skin rash, headache, fatigue, arthralgia, and abdominal pain.
TARGET ORGAN EFFECTS:	Prolonged or repeated exposure may cause liver and kidney toxicity, and immunosuppresion.
REPRODUCTIVE HAZARDS:	FDA Pregnancy Category D (see section 11).
CARCINOGENICITY:	Experimental (animal) non-genotoxic carcinogenic effects (see section 11).
MUTAGENICITY:	Imatinib mesylate was clastogenic in one in vitro assay, and non-mutagenic in three assays (see Section 11).

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: Pregnancy; known hypersensitivity to imatinib or any other components of the formulation; pre-existing liver impairment.

SECTION 4. EMERGENCY AND FIRST AID MEASURES

Skin Contact:	Wash contaminated area with soap and water.
Eye Contact:	Flush with running water for 15 minutes holding eyelids open.
Inhalation:	No specific treatment is necessary since this product is not likely to be hazardous by inhalation if capsule is left intact.
Ingestion:	Get medical attention immediately; induce vomiting if victim is conscious.

SECTION 5. FIRE FIGHTING MEASURES

Flash Point: Not applicable **Method Used**: Not applicable

Flammable Limits (% in air)

Lower: not applicable Upper: not applicable

Autoignition Temperature:	Not available
Extinguishing Media:	Use media suitable for fire in surrounding area.
Special Fire Fighting Procedures and Precautions:	Evacuate area and fight fire from safe distance.
Fire and Explosion Hazards:	Not available
Fire-Fighting Equipment:	Wear full protective clothing and positive pressure self-contained breathing apparatus.
Hazardous Products of Combustion:	COx, NOx, SOx

NFPA Ratings: Health = 1 Flammability = 0 Reactivity = 0 Special Hazard = None
Hazard Rating Scales: 0 = Minimal 1 = Slight 2 = Moderate 3 = Serious 4 = Severe U = Unknown

SECTION 6. ACCIDENTAL RELEASE MEASURES

Steps to be taken if Material is Released or Spilled: Using appropriate protective equipment, absorb/sweep up and containerize spilled material. All wastes must be disposed of in accordance with local, state and federal laws and regulations. Avoid disposal in sewers and waterways.

SECTION 7. HANDLING AND STORAGE

Storage Temperature:	Do not store above 86°F (30°C).
Shelf Life:	See container packaging.
Special Sensitivity:	None known.
Handling and Storage Precautions:	None known.

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Eye Protection:	Not required under normal conditions of therapeutic administration and use.
Skin Protection:	Not required under normal conditions of therapeutic administration and use. Protective gloves should be worn if contents of capsule are expelled.
Respiratory Protection:	Not required under normal conditions of therapeutic administration and use.
Ventilation Requirements:	Not required under normal conditions of therapeutic administration and use.
Additional Measures:	None

Exposure Limits (Definition of terms):

NPIEL: Novartis Pharma Internal Exposure Limit

Component	**Exposure Limit**
Imatinib mesylate	NPIEL = 0.013 mg/m^3

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance:	Tablet		
Color:	dark yellow to brownish orange		
Boiling Point:	Not applicable	**Odor Threshold:**	Not available
Melting/Freezing Pt.:	Not applicable	**Odor Characteristics:**	Not available
pH:	Not available	**Vapor Pressure (mm Hg):**	Not applicable
Specific Gravity:	Not available	**Vapor Density:**	Not applicable
Soluble In:	Water	**% Volatile by Wt:**	Not applicable

SECTION 10. STABILITY AND REACTIVITY

Stable (yes/no):	Yes
Hazardous Polymerization:	Will not occur.
Conditions and Materials to Avoid:	Protect from temperatures exceeding 86°F (30°C).
Incompatibility:	None known
Hazardous Decomposition Products:	None known

SECTION 11. TOXICOLOGICAL INFORMATION

No toxicological data on finished product; data are for drug substance.

Eye Irritation: No data available.

Skin Irritation/Sensitization: Non irritating to the skin of rabbits; not sensitizing to the skin of guinea pigs.

Oral Toxicity: MTD Oral (rat): > 600 mg/kg

Parenteral Toxicity: LD_{50} Intravenous (rat): > 100 mg/kg

Dermal Toxicity: No data available.

Inhalation Toxicity: Respiratory irritant (human)

Chronic/Carcinogenicity: In a 2-year feed study in rats, there was evidence for a carcinogenic effect of imatinib mesylate in the kidneys, urinary bladder, preputial gland, and clitoral gland. The no observed adverse effect levels (NOAEL) for the various target organs with neoplastic lesions could be established as follows: 30 mg/kg/day for kidney and urinary bladder and 15 mg/kg/day for preputial and clitoral gland.

Mutagenicity: Positive in the following tests: *in vitro* chromosome aberration test in ovarian cells of the Chinese hamster.
Negative in the following tests: *in vitro* bacterial cell assay (Ames test), *in vitro* mammalian cell assay (mouse lymphoma) and an *in vivo* rat micronucleus assay.

Reproductive Effects: Imatinib mesylate was teratogenic in rats when administered during organogenesis at doses ≥ 100 mg/kg, approximately equal to the maximum clinical dose of 800 mg/day, based on body surface area. Teratogenic effects included exencephaly or encephalocele, absent/reduced frontal and absent parietal bones. Female rats administered this dose also experienced significant post-implantation loss in the form of early fetal resorption. At doses higher than 100 mg/kg, total fetal loss was noted in all animals.
Women of childbearing potential should be advised to avoid becoming pregnant.

In a study of fertility, in male rats dosed for 70 days prior to mating, testicular and epididymal weights and percent motile sperm were decreased at 60 mg/kg, approximately equal to the maximum clinical dose of 800 mg/day. When female rats were dosed 14 days prior to mating and through to gestational day 6, there was no effect on mating or on number of pregnant females.

It is not known whether imatinib or its metabolites are excreted in human milk. However, in lactating female rats administered 100 mg/kg, a dose approximately equal to the maximum clinical dose of 800 mg/day based on body surface area, imatinib and/or its metabolites were extensively excreted in milk. **Therefore, women should be advised against breastfeeding while taking Gleevec.**

SECTION 12. ECOLOGICAL INFORMATION

No ecological data on finished product; data are for drug substance.

Bacteria toxicity (respiration inhibition): activated sludge (3h):
EC_{10}: 65mg/l
EC_{50}: 232mg/l
EC_{80}: 605mg/l
Fish toxicity: common carp (cyprinus carpio) (96h):
LC_0: 56mg/l
LC_{50}: 82mg/l
Daphnia toxicity: daphnia magna (water flea) (48h):
EC_{50}: 80mg/l
NoEC: 32mg/l
Algae toxicity: Selenastrum capricornutum. Green algae. (72h):
EbC_{50}: 2.5mg/l
EbC_{10}: 1.1mg/l
N0EC: 0.96mg/l
Biological elimination: 9 - 12% (aerobic) (28d)
Inhibitory effects can be excluded.

Bioaccumulation in water organisms is not likely based on the n-octanol/water partition coefficient (log pOW < 3.0). Avoid release into the environment

SECTION 13. DISPOSAL CONSIDERATIONS

Waste Disposal Method: Using appropriate protective equipment, absorb/sweep up and containerize spilled material. All wastes must be disposed of in accordance with local, state and federal laws and regulations. Avoid disposal in sewers and waterways.

EPA Hazardous Waste Number: None

SECTION 14. TRANSPORTATION INFORMATION

Ground Regulations:

Proper Shipping Description:	Drugs, N.O.I. NMFC Item 60000
DOT Proper Shipping Name:	Not Applicable
DOT Hazard Class:	Not Applicable
DOT Identification Number:	Not Applicable
Packing Group:	Not Applicable
Hazard Label:	Not Applicable
Package Weight Limits:	Not Applicable
Special Requirements:	Not Applicable
Exceptions:	Not Applicable
Non-Bulk Requirements:	Not Applicable
Bulk Requirements:	Not Applicable
Reportable Quantity (lbs.):	Not Applicable
Stowage:	Not Applicable
Other Requirements:	Not Applicable

Air Regulations:

Proper Shipping Description:	Drugs, N.O.I. NMFC Item 60000
IATA Proper Shipping Name:	Not Applicable
IATA Hazard Class:	Not Applicable
IATA Identification Number:	Not Applicable
Packing Group:	Not Applicable
Hazard Label:	Not Applicable
Special Requirements:	Not Applicable
Max. wgt/pkg - Passgr. Aircraft:	Not Applicable
Max. wgt/pkg - Cargo Only Air:	Not Applicable

SECTION 15. REGULATORY INFORMATION

OSHA (Occupational Safety & Health Administration): This Material Safety Data Sheet contains the information required by the Federal OSHA Hazard Communication Standard (29 CFR 1910.1200).

OSHA PSM (Process Safety Management): Not listed (29 CFR 1910.119, Appendix A)

NJ TCPA (Toxic Catastrophe Prevention Act): This product contains NONE of the substances subject to the reporting requirements of Section N.J.A.C. 7:31 of this act.

TSCA (Toxic Substance Control Act): Not applicable

CERCLA (Comprehensive Response Compensation & Liability Act): Not listed

SARA Title III (Superfund Amendments & Reauthorization Act):

Section 302 Extremely Hazardous Substances:	Not listed
Section 311/312 Hazard Categories:	None
Section 313 Reportable Ingredients:	Not listed

RCRA (Resource Conservation & Recovery Act): Not listed

Other State Regulatory Information:

New Jersey: NJ RTK Threshold Planning Quantity = 10,000 lbs.

Other USA Regulations: None

California Proposition 65: The following statement is made in order to comply with the California Safe Drinking Water and Toxic Enforcement Act of 1986. *This product does not contain any ingredient known to the State of California to cause cancer or reproductive toxicity.*

Canada: WHMIS Ingredient Disclosure List
Not listed

EU Classification (European Union): **Warning Symbol:** not available.
Risk Phrases: not available.
Safety Phrases: not available.

SECTION 16. OTHER INFORMATION

Reason for Issue: Revision #1 – Changes and/or additions to Sections 3,6,11,13 and 15.

Supercedes Date: 23 June 03

Written By:	C. Perino	**Date:**	03 July 07
Approved By:	G. King	**Date:**	03 August 07

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