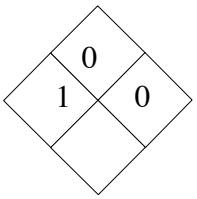
NOVARTIS



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:	**Tasigna® Capsules, 200 mg**
SYNONYMS:	Nilotinib Capsules
INDICATION:	Treatment of chronic phase and accelerated phase Philadelphia chromosome positive chronic myelogenous leukemia (CML).
GENERIC NAME:	None
CHEMICAL NAME:	Nilotinib hydrochloride
CHEMICAL FORMULA:	$C_{28}H_{22}F_3N_7O$ * HCl * H2 O
MOLECULAR WEIGHT:	584

SECTION 2. COMPOSITION/INFORMATION ON INGREDIENTS

COMPOSITION	CAS#	CONCENTRATION (% by wt.)
Active Ingredients		
Tasigna Active Ingredient	641571-10-0 (free base)	~ 55

SECTION 3. HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW

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FINISHED PHARMACEUTICAL PRODUCT
REFER TO PHYSICIANS' DESK REFERENCE OR PACKAGE INSERT
MAY CAUSE NAUSEA, VOMITING AND DIARRHEA
MAY CAUSE HEADACHE, FATIGUE
MAY CAUSE SKIN RASH
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, skin rash, pruritis, headache, fatigue, dizziness, palpitations and constipation. Common serious drug-related adverse reactions include thrombocytopenia and neutropenia. Sudden deaths and QT prolongation have been reported.
TARGET ORGAN EFFECTS:	Prolonged or repeated exposure may cause liver toxicity, elevated serum lipase, electrolyte abnormalities and myelosuppresion.
REPRODUCTIVE HAZARDS:	FDA Pregnancy Category D (see section 11).
CARCINOGENICITY:	Carcinogenicity studies have not been performed for nilotinib..
MUTAGENICITY:	Nilotinib was not mutagenic and/or clastogenic in three *in vitro* assays and one *in vivo* assay (see Section 11).

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: Pre-existing hypokalemia, hypomagnesemia, or long QT syndrome; known hypersensitivity to nilotanib or any other components of the formulation.

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.

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

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 capsules are handled.
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**
Nilotinib	NPIEL = 0.1 mg/m^3

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance:	Hard gelatin capsule		
Color:	Lt. yellow opaque		
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 (practically insoluble)	**% 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 in the murine Local Lymph Assay.

Oral Toxicity: LD_{50} Oral (rat-female): > 2000 mg/kg

Dermal Toxicity: No data available.

Inhalation Toxicity: No data available.

Chronic/Carcinogenicity: Carcinogenicity studies have not been performed.

Mutagenicity: Negative in the following tests: *in vitro* bacterial cell assay (Ames test), *in vitro* Comet assay (mouse lymphoma), *in vitro* chromosome aberration assay (human lymphocytes), and an *in vivo* rat micronucleus assay.

Reproductive Effects: **Tasigna can cause fetal harm when administered to pregnant women.**

Nilotinib was studied for effects on embryo-fetal development in pregnant rats and rabbits given oral doses of 10, 30, 100 mg/kg/day, and 30, 100, 300 mg/kg/day, respectively. In rats, nilotinib at doses of 100 mg/kg/day was associated with maternal toxicity (decreased gestation weight, gravid uterine weight, net weight gain, and food consumption). Nilotinib at doses $\geq$30 mg/kg/day resulted in embryo-fetal toxicity as shown by increased resorptions and post-implantation loss, and at 100 mg/kg/day a decrease in viable fetuses. In rabbits, maternal toxicity at 300 mg/kg/day was associated with mortality, abortion, decreased gestation weights and decreased food consumption. Embryonic toxicity (increased resorptions) and minor skeletal anomalies were observed at a dose of 300 mg/kg/day. Nilotinib is not considered teratogenic.

There were no effects on male or female rat and female rabbit mating or fertility at doses up to 180 mg/kg in rats or 300 mg/kg in rabbits. The effect of Tasigna on human fertility is unknown. In a study where male and female rats were treated with nilotinib at oral doses of 20-180 mg/kg/day during the pre-mating and mating periods and then mated, and dosing of pregnant rats continued through gestation day 6, nilotinib increased post-implantation loss and early resorptions, and decreased the number of viable fetuses and litter size at all doses tested.

SECTION 12. ECOLOGICAL INFORMATION

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

Bacteria toxicity (respiration inhibition):
EC_{50}: > 300 mg/l
Species: activated sludge
Exp. time: 3 hours
Method: Inhibition of Oxygen Consumption by activated sludge (87/302/EEC), Part C
Fish toxicity:
LC_{50}: > 100 mg/l
NoEC: >= 100 mg/l
Species: zebra fish (brachydanio rerio)
Exp. time: 96 hours
Method: 92/69/EEC (L383) C.1 * Acute toxicity for fish
nominal concentration due to the limited solubility
Daphnia toxicity:
EC_{50}: > 100 mg/l
NoEC: >= 100 mg/l
Species: daphnia magna (water flea)
Exp. time: 48 hours
Method: 92/69/EEC (L383) C.2 * Acute toxicity for daphnia
nominal concentration due to the limited solubility
Algae toxicity:
EbC_{50}: > 0.016 mg/l
ErC_{50}: > 0.016 mg/l
NoEC: 0.008 mg/l
Species: Selenastrum capricornutum. Green algae.
Exp. time: 72 hours
Method: 92/69/EC (L383) C.3 * Algal inhibition test.
Biological elimination:
Degradation: 22.3 % (aerobic: Temperature: 21.8 °C CO2)
Not readily degradable
Initial conc.: 23.62 mg/l, Duration: 28 days
Method: 92/69/EC (L383) C.4-C * Carbon dioxide (CO2) evolution

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: New

Written By:	C. Perino	**Date:**	07 Nov 07
Approved By:	G. King	**Date:**	14 Dec 07

To the best of our knowledge, the information contained herein is accurate. However, Novartis Pharmaceuticals Corporation does not assume any liability whatsoever for the accuracy or completeness of the information contained herein except for the product's administration/use as intended. Final determination of the suitability of any material is the sole responsibility of the user. All materials may present unknown hazards and should be used with caution. Although certain hazards are described herein, we cannot guarantee that these are the only hazards which exist.