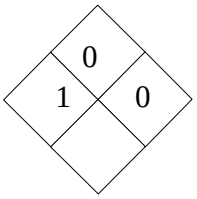
NOVARTIS



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:	**Femara**Ò **Tablets, 2.5 mg**
SYNONYMS:	Letrozole Tablets
THERAPEUTIC CATEGORY:	Treatment of breast cancer (nonsteroidal aromatase inhibitor)
GENERIC NAME:	None
CHEMICAL NAME:	4,4'-(1H-1,2,4-Triazol-1-ylmethylene)dibenzonitrile
CHEMICAL FORMULA:	$C_{17}H_{11}N_5$
MOLECULAR WEIGHT:	285.31

SECTION 2. COMPOSITION/INFORMATION ON INGREDIENTS

COMPOSITION	CAS#	CONCENTRATION (% by wt.)
Active Ingredients		
Femara Active Ingredient	112809-51-5	2.5
Inactive Ingredients		
Lactose	63-42-3	60-65
Avicel PH 102	Not Available	~20
Starch	9005-25-8	9-10

SECTION 3. HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW

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FINISHED PHARMACEUTICAL PRODUCT
REFER TO PHYSICIANS' DESK REFERENCE OR PACKAGE INSERT
MAY CAUSE NAUSEA, BONE PAIN AND ARTHRALGIA
EXPERIMENTAL TERATOGEN
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:	Bone pain, hot flushes, back pain, nausea, fatigue, dizziness, arthralgia and dyspnea.
TARGET ORGAN EFFECTS:	Letrozole has been found to accumulate in the skin, as well as produce changes in the liver and bone.
REPRODUCTIVE HAZARDS:	**FDA Pregnancy Category D** (see section 11). Given its inhibitory effect on estrogen synthesis, the potential exists for Letrozole to inhibit uterine implantation of the fertilized egg, produce menstrual irregularities, and adversely affect the developing fetus.
CARCINOGENICITY:	See section 11.
MUTAGENICITY:	Letrozole was clastogenic in two in vitro assays, and non-mutagenic in two in vitro assays and one in vivo assay (see Section 11).

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: Pregnancy; known hypersensitivity to letrozole or any other components of the formulation; pre-existing liver or kidney 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 tablet 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, sweep up and containerize spilled material. Avoid contamination of 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 tablet is crushed.
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**
Letrozole	NPIEL = 0.0001 mg/m^3

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance:	Tablet		
Color:	dark yellow, film-coated		
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:	Dichloromethane, ethanol (slt.)	**% 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 is for drug substance.

Eye Irritation: Not an irritant (rabbit).

Skin Irritation/Sensitization: Not an irritant (rabbit)

Oral Toxicity: LD_{50} > 2000 mg/kg (rat)
LD_{50} > 2000 mg/kg (mouse)
LD_{50} = 200 mg/kg (dog)

Dermal Toxicity: No data available.

Inhalation Toxicity: No data available

Chronic/Carcinogenicity: In a two-year carcinogenicity study in mice at oral doses of 0.6 to 60 mg/kg/day, and in rats at oral doses of 0.1 to 10 mg/kg/day, a dose-related increase in the incidence of benign ovarian stromal tumors was observed. This effect was seen in rats at the 10 mg/kg dose. In female rats, ovarian hyperplasia was observed at doses equal to or greater than 0.1 mg/kg/day.

Mutagenicity: Positive in the following tests: Potential clastogen in the *in vitro* CHO K1 and CCL 61 Chinese hamster ovary cells
Negative in the following tests: *in vitro* Ames and E. coli bacterial assays, and an *in vivo* rat micronucleus assay.

Reproductive Effects: Letrozole may cause fetal harm when administered to pregnant women.

Studies in rats at doses equal to or greater than 0.003 mg/kg administered during the period of organogenesis, have shown that letrozole is embryotoxic and fetotoxic, as indicated by intrauterine mortality, increased resorption, increased post implantation loss, decreased numbers of live fetuses and fetal anomalies including absence and shortening of renal papilla, dilation of ureter, edema and incomplete ossification of frontal skull and metatarsals. Letrozole was also teratogenic in rats, causing fetal domed heads and cervical/centrumvertebral fusion at a dose of 0.03 mg/kg.

In rabbits, Letrozole is embryotoxic at doses equal to or greater than 0.002 mg/kg and fetotoxic at 0.02 mg/kg.

There are no studies in pregnant women. Femara® is indicated for postmenopausal women. The patient should be apprised of the potential hazard to the fetus and potential risk for loss of the pregnancy It is also not known whether letrozole is excreted in human milk. Caution should be exercised when letrozole is administered to pregnant women.

SECTION 12. ECOLOGICAL INFORMATION

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

Biological elimination:
1 % (CO_2)
Initial conc. 23.4 mg/l
Not readily degradable
Method: OECD 301B * 1981 Mmod. Sturm (ready)

Biological elimination:
1 % (CO_2)
Initial conc. 26.3 mg/l
Not readily degradable
Method: OECD 301B * 1981 Mmod. Sturm (ready)

Fish toxicity: LC_0: 37 mg/l
LC_{50}: > 37 mg/l
LC_{100}: > 37 mg/l
(Species: rainbow trout (salmo gairdneri, oncorhynchus mykiss), Exp. time: 96 h)
Method: OECD 203 * 1984 acute tox.
Not toxic with reference to the 7th Amendment to Directive 67/548/EEC, 92/32/EEC

Daphnia toxicity: EC_0: 35 mg/l
EC_{50}: > 35 mg/l
EC_{100}: > 35 mg/l
(Species: daphnia magna (water flea), Exp. time: 48 h)
Method: OECD 202.I
Not toxic with reference to the 7th Amendment to Directive 67/548/EEC, 92/32/EEC

Algae toxicity: EC_{50}: > 100 mg/l
(Species: Scenedesmus subspicatus 86.81 sag. green algae, Exp time: 72 h)
Method: OECD 201 * 1984. Growth inhibition
Not toxic with reference to the 7th Amendment to Directive 67/548/EEC, 92/32/EEC

Bacteria toxicity (respiration inhibition):
EC_0: 20.2 mg/l
EC_{50}: > 20.2 mg/l
EC_{100}: > 20.2 mg/l
(Species: activated sludge, Exp. time: 696 h)
Method: evaluated

Bioaccumulation in water organisms is not likely based on the n-octanol/water partition coefficient (log pOW < 3.0). When low concentrations are discharged correctly into adapted biological sewage treatment plants, interference with the degradation activity of activated sludge is not likely.

SECTION 13. DISPOSAL CONSIDERATIONS

Waste Disposal Method: All wastes must be disposed of in accordance with local, state and federal laws and regulations. (Contact local or state environmental agency for specific rules).

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

EEC Classification (European Economic Community): **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:** 15 Oct 03
Approved By:	J. Affuso	**Date:** 28 Oct 03

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