SAFETY DATA SHEET

Prepared to U.S. OSHA, CMA, ANSI, Canadian WHMIS Standards, European Union CLP EC 1272/2008 and the Global Harmonization Standard

1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY UNDERTAKING

PRODUCT IDENTIFIER/TRADE/MATERIAL NAME: **TAMOXIFEN CITRATE TABLETS**

Tamoxifen Tablets, 10 mg and 20 mg

DESCRIPTION: Tamoxifen Tablets

OTHER DESIGNATIONS: None

CHEMICAL NAME: For Active Ingredient: (Z)2-[4-(1,2-diphenyl-1-butenyl) phenoxy]-N, N-dimethylethanamine 2 hydroxy-1,2,3-propanetricarboxylate (1:1)

CHEMICAL FAMILY: For Active Ingredient: Trans-Isomer of a Triphenylethylene Derivative/Non-Steroidal Antiestrogen

HOW SUPPLIED: 10 mg and 20 mg Tablets

NDC #: 0591-2472-18, 0591-2472-60, 0591-2473-19, 0591-2473-30

FORMULA: For Active Ingredient: $C_{26}H_{29}NO.C_6H_8O_7$

SUPPLIER OF THE SAFETY DATA SHEET

RESPONSIBLE PARTY U.S.:	**ACTAVIS, INC.**
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NOTE: ALL United States Occupational Safety and Health Administration Standard (29 CFR 1910.1200), U.S. State equivalent Standards, Canadian WHMIS [Controlled Products Regulations], EU Directives through EC 1907: 2006, and European Union CLP EC 1272/2008, required information is included in appropriate sections based on the U.S. ANSI Z400.1-2010 format. This compound has been classified in accordance with the hazard criteria of the countries listed above.

DATE OF PREPARATION: May13, 2016 **DATE OF REVISION:** New

2. HAZARDS IDENTIFICATION

EU CLP REGULATION (EC) 1272/2008 LABELING AND CLASSIFICATION: According to Article 1, item 5 (a) of CLP Regulation (EC) 1272/2008, medicinal products in the finished state for human use, as defined in 2001/83/EC, are excepted from classification and other criteria of 1272/2008.

Classification: Not Applicable Signal Word: Not Applicable Hazard Statement Codes: Not Applicable

EU LABELING AND CLASSIFICATION 67/548/EEC: According to Article 1 of European Union Council Directive 92/32/EEC, medical products in the finished state for human use (as defined by European Union Council Directives 67/548/EEC and 87/21/EEC) are not subject to the regulations and administrative provisions of European Union Council Directive 92/32/EEC.

Classification: Not Applicable Risk Phrases: Not Applicable Safety Phrases: Not Applicable

See Section 16 for full EU classification information of product and components and full text of hazard and precautionary statements.

EMERGENCY OVERVIEW:

Product Description: This product is supplied as white tablets.

Health Hazards: The chief health hazard associated with overexposures during normal use and handling is the potential for irritation of contaminated skin or eyes from damaged tablets. Non-therapeutic ingestion may be harmful. The most common adverse effects from therapeutic use have been nausea, anorexia, distaste for food, and abdominal cramps, dizziness, lightheadedness, headache, fatigue, and mental depression. May cause harm to fetus. Other adverse effects seen from therapeutic use are described in Section 11 (Toxicological information).

Flammability Hazards: Exposure to high heat or ignition source may cause product to burn. Involvement in fire will cause decomposition and production of irritating vapors and toxic compounds, including carbon, nitrogen, magnesium and sodium oxides.

Reactivity Hazards: This product is not reactive.

Environmental Hazards: Large quantities released to the aquatic and terrestrial environment may have an adverse effect.

Emergency Considerations: Emergency responders should wear appropriate protection for the situation to which they respond.

3. COMPOSITION and INFORMATION ON INGREDIENTS

CHEMICAL NAME	CAS #	EINECS #	% w/w	EU Classification (67/548/EEC) GHS & EU Classification (1272/2008 EC) Risk Phrases/Hazard Statements/Symbol
ACTIVE INGREDIENT:				
Tamoxifen Citrate	54965-24-1	259-415-2	Proprietary	SELF-CLASSIFICATION EU 67/548 Classification: Reproductive Toxicity Cat. 2, Harmful Risk Phrases: R22, R61 Hazard Symbol: T, Xn EU/GHS 1272/2008 Classification: Reproductive Toxicity Cat. 1, Acute Oral Toxicity Cat. 4 Hazard Statement Codes: H360D, H302 Hazard Symbol/Pictogram: GHS07, GHS08
EXCIPIENTS:				
Croscarmellose Sodium	9004-32-4	Not Listed	Proprietary	EU 67/548 Hazard Classification: Not Applicable EU/GHS 1272/2008 Classification: Not Applicable
Lactose Monohydrate	64044-51-8	200-559-2	Proprietary	EU 67/548 Hazard Classification: Not Applicable EU/GHS 1272/2008 Classification: Not Applicable
Magnesium Stearate	557-04-0	209-150-3	Proprietary	EU 67/548 Hazard Classification: Not Applicable EU/GHS 1272/2008 Classification: Not Applicable
Microcrystalline Cellulose	9004-34-6	232-674-9	Proprietary	EU 67/548 Hazard Classification: Not Applicable EU/GHS 1272/2008 Classification: Not Applicable
Pregelatinized Starch	9005-25-8	232-679-6	Proprietary	EU 67/548 Hazard Classification: Not Applicable EU/GHS 1272/2008 Classification: Not Applicable

See Section 16 for full EU classification information of product and components.

4 FIRST-AID MEASURES

PROTECTION OF FIRST AID RESPONDERS: First-aid responders should not attempt to treat victims of exposure to this material without adequate personal protective equipment. Rescuers should be taken for medical attention, if necessary.

DESCRIPTION OF FIRST AID MEASURES: Victim(s) must be taken for medical attention. Remove victim(s) to fresh air, as quickly as possible. Only trained personnel should administer supplemental oxygen and/or cardio-pulmonary resuscitation, when necessary. Take copy of label and MSDS to physician or other health professional with victim(s).

INHALATION: If dusts or particulates from this product are inhaled, remove victim to fresh air. If necessary, use artificial respiration to support vital functions. Seek medical attention if adverse effect occurs after removal to fresh air.

SKIN EXPOSURE: If the product contaminates the skin and adverse effect occurs, begin decontamination with running water. Minimum flushing is for 20 minutes. Do not interrupt flushing. Remove exposed or contaminated clothing, taking care not to contaminate eyes. Seek medical attention if adverse effect occurs after flushing.

EYE EXPOSURE: If particulates from this product enter the eyes, open victim's eyes while under gently running water. Use sufficient force to open eyelids. Have victim "roll" eyes. Minimum flushing is for 20 minutes. Do not interrupt flushing. Seek immediate medical attention after flushing if adverse effect occurs.

INGESTION EXPOSURE: If this product is swallowed, CALL PHYSICIAN OR POISON CONTROL CENTER FOR MOST CURRENT INFORMATION. If professional advice is not available, do not induce vomiting. Rinse mouth with water immediately. Victim should drink large quantities of water. If milk is available, victim should drink it after drinking water. Never induce vomiting or give diluents (milk or water) to someone who is unconscious, having convulsions, or unable to swallow.

IMPORTANT SYMPTOMS AND EFFECTS: See Sections 2 (Hazard Identification) and 11 (Toxicological Information).

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: When administered for therapeutic use, pre-existing hepatic, central nervous system, liver, deep-vein thrombosis or pulmonary embolism and eye conditions may be aggravated by exposure or therapeutic use of this product.

IMMEDIATE MEDICAL ATTENTION AND SPECIAL TREATMENT NEEDED: This product should only be given to patients by persons experienced in management of patients receiving the type of therapy intended for this product. Treat symptoms and eliminate exposure.

5. FIRE-FIGHTING MEASURES

FLASH POINT: For Active: 482.3°C (900.14°F)

AUTOIGNITION TEMPERATURE: Not established.

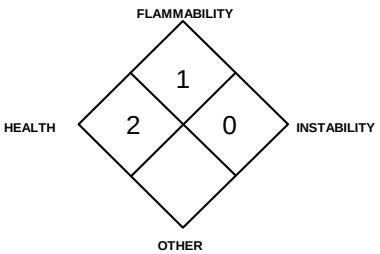
FLAMMABLE LIMITS & METHOD OF DETERMINATION (in air by volume, %): Not determined.

FIRE EXTINGUISHING MEDIA: Use extinguishing media appropriate for surrounding fire.

UNSUITABLE EXTINGUISHING MEDIA: None known.

SPECIAL FIRE AND EXPLOSION HAZARDS: This product may ignite if highly heated for a prolonged period of time. When involved in a fire, the products of thermal decomposition may include irritating fumes and toxic gases (e.g., carbon, nitrogen, magnesium and sodium oxides).

NFPA RATING



Hazard Scale: **0** = Minimal **1** = Slight **2** = Moderate **3** = Serious **4** = Severe

5. FIRE-FIGHTING MEASURES (Continued)

SPECIAL FIRE AND EXPLOSION HAZARDS (continued):

Explosion Sensitivity to Mechanical Impact: Not sensitive.

Explosion Sensitivity to Static Discharge: Not sensitive.

ADVICE TO FIRE-FIGHTERS: Incipient fire responders should wear eye protection. Structural firefighters must wear Self-Contained Breathing Apparatus (SCBA) and full protective equipment. Contaminated protective equipment should be thoroughly washed with running water prior to removal of SCBA respiratory protection. Firefighters whose protective equipment becomes contaminated should thoroughly shower with warm, soapy water and should receive medical evaluation if they experience any adverse effects.

6. ACCIDENTAL RELEASE MEASURES

PERSONAL PRECAUTIONS: In the event of a spill, clear the area and protect people.

PROTECTIVE EQUIPMENT:

Small Spills: For incidental spills (e.g., 1 vial of tablets), wear double latex or nitrile disposable gloves and eye protection.

Large Spills: For large spills (e.g., a pallet of vials), protective apparel should be used with a respirator when there is any danger of airborne dusts being generated. Minimum Personal Protective Equipment should be rubber gloves, rubber boots, face shield, and Tyvek suit.

METHODS FOR CLEANUP AND CONTAINMENT:

Small Spills: Pick-up or sweep-up spilled tablets.

Large Spills: Trained personnel following pre-planned procedures should handle non-incidental releases. Access to the spill areas should be restricted. Sweep up spilled product carefully, avoiding the generation of airborne dusts.

All Spills: Decontaminate the area of the spill thoroughly using detergent and water. Place all spill residue in an appropriate container and seal. Do not mix with wastes from other materials. If necessary, discard contaminated response equipment or rinse with soapy water before returning such equipment to service. Dispose of in accordance with applicable international, national, state, and local procedures (see Section 13, Disposal Considerations).

ENVIRONMENTAL PRECAUTIONS: Prevent material from entering sewer or confined spaces, waterways, soil or public waters. Do not flush to sewer. For spills on water, contain, minimize dispersion and collect.

7. HANDLING and USE

PRECAUTIONS FOR SAFE HANDLING: Employees must be trained to properly use this product. As with all chemicals, avoid getting this material ON YOU or IN YOU. Do not eat, drink, smoke, or apply cosmetics in work areas where this product is handled or stored. Wash thoroughly after handling this product or equipment and containers of this product. Follow SPECIFIC USE INSTRUCTIONS supplied with this product. Use of this product should be performed in a designated area for working with drugs. Particular care in working with this product must be practiced in pharmacies and other preparation areas, during manufacture of this compound, and during patient administration. If necessary, work areas must be regularly cleaned and decontaminated.

PRODUCT PREPARATION INSTRUCTIONS FOR MEDICAL PERSONNEL: Handle this material following standard medical practices and following the recommendations presented on the Package Insert.

CONDITIONS FOR SAFE STORAGE: Containers of this product must be properly labeled. Store this product in original container at controlled room temperature of 25°C (77°F); excursions permitted to 15-30°C (59-86°F). Inspect bottles containing this product for leaks or damage. Store away from incompatible materials (see Section 10, Stability and Reactivity).

SPECIFIC END USE(S): This product human pharmaceutical. Follow all industry standards for use of this product.

8. EXPOSURE CONTROLS - PERSONAL PROTECTION

EXPOSURE LIMITS/CONTROL PARAMETERS:

VENTILATION AND ENGINEERING CONTROLS: Use with adequate ventilation. Follow standard medical product handling procedures. During decontamination of work surfaces, workers should wear the same equipment recommended in Section 6 (Accidental Release Measures) of this MSDS.

OCCUPATIONAL/WORKPLACE EXPOSURE LIMITS/GUIDELINES:

CHEMICAL NAME	CAS #	EXPOSURE LIMITS IN AIR							
		ACGIH-TLVs		OSHA-PELs		NIOSH-RELs		NIOSH	OTHER
		TWA mg/m^3	STEL mg/m^3	TWA mg/m^3	STEL mg/m^3	TWA mg/m^3	STEL mg/m^3	IDLH mg/m^3	mg/m^3
Tamoxifen Citrate	54965-24-1	NE	NE	NE	NE	NE	NE	NE	OEL: 1 $\mu g/m^3$
Croscarmellose Sodium	9004-32-4	NE	NE	NE	NE	NE	NE	NE	NE
Lactose Monohydrate	64044-51-8	NE	NE	NE	NE	NE	NE	NE	NE
Magnesium Stearate Exposure limits are for Stearates	557-04-0	10	NE	NE	NE	NE	NE	NE	Carcinogen: TLV-A4
Microcrystalline Cellulose	9004-34-6	10	NE	15 (total dust), 5 (respirable fraction)	NE	10 (total dust), 5 (respirable fraction)	NE	NE	NE
Pregelatinized Starch	9005-25-8	10	NE	15 (total dust), 5 (respirable fraction)	NE	10 (total dust), 5 (respirable fraction)	NE	NE	Carcinogen: TLV-A4

NE = Not Established.

8. EXPOSURE CONTROLS - PERSONAL PROTECTION (Continued)

EXPOSURE LIMITS/CONTROL PARAMETERS (continued):

INTERNATIONAL OCCUPATIONAL EXPOSURE LIMITS: In addition to the exposure limit values cited in this section, other exposure limits have been established by various countries for the components of this product. The exposure limits given may not be the most current; individual country authorities should be contacted to check on more current limits.

CROSCARMELLOSE SODIUM:
Russia: STEL = 10 mg/m^3, JUN 2003

MAGNESIUM STEARATE:
New Zealand: TWA = 10 mg/m^3 (inspirable dust), JAN 2002
Sweden: TWA = 5 mg/m^3, JUN 2005

MICROCRYSTALLINE CELLULOSE:
Belgium: TWA = 10 mg/m^3, MAR 2002
France: VME = 10 mg/m^3, FEB 2006
Korea: TWA = 10 mg/m^3, 2006
Mexico: TWA = 10 mg/m^3; STEL = 20 mg/m^3, 2004
The Netherlands: MAC-TGG = 2 mg/m^3, 2003
New Zealand: TWA = 10 mg/m^3 (inspirable dust), JAN 2002
Russia: STEL = 10 mg/m^3, JUN 2003
Switzerland: MAK-W = W 6 mg/m^3, DEC 2006

MICROCRYSTALLINE CELLULOSE (continued):
United Kingdom: TWA = 10 mg/m^3 (inhalable), 2005
United Kingdom: TWA = 4 mg/m^3; STEL = 20 mg/m^3 (respirable), 2005
In Argentina, Bulgaria, Colombia, Jordan, Singapore, Vietnam, check ACGIH TLV

PREGELATINIZED STARCH:
Belgium: TWA = 10 mg/m^3, MAR 2002
Korea: TWA = 10 mg/m^3, 2006
New Zealand: TWA = 10 mg/m^3 (inspirable dust), JAN 2002
Russia: STEL = 10 mg/m^3, JUN 2003
Switzerland: MAK-W = 3 mg/m^3, DEC 2006
United Kingdom: TWA = 10 mg/m^3 (inhalable), 2005
United Kingdom: TWA = 4 mg/m^3 (respirable), 2005
In Argentina, Bulgaria, Colombia, Jordan, Singapore, Vietnam check ACGIH TLV

PERSONAL PROTECTIVE EQUIPMENT: Use of personal protective equipment must be in compliance with U.S. OSHA 29 CFR Subpart I (beginning at 1910.132), Canadian CSA Standards Z94.4-02 and Z94.3-02, EU EN 529:2005, CEN/TR 15419:2006, and CR 13464:1999. Please reference applicable regulations and standards for relevant details.

RESPIRATORY PROTECTION: Respiratory protection is generally not needed during routine conditions of use of this product. If respiratory protection is needed, use only respiratory protection authorized under appropriate regional regulations.

EYE PROTECTION: No eye protection is normally needed during medical administration of this product. During operations in which dusts of the product may be generated, splash goggles or safety glasses should be considered.

HAND PROTECTION: During medical administration of this product, medical latex or nitrile gloves should be worn to avoid absorption of the product. During manufacture or other similar industrial operations, wear the appropriate hand protection for the process. Use double gloves for spill response, as stated in Section 6 (Accidental Release Measures) of this MSDS.

BODY PROTECTION: Use appropriate protective clothing for the task (e.g., lab coat, etc.)

9. PHYSICAL and CHEMICAL PROPERTIES

The following values are available for the active ingredient, Tamoxifen Citrate:

FORM: Crystalline solid.
COLOR: White.
MOLECULAR WEIGHT: 563.62
MOLECULAR FORMULA: $C_9H_7N_5Cl_2$
ODOR: Odorless.
ODOR THRESHOLD: Not applicable.
BOILING POINT @ 760 mmHg: 482.3°C (900.14°F)
MELTING POINT: 140-144°C (284-291.2°F)
VAPOR PRESSURE (air = 1) @ 25°C: 1.85E-09mmHg
SPECIFIC GRAVITY (water = 1): Not available.
EVAPORATION RATE (nBuAc = 1): Not applicable.
FLASH POINT: 140°C (284°F)
SOLUBILITY IN WATER @ 37°C: 0.5 mg/mL
OTHER SOLUBILITIES@ 37°C: in 0.02 N HCl it is 0.2 mg/mL; Soluble to 5 mM in ethanol and to 100 mM in DMSO
COEFFICIENT WATER/OIL DISTRIBUTION: Log P(oct) = 7.882 (est.)

The following information is for the product.

FORM: Tablets. **COLOR:** White. **ODOR:** Odorless. **ODOR THRESHOLD:** Not applicable.

HOW TO DETECT THIS SUBSTANCE (identification properties): The appearance of this product is a distinguishing characteristic.

10. STABILITY and REACTIVITY

REACTIVITY/CHEMICAL STABILITY: This product is not reactive.

DECOMPOSITION PRODUCTS: *Combustion:* If exposed to extremely high temperatures, the products of thermal decomposition may include irritating fumes and toxic gases (e.g. carbon, nitrogen, magnesium and sodium oxides). *Hydrolysis:* None known.

MATERIALS WITH WHICH SUBSTANCE IS INCOMPATIBLE: This product is generally compatible with other common materials in a medical facility. Acids and alkalies, and other chemicals that could affect its performance should be avoided.

POSSIBILITY HAZARDOUS POLYMERIZATION: Will not occur.

CONDITIONS TO AVOID: Avoid heat, light, and contact with incompatible chemicals.

11. TOXICOLOGICAL INFORMATION

SYMPTOMS OF OVEREXPOSURE BY ROUTE OF EXPOSURE: The health hazard information provided below is pertinent to medical employees using this product in an occupational setting. The following paragraphs describe the symptoms of exposure by route of exposure.

INHALATION: Inhalation of airborne dusts generated by damaged tablets of this product may slightly irritate the nose, throat, and lungs. Symptoms are generally alleviated upon breathing fresh air.

CONTACT WITH SKIN or EYES: Contact with the skin may cause mild irritation, which is alleviated upon rinsing. Prolonged or repeated skin contact may cause dermatitis (dry, red skin). Contact with the eyes of airborne dusts generated by damaged tablets of this product may cause mild to moderate irritation, redness, and tearing.

SKIN ABSORPTION: The components of this product are not known to be absorbed through intact skin.

11. TOXICOLOGICAL INFORMATION (Continued)

INGESTION: Ingestion is not a significant route of occupational overexposure. If swallowed, irritation of the gastrointestinal tract may occur with nausea, vomiting, abdominal discomfort, and diarrhea. Other symptoms of prolonged or repeated ingestion, as may occur when poor industrial hygiene is practiced, may include those described for "Other Potential Health Effects".

INJECTION: Local pain and inflammation may result from subcutaneous injection.

OTHER POTENTIAL HEALTH EFFECTS-Therapeutic Doses: Employees administering the product should not experience adverse effects if handled properly. Adverse effects from therapeutic doses have included those described below.

- ***Body as a Whole:*** Asthenia, pain, back pain, headache, abdominal pain, infection, infection, flu syndrome, chest pain, neoplasm, cyst.
- ***Cardiovascular:*** Vasodilatation, hypertension.
- ***Digestive:*** Nausea, constipation, diarrhea, gastrointestinal disorder.
- ***Hemic and Lymphatic:*** Lymphoedema, anemia.
- ***Metabolic and Nutritional:*** Peripheral edema, weight gain, hypercholesterolemia.
- ***Musculoskeletal:*** Arthritis, arthralgia, osteoporosis, fracture, bone pain, arthrosis, joint disorder, myalgia.
- ***Nervous System:*** Depression, insomnia, dizziness, anxiety, paraesthesia.
- ***Respiratory:*** Pharyngitis, cough, dyspnea, sinusitis, bronchitis.
- ***Skin and Appendages:*** Rash, sweating.
- ***Eyes:*** Cataract.
- ***Urogenital:*** Leukorrhea, Urinary tract infection, breast pain, breast neoplasm, vulvovaginitis, vaginal hemorrhage, vaginitis.

HAZARDOUS MATERIAL IDENTIFICATION SYSTEM

HEALTH HAZARD	(BLUE)	2*
FLAMMABILITY HAZARD	(RED)	1
PHYSICAL HAZARD	(YELLOW)	0

PROTECTIVE EQUIPMENT

EYES	RESPIRATORY	HANDS	BODY
	SEE SECTION 8		SEE SECTION 8

For Routine Industrial Use and Handling Applications

Hazard Scale: **0** = Minimal **1** = Slight **2** = Moderate **3** = Serious **4** = Severe * = Chronic hazard

HEALTH EFFECTS OR RISKS FROM EXPOSURE: An Explanation in Lay Terms. Overexposure to this product may cause the following health effects:

ACUTE: May cause irritation if inhaled. Eye contact of dusts may cause mechanical irritation. Ingestion may be harmful.

CHRONIC: In the event of chronic exposures to therapeutic doses of this product, effects described in "Other Potential Health Effects" may result.

TARGET ORGANS: ACUTE: Industrial Exposure: Skin, eyes. Therapeutic Doses: Gastrointestinal, cardiac systems. CHRONIC: Industrial Exposure: Skin. Therapeutic Doses: Respiratory, digestive, nervous, urogenital and musculoskeletal systems.

IRRITANCY OF PRODUCT: This product is not expected to irritate contaminated tissue unless particulates are generated; mild irritation may result.

SENSITIZATION OF PRODUCT: No specific information is available on possible sensitization effects.

TOXICITY DATA: Only currently available toxicity data for the active component presented in this MSDS. Additional data for excipients are available but are not presented in this MSDS. Contact Actavis for more information.

TAMOXIFEN CITRATE:

TDLo (Oral-Woman) 154 mg/kg/1 year-intermittent: Sense Organs and Special Senses (Eye): visual field changes, retinal changes (pigmentary depositions, retinitis, other)

TDLo (Oral-Woman) 3600 µg/kg/9 days-intermittent: Behavioral: somnolence (general depressed activity); Gastrointestinal: nausea or vomiting; Nutritional and Gross Metabolic: changes in calcium

TDLo (Oral-Woman) 1216 µg/kg: female 22 week(s) pre-mating: Reproductive: Maternal Effects: uterus, cervix, vagina, menstrual cycle changes or disorders, other effects

LD_{50} (Oral-Rat) 1190 mg/kg: Behavioral: somnolence (general depressed activity); Lungs, Thorax, or Respiration: respiratory depression, weight loss or decreased weight gain

LD_{50} (Oral-Mouse) 3100 mg/kg

LD_{50} (Intraperitoneal-Rat) 575 mg/kg: Behavioral: somnolence (general depressed activity); Lungs, Thorax, or Respiration: respiratory depression; Nutritional and Gross Metabolic: weight loss or decreased weight gain

LD_{50} (Intraperitoneal-Mouse) 218 mg/kg: Skin and Appendages: hair

LD_{50} (Subcutaneous-Rat) > 5 gm/kg: Behavioral: convulsions or effect on seizure threshold

TAMOXIFEN CITRATE (continued):

LD_{50} (Subcutaneous-Mouse) > 5 gm/kg: Behavioral: convulsions or effect on seizure threshold

LD_{50} (Intravenous-Rat) 62,500 µg/kg

LD_{50} (Intravenous-Mouse) 62,500 µg/kg

TDLo (Oral-Rat) 2450 µg/kg/5 weeks-intermittent: Kidney/Ureter/Bladder: changes in bladder weight; Blood: changes in platelet count; Related to Chronic Data: changes in prostate weight

TDLo (Oral-Rat) 127 mg/kg/26 weeks-intermittent: Liver: changes in liver weight; Blood: changes in serum composition (e.g. TP, bilirubin, cholesterol), changes in leukocyte (WBC) count

TDLo (Oral-Rat) 67,200 µg/kg/12 weeks-intermittent: Blood: changes in serum composition (e.g. TP, bilirubin, cholesterol); Biochemical: Enzyme inhibition, induction, or change in blood or tissue levels: dehydrogenases, Enzyme inhibition, induction, or change in blood or tissue levels: other transferases

TDLo (Oral-Rat) 147 mg/kg/7 weeks-continuous: Reproductive: Maternal Effects: menstrual cycle changes or disorders

TDLo (Oral-Rat) 840 µg/kg/28 days-intermittent: Endocrine: differential effect of sex or castration on observed toxicity; Nutritional and Gross Metabolic: weight loss or decreased weight gain

TAMOXIFEN CITRATE (continued):

TDLo (Oral-Rat) 5600 µg/kg/28 days-intermittent: Nutritional and Gross Metabolic: weight loss or decreased weight gain; Related to Chronic Data: changes in prostate weight, changes in uterine weight

TDLo (Oral-Rat) 15,512 mg/kg/1 year-intermittent: Tumorigenic: carcinogenic by RTECS criteria; Liver: tumors

TDLo (Oral-Rat) 3640 mg/kg/36 weeks-intermittent: Tumorigenic: equivocal tumorigenic agent by RTECS criteria; Liver: tumors

TDLo (Oral-Rat) 200 µg/kg: female 4 day(s) after conception: Reproductive: Fertility: female fertility index (e.g. # females pregnant per # sperm positive females; # females pregnant per # females mated)

TDLo (Oral-Rat) 90 µg/kg: female 2-4 day(s) after conception: Reproductive: Fertility: pre-implantation mortality (e.g. reduction in number of implants per female; total number of implants per corpora lutea)

TDLo (Oral-Rat) 300 µg/kg: female 3 day(s) pre-mating: Reproductive: Maternal Effects: uterus, cervix, vagina

TDLo (Oral-Rat) 24,500 µg/kg: male 35 day(s) pre-mating: Reproductive: Paternal Effects: testes, epididymis, sperm duct, prostate, seminal vesicle, Cowper's gland, accessory glands

11. TOXICOLOGICAL INFORMATION (Continued)

TOXICITY DATA (continued):

TAMOXIFEN CITRATE (continued):

TDLo (Oral-Rat) 100 µg/kg: female 1 day(s) pre-mating: Reproductive: Fertility: other measures of fertility

TDLo (Oral-Rat) 500 µg/kg: female 1 day(s) pre-mating: Reproductive: Maternal Effects: ovaries, fallopian tubes, uterus, cervix, vagina

TDLo (Oral-Rat) 10 mg/kg:Multi-generations: Reproductive: Fertility: other measures of fertility; Effects on Newborn: sex ratio

TDLo (Oral-Rat) 490 mg/kg: female 6 week(s) pre-mating 1 week(s) after conception: Reproductive: Maternal Effects: parturition; Fertility: female fertility index (e.g. # females pregnant per # sperm positive females; # females pregnant per # females mated)

TDLo (Oral-Rat) 1050 mg/kg: female 14 day(s) pre-mating 7 day(s) after conception: Reproductive: Effects on Newborn: live birth index (measured after birth)

TDLo (Oral-Mouse) 5 mg/kg: female 3-7 day(s) after conception: Reproductive: Fertility: pre-implantation mortality (e.g. reduction in number of implants per female; total number of implants per corpora lutea)

TDLo (Oral-Rabbit) 34 mg/kg: female 10-26 day(s) after conception: Reproductive: Fertility: post-implantation mortality (e.g. dead and/or resorbed implants per total number of implants); Effects on Newborn: live birth index (measured after birth)

TAMOXIFEN CITRATE (continued):

TDLo (Oral-Rabbit) 14 mg/kg: female 20-26 day(s) after conception: Reproductive: Maternal Effects: parturition

TDLo (Oral-Hamster) 500 µg/kg: female 1 day(s) pre-mating: Reproductive: Fertility: other measures of fertility

TDLo (Oral-Dog) 9100 mg/kg/13 weeks-intermittent: Gastrointestinal: hypermotility, diarrhea; Blood: changes in leukocyte (WBC) count; Related to Chronic Data: changes in ovarian weight

TDLo (Subcutaneous-Rat) 14 mg/kg/2 weeks-intermittent: Biochemical: Metabolism (Intermediary): other proteins; Related to Chronic Data: changes in uterine weight

TDLo (Subcutaneous-Mouse) 10 mg/kg: Behavioral: alteration of operant conditioning

TDLo (Intravenous-Rat) 50 µg/kg: female 4 day(s) after conception: Reproductive: Fertility: pre-implantation mortality (e.g. reduction in number of implants per female; total number of implants per corpora lutea)

TDLo (Intravenous-Rat) 500 µg/kg: female 1 day(s) pre-mating: Reproductive: Fertility: other measures of fertility

TDLo (Intravenous-Rat) 3 µg/kg: female 3 day(s) pre-mating: Reproductive: Maternal Effects: uterus, cervix, vagina

TAMOXIFEN CITRATE (continued):

TDLo (Intramuscular-Rabbit) 1500 µg/kg: female 1-3 day(s) after conception: Reproductive: Fertility: female fertility index (e.g. # females pregnant per # sperm positive females; # females pregnant per # females mated), pre-implantation mortality (e.g. reduction in number of implants per female; total number of implants per corpora lutea)

TDLo (Intraperitoneal-Non Mammalian Species) 30 mg/kg/11 days-intermittent: Endocrine: other changes

DNA Adduct (Intraperitoneal-Rat) 60 mg/kg/3 days-continuous

DNA Adduct (Intraperitoneal-Hamster) 10 mg/kg

Cytogenetic Analysis (Oral-Rat) 35 mg/kg

Cytogenetic Analysis (Oral-Mouse) 1 mg/kg/10 days-intermittent

Micronucleus Test (Oral-Mouse) 1 mg/kg/10 days-intermittent

Sperm Morphology (Oral-Mouse) 1 mg/kg/10 days

Specific Locus Test (Multiple Routes-Insect-*Drosophila melanogaster*) 936 mg/L/48 hours

Sex Chromosome Loss and Non-Disjunction (Oral-Rat) 35 mg/kg

Gene Conversion and Mitotic Recombination (Oral-Insect-*Drosophila melanogaster*) 1.66 mmol/L/48 hours

CARCINOGENIC POTENTIAL OF COMPONENTS: A conventional carcinogenesis study in rats at doses of 5, 20, and 35 mg/kg/day (about one, three and seven-fold the daily maximum recommended human dose on a mg/m²basis) administered by oral gavage for up to 2 years) revealed a significant increase in hepatocellular carcinoma at all doses. The incidence of these tumors was significantly greater among rats administered 20 or 35 mg/kg/day (69%) compared to those administered 5 mg/kg/day (14%). In a separate study, rats were administered Tamoxifen at 45 mg/kg/day (about nine-fold the daily maximum recommended human dose on a mg/m² basis); hepatocellular neoplasia was exhibited at 3 to 6 months. Granulose cell ovarian tumors and interstitial cell testicular tumors were observed in two separate mouse studies. The mice were administered the trans and racemic forms of Tamoxifen for 13 to 15 months at doses of 5, 20 and 50 mg/kg/day (about one-half, two and five-fold the daily recommended human dose on a mg/m² basis).

The excipient components are listed by agencies tracking the carcinogenic potential of chemical compounds, as follows:

MAGNESIUM STEARATE (as a stearate): ACGIH TLV-A4 (Not Classifiable as a Human Carcinogen)

STARCH: ACGIH TLV-A4 (Not Classifiable as a Human Carcinogen)

No other component of this product are not found on the following lists: U.S. EPA, U.S. NTP, U.S. OSHA, U.S. NIOSH, GERMAN MAK, IARC, or ACGIH and therefore are neither considered to be nor suspected to be cancer-causing agents by these agencies.

REPRODUCTIVE TOXICITY INFORMATION: This product is rated Pregnancy Category D (POSITIVE EVIDENCE OR RISK, There is a risk to fetus after drug is administered, but under certain circumstances [e.g., treatment of life-threatening illnesses], the benefits can outweigh the risk.) There are no adequate and well-controlled trials of Tamoxifen in pregnant women. There have been a small number of reports of vaginal bleeding, spontaneous abortions, birth defects, and fetal deaths in pregnant women.

Mutagenicity: No genotoxic potential was found in a conventional battery of *in vivo* and *in vitro* tests with pro- and eukaryotic test systems with drug metabolizing systems. However, increased levels of DNA adducts were observed by ^{32}P post-labeling in DNA from rat liver and cultured human lymphocytes. Tamoxifen also has been found to increase levels of micronucleus formation *in vitro* in human lymphoblastoid cell line (MCL-5). Based on these findings, Tamoxifen is genotoxic in rodent and human MCL-5 cells.

Embryotoxicity/Teratogenicity: In reproductive studies in rats at dose levels equal to or below the human dose, non-teratogenic developmental skeletal changes were seen and were found reversible. In addition, in fertility studies in rats and in teratology studies in rabbits using doses at or below those used in humans, a lower incidence of embryo implantation and a higher incidence of fetal death or retarded in utero growth were observed, with slower learning behavior in some rat pups when compared to historical controls. Several pregnant marmosets were dosed with 10 mg/kg/day (about 2-fold the daily maximum recommended human dose on a mg/m² basis) during organogenesis or in the last half of pregnancy. No deformations were seen and, although the dose was high enough to terminate pregnancy in some animals, those that did maintain pregnancy showed no evidence of teratogenic malformations.

Reproductive Toxicity: Tamoxifen does not cause infertility, even in the presence of menstrual irregularity in women. Effects on reproductive functions are expected from the antiestrogenic properties of the drug. Tamoxifen produced impairment of fertility and conception in female rats at doses of 0.04 mg/kg/day (about 0.01-fold the daily maximum recommended human dose on a mg/m² basis) when dosed for two weeks prior to mating through day 7 of pregnancy. At this dose, fertility and reproductive indices were markedly reduced with total fetal mortality. Fetal mortality was also increased at doses of 0.16 mg/kg/day (about 0.03-fold the daily maximum recommended human dose on a mg/m² basis) when female rats were dosed from days 7-17 of pregnancy.

11. TOXICOLOGICAL INFORMATION (Continued)

REPRODUCTIVE TOXICITY INFORMATION (continued):

Reproductive Toxicity (continued): Tamoxifen has been reported to inhibit lactation. Two placebo-controlled studies in over 150 women have shown that Tamoxifen significantly inhibits early postpartum milk production. In both studies Tamoxifen was administered within 24 hours of delivery for between 5 and 18 days. The effect of Tamoxifen on established milk production is not known.

ACGIH BIOLOGICAL EXPOSURE INDICES (BEIs): Currently, ACGIH Biological Exposure Indices (BEIs) have not been determined for the components of this product.

12. ECOLOGICAL INFORMATION

ALL WORK PRACTICES MUST BE AIMED AT ELIMINATING ENVIRONMENTAL CONTAMINATION.

MOBILITY: This product has not been tested for mobility in soil.

PERSISTENCE AND BIODEGRADABILITY: This product has not been tested for persistence or biodegradability. It is expected that the components will slowly degrade in the environment and form a variety of organic and inorganic materials; however, no specific information is known.

BIO-ACCUMULATION POTENTIAL: This product has not been tested for bio-accumulation potential.

ECOTOXICITY: All releases to terrestrial, atmospheric and aquatic environments should be avoided. No specific data is available for this product. No aquatic toxicity data are available for the active component.

OTHER ADVERSE EFFECTS: This product does not contain any component with known ozone depletion potential.

RESULTS OF PBT AND vPvB ASSESSMENT: No Data Available. PBT and vPvB assessments are part of the chemical safety report required for some substances in European Union Regulation (EC) 1907/2006, Article 14.

ENVIRONMENTAL EXPOSURE CONTROLS: Controls should be engineered to prevent release to the environment, including procedures to prevent spills, atmospheric release and release to waterways.

13. DISPOSAL CONSIDERATIONS

WASTE TREATMENT/DISPOSAL METHODS: Waste disposal must be in accordance with appropriate Federal, State, and local regulations.

PRECAUTIONS TO BE FOLLOWED DURING WASTE HANDLING: Wear proper protective equipment when handling waste materials.

U.S. EPA WASTE NUMBER: Not applicable to wastes consisting only of this product.

EUROPEAN WASTE CODES: Wastes from Human or Animal Health Care or Related Research: 18 01 06: Chemicals consisting of or containing dangerous substances.

14. TRANSPORTATION INFORMATION

U.S. DEPARTMENT OF TRANSPORTATION REGULATIONS: This product is not classified as dangerous goods, per U.S. DOT regulations, under 49 CFR 172.101.

TRANSPORT CANADA, TRANSPORTATION OF DANGEROUS GOODS REGULATIONS: This product is not classified as Dangerous Goods, per regulations of Transport Canada.

INTERNATIONAL AIR TRANSPORT ASSOCIATION (IATA): This product is not classified as Dangerous Goods, by rules of IATA.

INTERNATIONAL MARITIME ORGANIZATION (IMO) DESIGNATION: This product is not classified as Dangerous Goods by the International Maritime Organization.

EUROPEAN AGREEMENT CONCERNING THE INTERNATIONAL CARRIAGE OF DANGEROUS GOODS BY ROAD (ADR): This product is not classified by the United Nations Economic Commission for Europe to be dangerous goods.

TRANSPORT IN BULK ACCORDING TO THE IBC CODE: Not applicable.

ENVIRONMENTAL HAZARDS: This compound is neither environmentally hazardous according to the criteria of the UN Model Regulations (as reflected in the IMDG Code, ADR, RID, and ADN) nor a marine pollutant according to the IMDG Code and is not listed in Annex III under MARPOL 73/78.

15. REGULATORY INFORMATION

UNITED STATES REGULATIONS:

U.S. SARA REPORTING REQUIREMENTS: The components of this product are not subject to the reporting requirements of Sections 302, 304, and 313 of Title III of the Superfund Amendments and Reauthorization Act.

U.S. SARA THRESHOLD PLANNING QUANTITY: There are no specific Threshold Planning Quantities for any component of this product. The default Federal MSDS submission and inventory requirement filing threshold of 10,000 lb (4,540 kg) therefore applies, per 40 CFR 370.20.

U.S. CERCLA REPORTABLE QUANTITIES (RQ): Not applicable.

U.S. TSCA INVENTORY STATUS: This product is regulated under Food and Drug Administration standards; it is not subject to requirements under TSCA.

CALIFORNIA SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT (PROPOSITION 65): The active ingredient of this product, Tamoxifen Citrate, is on the California Proposition 65 Lists. WARNING! This product contains a compound that is known to the State of California to cause developmental harm.

15. REGULATORY INFORMATION (Continued)

CANADIAN REGULATIONS:

CANADIAN DSL INVENTORY STATUS: This product regulated by the Therapeutic Products Programme (TPP) of Health Canada and so it excepted from requirements of the DSL/NDSL Inventory.

CANADIAN ENVIRONMENTAL PROTECTION ACT (CEPA) PRIORITIES SUBSTANCES LISTS: The components of this product are not on the CEPA Priorities Substances Lists.

CANADIAN WHMIS CLASSIFICATION AND SYMBOL: The WHMIS Requirements of the Hazardous Products Act does not apply in respect of the advertising, sale or importation of any cosmetic, device, drug or food within the meaning of the Food and Drugs Act.

EUROPEAN REGULATIONS:

SAFETY, HEALTH, AND ENVIRONMENTAL REGULATIONS/LEGISLATION SPECIFIC FOR THE PRODUCT: When formulated in a finished medicinal product for human use, this material is subject to Directive 2001/83/EC and subsequent amendments to the directive.

CHEMICAL SAFETY ASSESSMENT: No Data Available. The chemical safety assessment is required for some substances according to European Union Regulation (EC) 1907/2006, Article 14.

16. OTHER INFORMATION

ANSI LABELING (Based on 129.1, Provided to Summarize Occupational Exposure Hazards): WARNING! INGESTION MAY BE HARMFUL. MAY CAUSE EYE IRRITATION. CONTAINS SUSPECT REPRODUCTIVE TOXIN. Avoid unnecessary contact with skin, eyes, and clothing. Wash thoroughly after handling. Wear gloves, goggles, and appropriate body protection during handling or administration. FIRST-AID: In case of contact, flush skin or eyes with plenty of water. If adverse respiratory reaction occurs, give oxygen and seek immediate medical attention. If ingested, DO NOT induce vomiting-seek immediate medical attention. IN CASE OF FIRE: Use water fog, dry chemical, CO_2, or "alcohol" foam. IN CASE OF SPILL: Pick up or sweep up spilled product. Place residual in appropriate container and seal. Dispose of according to applicable regulations. Consult Safety Data Sheet for additional information.

GLOBAL HARMONIZATION AND EU CLP REGULATION (EC) 1272/2008 LABELING AND CLASSIFICATION: According to Article 1, item 5 (a) of CLP Regulation (EC) 1272/2008, medicinal products in the finished state for human use, as defined in 2001/83/EC, are excepted from classification and other criteria of 1272/2008.

EU LABELING AND CLASSIFICATION 67/548/EEC: According to Article 1 of European Union Council Directive 92/32/EEC, medical products in the finished state for human use (as defined by European Union Council Directives 67/548/EEC and 87/21/EEC) are not subject to the regulations and administrative provisions of European Union Council Directive 92/32/EEC.

CLASSIFICATION OF COMPONENTS:

CLP Regulation (EC) 1272/2008

Tamoxifen Citrate: This is a self-classification.

Classification: Reproductive Toxicity Category 1, Acute Oral Toxicity Category 4

Signal Word: Danger

Hazard Statements: H360D: May damage the unborn child. H302: Harmful if swallowed.

Hazard Symbols/Pictograms: GHS08, GHS07

All Other Components:

An official classification for these substances has not been published in the CLP 1272: 2008 and a self-classification is not applicable.

67/548/EEC:

Tamoxifen Citrate: This is a self-classification.

Hazard Classification: Reproductive Toxicity Category 2, Harmful

Risk Phrases: R61: May cause harm to the unborn child. R22: Harmful if swallowed.

Symbols: T, Xn

All Other Components:

Classification: An official classification for these substances has not been published in Commission Directives.

REFERENCES AND DATA SOURCES: Contact the supplier for information.

METHODS OF EVALUATING INFORMATION FOR THE PURPOSE OF CLASSIFICATION: Bridging principles were used to classify this product.

REVISION DETAILS: New

This Safety Data Sheet is offered pursuant to OSHA's Hazard Communication Standard, 29 CFR, 1910.1200. Other government regulations must be reviewed for applicability to this product. To the best of Actavis knowledge, the information contained herein is reliable and accurate as of this date; however, accuracy, suitability or completeness are not guaranteed and no warranties of any type, either express or implied, are provided. The information contained herein relates only to this specific product. If this product is combined with other materials, all component properties must be considered. Data may be changed from time to time. Be sure to consult the latest edition.

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