Safety Data Sheet

Docetaxel Injection, USP

Section 1: Chemical Product and Company Identification

Product Name: Docetaxel Injection, USP
Chemical Name(s): (2R,3S)-N-carboxy-3-phenylisoserine,N-*tert*-butyl ester, 13-ester with 5b-20-epoxy-1,2a,4,7b,10b,13a-hexahydroxytax-11-en-9-one 4-acetate 2-benzoate
Synonym: Docetaxel Injection
CAS Number: 148408-66-6, 77-92-9, 9005-65-6, 64-17-5, 7789-20-0
RTECS #: Not available
Trade Name: *Taxotere*
Chemical Formula: $C_{43}H_{53}NO_{14}$

Contact Information:
X-GEN Pharmaceuticals, Inc.
PO Box 445, Big Flats, NY 14814
Technical Assistance: 607-562-2700
Online Assistance: www.x-gen.us

Emergency phone number:
National Poison Control
1-800-222-1222

**For information regarding recommended uses and restrictions on usage refer to the product package insert.

Section 2: Hazard Identification

Hazard pictograms (GHS-US):

Hazard Overview: Docetaxel Injection, USP is a solution containing docetaxel, a semisynthetic taxane similar to paclitaxel. Clinically, docetaxel is used to treat some types of cancers. It is cytotoxic and neurotoxic. The formulated product is a flammable liquid. In the workplace, this product also should be considered a potential occupational reproductive hazard. Following an accidental over-exposure, possible target organs may include the bone marrow, gastrointestinal system, peripheral nervous system, cardiovascular system, liver, testes, skin and the fetus.

Potential Acute Health Effects: Hazardous in cases of inhalation. Slightly harmful in cases of skin contact or eye contact (based on components).

Potential Chronic Health Effects: It may cause blood cell changes, nervous system/brain toxicity (neurotoxicity). Serious allergic reactions, including anaphylaxis, have been reported. Repeat-dose studies in animals have shown a potential to cause adverse effects on central nervous system, gastrointestinal system, blood and blood forming organs, and testes.
Chronic Effects: If the compound is bioavailable via the route of exposure and exposure occurs for prolonged periods of time, potential adverse effects include neurotoxicity, myelosuppression, leucopenia, necrosis of the intestinal epithelium, testicular atrophy and lymphoid organ depletion.
The compound was negative in the Ames test but positive in other genotoxicity assays. The Guinea-Pig Anaphylaxis assay was negative.

Carcinogenic Effects: Long term studies in animals to assess the carcinogenic potential of docetaxel have not been conducted.

IARC: Not listed
NTP: Not Listed
OSHA: Not Listed

Mutagenic Effects: Docetaxel was clastogenic in an *in vitro* chromosome aberration assay in CHO-K1 cells, and in an *in vivo* micronucleus test in the mouse, but it did not induce mutagenicity in the Ames test or the CHO/HGPRT gene mutation assays.

Teratogenic Effects: There are scientific studies that suggest that personnel (e.g. nurses, pharmacists, etc.) who prepare and administer parenteral antineoplastic (e.g. in hospitals) may be at some risk of these materials if workplace exposures are not properly controlled. The actual risk in the workplace is unknown. Avoid liquid aerosol generation and skin contact. Avoid sparks, flames, and other sources of ignition when working with open containers.

Developmental Toxicity: Single exposure: NA. Repeated exposure: Following an accidental over-exposure, possible target organs may include the bone marrow, peripheral nervous system, cardiovascular system, gastrointestinal system, liver, and testes.

Adverse effects: See package insert

Section 3: Composition and Information on Ingredients

Principle Components:
This product contains Docetaxel Anhydrous as active ingredient, Anhydrous Citric Acid, Polysorbate 80, Dehydrated Alcohol and water for Injection, in glass vials. Active ingredient: Docetaxel Injection 20 mg/ml. Contains 2% docetaxel in a 50:50 solution of ethanol and Polysorbate (complete to 100%) for injection.

Name	CAS #
Docetaxel	148408-66-6
Anhydrous Citric Acid	77-92-9
Ethanol	64-17-5
Polysorbate	9005-65-6

Section 4: First Aid Measures

Inhalation: If mist is inhaled remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Seek medical attention immediately.

Skin contact: Remove from source of exposure. Flush with copious amounts of soap and water. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Seek medical attention immediately.

Eye contact: Remove from source of exposure. Flush with copious amounts of water for fifteen minutes. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Seek medical attention immediately.

Ingestion: Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary. Seek medical attention immediately.

Notes to physician: Seek product package insert for complete information.

Overdose Treatment: No information available.

Section 5: Fire Fighting Measures

Flammability of the product: Highly flammable liquid and vapor. Flash Point, 50% ethanol: 75º F (24ºC).

Combustion Products: Formation of toxic gases is possible during heating or fire. CO, CO_2 and oxides of nitrogen may be generated in a fire.

Unusual Fire and Explosion Hazards: GHS Flammable liquid - Category 2. When heated, product may produce combustible vapors due to the alcohol content. Keep away from flames, sparks, and other sources of ignition.

Extinguishing Media and instruction: As with any fire, use extinguishing media appropriate for primary cause of fire such as water, carbon dioxide, dry chemical extinguishing powder or foam.

Protective equipment & precautions for firefighters: As with all fires, evacuate personnel to a safe area. No special provisions required beyond normal firefighting equipment such as flame and chemical resistant clothing and self-contained breathing apparatus.

Special remarks on fire hazard: Not available

Special remarks on explosion hazard: Not available

Section 6: Accidental Release Measures

Release to land: Isolate the area around spill and remove all sources of ignition. Put on suitable protective clothing and equipment as specified by site spill control procedures. Absorb the liquid with suitable inert material and clean affected area with soap and water. An undiluted solution of household bleach may be applied to the spill for ten minutes to inactivate docetaxel. Use care to avoid splashing when applying the bleach solution. Absorb the liquid with an inert absorbent material (e.g. absorbent pad). Clean again with soap and water. Dispose of spill materials per applicable federal, state, or local regulations (reference section 13 of the SDS).
Small Spill: Use nitrile NBR gloves and eye protection. Absorb liquid.
Large Spill: Use nitrile NBR gloves, Tyvek other clothing and face protection. Absorb liquid.

Release to air: If dust is generated, wear a disposable dust respirator (N95), and reduce exposures by ventilating area. Clean up spill immediately.

Release to Water: Refer to local water authority; drain disposal is not recommended.

Protective equipment: Keep unnecessary personnel away. Wear latex or nitrile gloves, safety glasses, and a disposable dust mask (N95), wear protective coveralls and shoe covers for spills.

Section 7: Handling and Storage

Handling: Generally, when handling ***Docetaxel Injection, USP***, avoid ingestion, inhalation, skin contact, and eye contact. When handling, precautions may include the use of a containment cabinet during the weighing, reconstitution and/or solubilizing of this anti-neoplastic agent. The use of disposable gloves and respiratory protection is recommended. Proper disposal of contaminated vials, syringes, or other materials is recommended when working with this material. Protect package from damage.

Storage: Keep container tightly closed. Keep container in a cool, dry, well ventilated area (see USP CRT storage conditions). Store at controlled room temperature between 2° - 25°C (36° - 77°F). DO NOT FREEZE. Retain in the original package to protect from bright light. Refer to label instructions to ensure product integrity.

Incompatibilities: Keep away from direct light, heat, sparks, open flames and hot surfaces. – No smoking

Section 8: Exposure Controls / Personal Protection

Exposure Guidelines: Exposure Limits: In 8-hour TWA exposure limit of 1 mcg/m3 to Docetaxel, the active ingredient in Docetaxel Injection 20mg/ml. For Ethanol, the OSHA 8-hour TWA is 1000 ppm.

Engineering Controls: Operations should be designed to offer no significant exposure to the liquid. Local exhaust ventilation is recommended to minimize employee exposure. The use of an enclosure, such as an approved ventilated cabinet designed to minimize airborne exposures, is also recommended.

Personal Protection: When handling this material, at a minimum, the use of chemical safety goggles is recommended. Disposable gloves should be worn always. Further, the use of double gloves is recommended. Disposable gloves made from nitrile, neoprene, polyurethane or natural latex generally have low permeability to this material. Persons known to be allergic to latex rubber should select a non-latex glove. Gloves should be changed regularly, and removed immediately after known contamination. Care should be taken to minimize inadvertent contamination when removing and/or disposing of gloves.

Respiratory Protection: Respiratory protection is normally not needed during intended product use. However, if the generation of aerosols or vapors is likely, and engineering controls are not considered adequate to control potential airborne exposures, the use of an approved air-purifying respirator with a HEPA cartridge (N99 or equivalent) with an organic vapor cartridge is recommended under conditions where airborne aerosol or vapor concentrations are not expected to be excessive. For uncontrolled release events, or if exposure levels are not known, provide respirators that offer a high protection factor such as a powered air purifying respirator or supplied air. A respiratory protection program that meets OSHA's 29 CFR 1910.134 and ANSI Z88.2 requirements must be followed whenever workplace conditions require respirator use. Personnel who wear respirators should be fit tested and approved for respirator use as required.

Exposure limit: Not available

Section 9: Physical and Chemical Properties

Physical appearance: Solution
Color: A clear colorless to pale yellow material
Molecular Weight: 807.879 g/mole
Taste: NA
Odor: Characteristic alcohol odor.
Odor Threshold: NA
pH: Approximately neutral (6.5 at 250 g/l in water)
Melting Point: NA
Freezing Point: NA
Boiling Point: NA - (For pure ethanol) 78.5°C
Flash Point: 50% ethanol: 75º F (24º C).
Evaporation rate: NA
Flammability: NA
Upper Flammable Limit: NA - (pure ethanol) 19%
Lower Flammable Limit: NA - (pure ethanol) 3.3%
Vapor Pressure: NA - (For pure ethanol) 40 mm Hg @ 19°C
Vapor Density: NA - (For pure ethanol) 1.59
Relative density: Not available
Partition Coefficient: Not available
Auto-Ignition Temperature: NA - (pure ethanol) 786ºF (419ºC)
Decomposition Temperature: Not available
Viscosity: Not available
Dispersion Properties: Not available
Solubility: Soluble in water at approximately 0.1 mg/ml.

Section 10: Stability and Reactivity

Reactivity: Not Determined

Chemical stability: Stable under standard use and storage conditions.

Possibility of hazardous reaction: Not available

Conditions to avoid: Store away from light and heat.

Incompatible materials: Not Determined

Hazardous decomposition products: No data available

Corrosivity: None anticipated from normal handling of this product.

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of exposure: Absorbed through skin, eye contact, inhalation and ingestion.

Ingredient(s)	Percent	Test Type	Route of Administration	Value	Units	Species
*Taxotere for Injection	4	LD50	Oral	>2000	mg/kg	Rat
Docetaxel (anhydrous)	100	LD50	Intravenous	156	mg/kg	Mouse
Docetaxel (anhydrous)	100	LDLo	Intravenous	> 20	mg/kg	Rat
Docetaxel (anhydrous)	100	LD50	Intravenous	2.5	mg/kg	Dog
Polysorbate 80	100	LD50	Oral	~36,570 25,000	mg/kg mg/kg	Rat Mouse
Polysorbate 80	100	LD50	Intravenous	1790 1790	mg/kg mg/kg	Rat Mouse
Ethyl Alcohol	100	Oral	LD50	3450 – 11,500	mg/kg	Guinea Pig, Rat, Mouse, Dog
Ethyl Alcohol	100	Intravenous	LD50	1973, 2209	mg/kg	Mouse
Ethyl Alcohol	100	Inhalation	LC50 (10h)	20,000	ppm	Rat
Ethyl Alcohol	100	Inhalation	LC50 (4h)	39,000	mg/m3	Mouse

Symptoms:
Short term: Hazardous in cases of inhalation. Slightly hazardous in case of skin contact (irritant).
Long term: May cause damage to the following organs: Kidneys.

Reproductive toxicity: Due to lack of data the classification is not possible. Reproductive studies in animals yield mixed results.

FDA Pregnancy Category: D

Toxicity to animals: Docetaxel: >2000 mg/kg p.o. rat LD50. Moderately toxic by ingestion. Sub-chronic animal bioassays indicate potential for neurotoxicity, myelosuppression, leukopenia, necrosis of the intestinal epithelium, testicular atrophy and lymphoid organ depletion. The compound was negative in the Ames test but positive in the in vitro and in vivo Micronucleus assay. The Guinea-pig Anaphylaxis assay was negative.

Ethanol: 20,000 ppm/10 hrs inhalation-rat LC50; 2000 mg/kg oral-child LDLo. Slightly toxic by inhalation and ingestion. Central nervous system depressant; hepatotoxin.

Measures of toxicity: Not available

Additional reproductive health and toxicity data is available from the National Institute for Occupational Safety and Health (NIOSH) and/or Registry of Toxic Effects of Chemical Substance (RTECS).

Section 12: Ecological Information

Ecotoxicity: No data for the finished product. Based upon water solubility and Log P value (octanol/water partition coefficient) of 3.2, the active ingredient docetaxel should partition to the aquatic compartment exclusively.

Bioaccumulation potential: Not determined for product because of its low octanol: water partition coefficient, ethanol is not anticipated to bioaccumulate.

Products of biodegradation: Not determined for product. Ethanol was reported to be degraded between 45% and 74% in five days in two aqueous biodegradation assays.

Toxicity of the products of biodegradation: Not determined

Section 13: Disposal Information

Waste classification: Hazardous

Waste from residues/unused products: All waste materials must be properly characterized. Further, disposal should be performed in accordance with the federal, state or local regulatory requirements. Product is classified as hazardous waste (D001) based on ignitability.

Waste Disposal: Dispose of containers and unused contents in accordance with all applicable federal, state and local laws. Incineration is the preferred method.

Section 14: Transport Information

ADR/ADG/DOT STATUS	Regulated
Proper Shipping Name	Ethanol Solution
Hazard Class	3
UN Number	UN 1170
Packing Group	II
Reportable Quantity	NA

ICAO/IATA STATUS	Regulated
Proper Shipping Name	Ethanol Solution
Hazard Class	3
UN Number	UN 1170
Packing Group	II
Reportable Quantity	NA

IMDG STATUS	
Proper Shipping Name	Regulated
Proper Shipping Name	Ethanol Solution
Hazard Class	3
UN Number	UN 1170
Packing Group	II
Reportable Quantity	NA

Notes: DOT - US Department of Transportation Regulations

Section 15: Regulatory Information

Federal and State Regulations:
US TSCA Status: Exempt. However, ethyl alcohol is listed on the TSCA inventory.
US CERCLA Status: Not listed
US SARA 302 Status: Not listed
US SARA 313 Status: Not listed
US RCRA Status: Classified as D001 hazardous waste based on ignitability.
US PROP 65 (Calif.): Ethyl alcohol in alcoholic beverages is known to the State of California to cause cancer and developmental toxicity.

Notes: TSCA, Toxic Substance Control Act; CERCLA, US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act; SARA, Superfund Amendments and Reauthorization Act; RCRA, US EPA, Resource Conservation and Recovery Act; Prop 65, California Proposition 65

Other Classifications:
GHS/CLP Classification* *In the EU, classification under GHS/CLP does not apply to certain substances and mixtures, such as medicinal products as defined in Directive 2001/83/EC, which are in the finished state, intended for the final user.

Hazard Class	Hazard Category	Pictogram	Signal Word	Hazard Statement
NA	NA	NA	NA	NA

EU Classification* *Medicinal products are exempt from the requirements of the EU Dangerous Preparations Directive.
Classifications: NA
Symbol: NA
Indication of danger: NA
Risk Phrases: NA
Safety Phrases: S16: Keep away from sources of ignition - No smoking.
S23: Do not breathe vapor/spray
S24: Avoid contact with the skin
S25: Avoid contact with eyes
S37/39 Wear suitable gloves and eye/face protection.

HMIS (U.S.A.):
Health Hazard: 3
Fire Hazard: 2
Reactivity: 0
Personal Protection: E

National Fire Protection Association (U.S.A.):
Health: 3
Flammability: 2
Reactivity: 0

Protective Equipment: Gloves. Lab coat. Safety glasses. Dust Respirator. Be sure to use an approved/certified respirator or equivalent.

Section 16: Other Information

References: Not available
Created: 4/20/2017
Last Updated: 4/21/2017
Prepared & Approved by: X-GEN Pharmaceuticals, Inc. Quality Department & Safety Committee

The above information is believed to be accurate and represents the best information currently available to us. The use of this product should be through or under the direction of a physician. This SDS does not address therapeutic use of this material. X-GEN Pharmaceuticals, Inc. makes no warranties, express or implied with respect to such information, and we assume no liability resulting from its use. Users should make their own investigations to determine the suitability of the information. In no event should X-GEN Pharmaceuticals be liable for any claim, loss, or damage of any third party, even if X-GEN Pharmaceuticals has been advised of the possibility of such damages to occur.