

MATERIAL SAFETY DATA SHEET

Product Name: Docetaxel Injection

1. CHEMICAL PRODUCT AND COMPANY INFORMATION

Manufacturer Name And Address Hospira Inc.
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Lake Forest, Illinois USA
60045

ZHOPL Hospira Oncology Pvt. Ltd.
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Hospira, Inc., Non-Emergency 224-212-2000

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Synonyms (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

2. COMPOSITION/INFORMATION ON INGREDIENTS

Active Ingredient Name Docetaxel Anhydrous

Chemical Formula $C_{43}H_{53}NO_{14}$

Preparation Hazardous ingredients present at less than 1% include citric acid.

Component	Approximate Percent by Weight	CAS Number	RTECS Number
Docetaxel Anhydrous	1	114977-28-5	DA4172750
Poly(ethylene glycol)	55	25322-68-3	TQ4100000/PEG6000; TQ3675000/PEG400
Ethyl Alcohol	18	64-17-5	KQ6300000
Polysorbate 80	26	9005-65-6	WG2932500

3. HAZARD INFORMATION

Carcinogen List

Substance	IARC	NTP	OSHA
Docetaxel Anhydrous	Not Listed	Not Listed	Not Listed
Ethyl Alcohol	Not Listed	Not Listed	Not Listed
Poly(ethylene glycol)	Not Listed	Not Listed	Not Listed
Polysorbate 80	Not Listed	Not Listed	Not Listed

Emergency Overview Docetaxel Injection is a solution containing docetaxel, a semisynthetic taxane similar to paclitaxel. Docetaxel induces microtubule formation and stabilization of microtubules, thereby disrupting normal cell division in the G2 and M phases of the cell cycle. Clinically, docetaxel is used to treat some types of cancers. It is cytotoxic and neurotoxic. The formulated product is a

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flammable liquid. In the workplace, this product also should be considered a potential occupational reproductive hazard, harmful to the fetus, and a potential human carcinogen. 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.

Occupational Exposure Potential	Information on the absorption of this product via inhalation or skin contact is not available. There are scientific studies that suggest that personnel (e.g. nurses, pharmacists, etc.) who prepare and administer parenteral antineoplastics (e.g. in hospitals) may be at some risk due to potential mutagenicity, teratogenicity, and/or carcinogenicity of these materials if workplace exposures are not properly controlled. The actual risk in the workplace is not known. Avoid liquid aerosol generation and skin contact. Avoid sparks, flames, and other sources of ignition when working with open containers.
Signs and Symptoms	During occupational use, this material should be considered irritating to the skin, eyes and respiratory tract. In clinical use, adverse effects have included myelosuppression, fever, edema, fatigue, nausea, vomiting and diarrhea, hypotension and abnormal ECG, hepatotoxicity, peripheral neuropathy, hair loss, skin reactions, joint and muscle pain, and hypersensitivity reactions.
Medical Conditions Aggravated by Exposure	Pre-existing hypersensitivity to docetaxel or other taxanes. Pre-existing bone marrow, blood, gastrointestinal, cardiovascular, peripheral nervous system, liver, testes, or skin ailments; or pregnancy.

4. FIRST AID MEASURES

Eye contact	Remove from source of exposure. Flush with copious amounts of water. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.
Skin contact	Remove from source of exposure. Flush with copious amounts of water. If irritation persists or signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.
Inhalation	Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.
Ingestion	Remove from source of exposure. If signs of toxicity occur, seek medical attention. Provide symptomatic/supportive care as necessary.

5. FIRE FIGHTING MEASURES

Flammability	Flashpoint 61°F.
Fire & Explosion Hazard	Flammable liquid and vapor. Keep away from flames, sparks, and other sources of ignition. This product will burn in a fire. Vapors may form an explosive mixture with air. In the event of a large spill, the vapors are heavier than air, and may travel along the ground or be moved by ventilation and ignited by heat or other flames/ignition. Containers may explode in the heat of a fire.
Extinguishing media	As with any fire, use extinguishing media appropriate for primary cause of fire.
Special Fire Fighting Procedures	Firefighters should wear self-contained breathing apparatus. Protective equipment and clothing should be worn to minimize contact with the respiratory tract, skin and eyes.

6. ACCIDENTAL RELEASE MEASURES

Spill Cleanup and Disposal

Isolate the area around spill and remove all sources of ignition. Put on suitable protective clothing and equipment as specified by site spill 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 according to applicable federal, state, or local regulations.

7. HANDLING AND STORAGE

Handling

Docetaxel is a cytotoxic anti-neoplastic agent. Appropriate procedures should be implemented during the handling and disposal of cytotoxic anti-neoplastics agents to minimize potential exposures. Several guidelines on handling cytotoxic anti-neoplastic agents have been published. There is no general agreement that all of the procedures recommended in the guidelines are necessary or appropriate. Consult your hygienist or safety professional for your site requirements.

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 solubilization 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.

Storage

No special storage is required for hazard control. However, employees should be trained on the proper storage procedures for anti-neoplastic agents. For product protection, follow storage recommendations noted on the product case label, the primary container label, or the product insert.

Special Precautions

No special precautions required for hazard control. Persons with known hypersensitivities to docetaxel or other taxanes, women who are pregnant, or women who want to become pregnant, should consult a health and/or safety professional prior to handling open containers of this material.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Guidelines

Component	Type	Exposure limits			
		mg/m ³	ppm	µg/m ³	Note
Ethyl Alcohol	ACGIH 8 Hr TLV	N/A	1000	N/A	
Ethyl Alcohol	US OSHA 8 Hr PEL	N/A	1000	1900	
Ethyl Alcohol	Australia NOHSC	N/A	1000	N/A	
Poly(ethylene glycol)	AIHA WEEL	10	N/A	N/A	8-hr TWA
Polysorbate 80	Not Applicable	N/A	N/A	N/A	None Established
Docetaxel Anhydrous	Not Applicable	N/A	N/A	N/A	None Established

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 (P100 or equivalent) with an organic vapor cartridge is

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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.

Skin protection	When handling this material, disposable gloves should be worn at all times. 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.
Eye protection	As a minimum, the use of chemical safety goggles is recommended when handling this material.
Engineering Controls	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.

9. PHYSICAL/CHEMICAL PROPERTIES

Appearance/Physical State	Liquid
Color	Clear, colorless to pale yellow
Odor	NA
Odor Threshold:	NA
pH:	NA
Melting point/Freezing point:	NA
Initial Boiling Point/Boiling Point	NA
Range:	
Evaporation Rate:	NA
Flammability (solid, gas):	NA
Upper/Lower Flammability or Explosive Limits:	LEL: 3.3% UEL: 19% based on ethanol
Vapor Pressure:	NA
Vapor Density:	NA
Specific Gravity:	NA
Solubility:	Soluble in water at approximately 0.1 mg/ml.
Partition coefficient: n-octanol/water:	NA
Auto-ignition temperature:	NA
Decomposition temperature:	NA

10. STABILITY AND REACTIVITY

Reactivity	NA
Chemical Stability	Consult package insert for product stability information

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Hazardous Reactions	NA
Conditions to avoid	Heath, flames, sparks or other sources of ignition
Incompatibilities	Not determined
Hazardous decomposition products	Not determined. During thermal decomposition, it may be possible to generate irritating vapors and/or toxic fumes of carbon oxides (COx) and nitrogen oxides (NOx).
Hazardous Polymerization	Not anticipated to occur with this material.

11. TOXICOLOGICAL INFORMATION

Acute Toxicity

Not determined for the product formulation. Information for the ingredients is as follows:

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
PEG 300	100	LD50	Oral	27,500, 31,000 17,300 19,600	mg/kg mg/kg mg/kg	Rat Rabbit Guinea Pig
PEG 300	100	LD50	Dermal	>20,000	mg/kg	Rabbit
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	mg/kg	Mouse
Ethyl Alcohol	100	Inhalation	LC50 (10h)	20,000	ppm	Rat
Ethyl Alcohol	100	Inhalation	LC50 (4h)	39,000	mg/m3	Mouse

Aspiration Hazard	None anticipated from normal handling of this product. However, inadvertent inhalation of the product aerosol may produce respiratory irritation.
Dermal Irritation/Corrosion	None anticipated from normal handling of this product. However, inadvertent skin contact with this product may produce mild irritation with redness and discomfort. Ethanol may produce mild skin irritation with redness and dryness.
Ocular Irritation/Corrosion	None anticipated from normal handling of this product. However, inadvertent eye contact of this product with eyes may produce irritation with stinging with redness, watering, and discomfort. Exposure to ethanol has produced severe eye irritation in studies in animals.
Dermal or Respiratory Sensitization	None anticipated from normal handling of this product. However, in clinical use, severe hypersensitivity reactions, characterized by hypotension and/or

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bronchospasm, or generalized rash/erythema, have occurred in about 2% of pre-medicated patients. The incidence of hypersensitivity reactions is higher in patients without pre-medication.

Reproductive Effects

*Docetaxel did not impair fertility in rats when administered in multiple intravenous dosages of up to 0.3 mg/kg, but decreased testicular weights were reported. Similarly, in a 10-cycle toxicity study in rats and dogs (dosing once every 21 days for 6 months), testicular atrophy or degeneration were observed at intravenous dosages of 5 mg/kg in rats and 0.375 mg/kg in dogs.

In other studies in both rats and rabbits, administration of docetaxel at dosages ≥ 0.3 and 0.03 mg/kg/day, respectively, during the period of organogenesis, produced embryotoxicity and fetotoxicity (as characterized by intrauterine mortality, increased resorption, reduced fetal weight, and fetal ossification delay). These dosages also caused maternal toxicity.

Chronic prenatal exposure to ethanol has been associated with a distinct pattern of congenital malformations that have collectively been termed the "fetal alcohol syndrome".

Mutagenicity

*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.

Carcinogenicity

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

Target Organ Effects

This material should be considered irritating to the skin, eyes and respiratory tract. Following an accidental over-exposure, possible target organs may include the bone marrow, peripheral nervous system, cardiovascular system, gastrointestinal system, liver, skin, testes and the fetus.

12. ECOLOGICAL INFORMATION

Aquatic Toxicity

Not determined for product

LC50(24 hr) = 12,900 - 15,300 mg/L in rainbow trout for ethanol
LC50 (24 hr) = 11,200 mg/L in fingerling trout for ethanol
LC50(48 hr) = 9,268 - 14,221 mg/L in Daphnia magna for ethanol
EC50 = 9310 mg/L in Chlorella pyrenoidosa (green algae) for ethanol

Persistence/Biodegradability

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

Bioaccumulation

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

Mobility in Soil

Not determined for product.

13. DISPOSAL CONSIDERATIONS

Waste Disposal	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.
Container Handling and Disposal	Dispose of containers and unused contents in accordance with federal, state and local regulations.

14. TRANSPORTATION INFORMATION

ADR/ADG/ DOT STATUS:	Regulated
Proper Shipping Name:	Ethanol Solution
Hazard Class:	3
UN number:	UN1170
Packing group:	II
Reportable Quantity:	N/A
IMDG STATUS:	Regulated
Proper Shipping Name:	Ethanol Solution
Hazard Class:	3
UN number:	UN1170
Packing group:	II
Reportable Quantity:	N/A
ICAO/IATA STATUS:	Regulated
Proper Shipping Name:	Ethanol Solution
Hazard Class:	3
UN number:	UN1170
Packing group:	II
Reportable Quantity:	N/A
Transport Comments:	None

15. REGULATORY INFORMATION

USA Regulations

Substance	TSCA Status	CERCLA Status	SARA 302 Status	SARA 313 Status	PROP 65 Status
Docetaxel Anhydrous	Not Listed	Not Listed	Not Listed	Not Listed	Not Listed
Ethyl Alcohol	Listed	Not Listed	Not Listed	Not Listed	Listed
Poly(ethylene glycol)	Listed	Not Listed	Not Listed	Not Listed	Not Listed
Polysorbate 80	Listed	Not Listed	Not Listed	Not Listed	Not Listed

RCRA Status	Not Listed
<u>U.S. OSHA</u>	Possible Carcinogen
<u>Classification</u>	Target Organ Toxin
	Reproductive Toxin
	Flammable Liquid
	Possible Irritant

GHS *In the EU, classification under GHS/CLP does not apply to certain substances and mixtures, such as

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<u>Classification</u>	medicinal products as defined in Directive 2001/83/EC, which are in the finished state, intended for the final user:
Hazard Class	Not Applicable
Hazard Category	Not Applicable
Signal Word	Not Applicable
Symbol	Not Applicable
Prevention	P260 - Do not breathe dust/fume/gas/mist/vapors/spray.
Hazard Statement	Not Applicable
Response:	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists, get medical attention. Wash hands after handling. Get medical attention if you feel unwell.

EU Classification*

*Medicinal products are exempt from the requirements of the EU Dangerous Preparations Directive. Information provided below is for the pure drug substance Docetaxel Anhydrous

Classification(s):	Not Applicable
Symbol:	Not Applicable
Indication of Danger:	Not Applicable
Risk Phrases:	Not Applicable
Safety Phrases:	S23 - Do not breathe vapor. S24/25 - Avoid contact with skin and eyes. S37/39 - Wear suitable gloves and eye/face protection.

16. OTHER INFORMATION:

Notes:

ACGIH TLV	American Conference of Governmental Industrial Hygienists – Threshold Limit Value
CAS	Chemical Abstracts Service Number
CERCLA	US EPA law, Comprehensive Environmental Response, Compensation, and Liability Act
DOT	US Department of Transportation Regulations
EEL	Employee Exposure Limit
IATA	International Air Transport Association
LD50	Dosage producing 50% mortality
NA	Not applicable/Not available
NE	Not established
NIOSH	National Institute for Occupational Safety and Health
OSHA PEL	US Occupational Safety and Health Administration – Permissible Exposure Limit
Prop 65	California Proposition 65
RCRA	US EPA, Resource Conservation and Recovery Act
RTECS	Registry of Toxic Effects of Chemical Substances
SARA	Superfund Amendments and Reauthorization Act

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STEL	15-minute Short Term Exposure Limit
TSCA	Toxic Substance Control Act
TWA	8-hour Time Weighted Average

MSDS Coordinator: Hospira GEHS

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