

SECTION 1: PRODUCT IDENTIFICATION

PRODUCT NAME	TRETINOIN, USP (Retinoic Acid)
PRODUCT CODE	0001
SUPPLIER	MEDISCA Inc. Tel.: 1.800.932.1039 Fax.: 1.855.850.5855 661 Route 3, Unit C, Plattsburgh, NY, 12901 3955 W. Mesa Vista Ave., Unit A-10, Las Vegas, NV, 89118 6641 N. Belt Line Road, Suite 130, Irving, TX, 75063 MEDISCA Pharmaceutique Inc. Tel.: 1.800.665.6334 Fax.: 514.338.1693 4509 Rue Dobrin, St. Laurent, QC, H4R 2L8 21300 Gordon Way, Unit 153/158, Richmond, BC V6W 1M2 MEDISCA Australia PTY LTD Tel.: 1.300.786.392 Fax.: 61.2.9700.9047 Unit 7, Heritage Business Park 5-9 Ricketty Street, Mascot, NSW 2020
EMERGENCY PHONE	CHEMTREC Day or Night Within USA and Canada: 1-800-424-9300 NSW Poisons Information Centre: 131 126
USES	Keratolytic; antineoplastic; dermatological applications.

SECTION 2: HAZARDS IDENTIFICATION

GHS CLASSIFICATION	Acute Toxicity - Oral (Category 4) Acute Toxicity - Dermal (Category 5) Toxic to Reproduction (Category 1A) Carcinogenicity (Category 2) Skin Irritation (Category 2) Eye Irritation (Category 2A) Chronic Aquatic Toxicity (Category 1)
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PICTOGRAM

SIGNAL WORD

Danger

HAZARD STATEMENT(S)

Cytotoxic! Extremely hazardous to all tissues.
 Harmful if swallowed.
 May be harmful if in contact with skin.
 May damage fertility or the unborn child.
 Suspected of causing cancer
 Causes skin irritation.
 Causes serious eye irritation.
 Very toxic to aquatic life with long lasting effects.

AUSTRALIA-ONLY HAZARDS

Not Available.

PRECAUTIONARY STATEMENT(S)

Prevention
 Wash thoroughly after handling.
 Do not eat, drink or smoke when using this product.
 Obtain special instructions before use.
 Do not handle until all safety precautions have been read and understood.
 Wear protective gloves, protective clothing, eye protection, face protection.
 Avoid release to the environment.

Response IF SWALLOWED: Immediately call a poison center or medical professional; Rinse mouth.
 IF ON SKIN (HAIR): Wash with plenty of water. If skin irritation occurs: Get medical advice/attention. Take off contaminated clothing and wash it before reuse.
 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 advice/attention.
 IF EXPOSED OR CONCERNED: Get medical advice/attention.
 COLLECT SPILLAGE

Storage Store locked up.

Disposal Dispose of contents and/or container in accordance with local regulations.

HMIS CLASSIFICATION

Health Hazard 4 **Flammability** 0

Reactivity 0 **Personal Protection** K

SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

CHEMICAL NAME Tretinoin
BOTANICAL NAME Not applicable
SYNONYM Vitamin A acid, all-trans-Retinoic acid
CHEMICAL FORMULA C₂₀H₂₈O₂
CAS NUMBER 302-79-4
ALTERNATE CAS NUMBER Not applicable
MOLECULAR WEIGHT 300.44

COMPOSITION

CHEMICAL NAME	CAS NUMBER	% BY WEIGHT
TRETINOIN (Retinoic Acid)	302-79-4	100

There are no additional ingredients present which, within the current knowledge of the supplier and in the concentrations applicable, are classified as health hazards and hence require reporting in this section.

NOTES

Chemical family: Retinoid.

SECTION 4: FIRST-AID MEASURES

IN CASE OF EYE CONTACT Flush with copious amounts of water for 15 minutes, separating eyelids with fingers. If irritation persists seek medical aid.

IN CASE OF SKIN CONTACT Wash with soap & water for 15 minutes. If irritation persists seek medical aid. If at any time there is skin contact with any cytotoxic drug, thoroughly wash the affected area with soap and water for 15 minutes. The worker should not scrape or abrade the skin by using a scrub brush as this could increase exposure. It is always recommended to seek a medical evaluation by a physician.

IF SWALLOWED Call a physician. Wash out mouth with water. Do not induce vomiting without medical advice.

IF INHALED Remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Call a physician.

SYMPTOMS AND EFFECTS Refer to section 11

SECTION 5: FIREFIGHTING MEASURES

SPECIFIC HAZARDS ARISING FROM THE CHEMICAL Not applicable

FLAMMABLE PROPERTIES	May be combustible at high temperature
HAZARDOUS COMBUSTION PRODUCTS	Under fire conditions, hazardous fumes will be present.
EXTINGUISHING MEDIA	Small fire: dry chemical, CO ₂ or water spray. Large fire: dry chemical, CO ₂ , alcohol resistant foam or water spray. Do not get water inside containers.
PROTECTIVE EQUIPMENT AND PRECAUTIONS FOR FIREFIGHTERS	Wear self-contained breathing apparatus and protective clothing to prevent contact with skin and eyes.

SECTION 6: ACCIDENTAL RELEASE MEASURES

PERSONAL PRECAUTIONS	Wear respiratory protection. Avoid dust formation. Avoid breathing vapours, mist or gas. Ensure adequate ventilation. Evacuate personnel to safe areas. Avoid breathing dust.
METHODS & MATERIAL FOR CONTAINMENT	On land, sweep or shovel into suitable containers. Minimize generation of dust. The use of chemical inactivates is not recommended as they may create a hazardous by-product. All contaminated areas should be cleaned a minimum of three times, and all contaminated products and equipment should be disposed of or cleaned in an appropriate manner.
CLEANUP PROCEDURE	A clearly labelled cytotoxic spill kit should be kept wherever cytotoxic medications are being prepared, stored, administered or received (shipping). A spill needs to be cleaned by members of the staff that have received the appropriate training and have the appropriate protective equipment; others should vacate the area as soon as it is safe to do so until the spill is cleaned. All spills should be immediately marked with a warning sign to prevent exposure to others. Glass should never be handled by hand; always use a scoop. The cleanup should be done by as few people as feasible, but there should be at least two people involved.

SECTION 7: HANDLING AND STORAGE

PRECAUTIONS FOR SAFE HANDLING	Cytotoxic! Extremely hazardous to all tissues. Avoid all contact. Wash thoroughly after handling. Store away from incompatible materials, in a well-ventilated area. Eliminate all sources of ignition. Store in accordance with local regulations. Do not store in unlabeled containers. Containers that have been opened must be carefully resealed and kept upright to prevent leakage. Use appropriate containment to avoid environmental contamination.
STORAGE CONDITIONS	Store in original container, tightly sealed, protected from direct sunlight and moisture. Preserve in tight containers, protected from light.

SECTION 8: EXPOSURE CONTROLS/ PERSONAL PROTECTION

Chemical Name: TRETINOIN (Retinoic Acid) CAS #: 302-79-4

	TWA	Ceiling	STEL	REL	IDLH	Remarks
OSHA PEL	N/L	N/L	-	-	-	-
ACGIH TLV	N/L	N/L	N/L	-	-	-
NIOSH	N/L	N/L	N/L	N/L	N/L	-
AIHA WEEL	N/L	N/L	N/L	-	-	-
Safe Work Australia HSIS	N/L	N/L	N/L	-	-	-
HSE	N/L	N/L	N/L	-	-	-

N/L = Not Listed

EXPOSURE GUIDELINES	Cytotoxic: There are no exposure limits set for cytotoxic drugs. Exposure must be kept to a minimum.
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PERSONAL PROTECTIVE EQUIPMENT

Eyes: Chemical splash goggles, and if necessary, full-face protection. Wear appropriate protective eyeglasses or chemical safety goggles as described by WHMIS or OSHA's eye and face protection regulations in 29 CFR 1910.133 or European Standard EN166. **Skin:** Protective gloves made of vinyl or nitrile rubber. Gloves should be changed frequently, or immediately if punctured, cut, or torn. It is also recommended that workers wear two pairs at a time for additional protection. **Clothing:** Wear appropriate protective clothing to minimize contact with skin. A moisture resistant, long sleeved gown with elastic cuffs. To prevent the spread of medication, protective clothing should not be worn outside of the preparation area. **Respirators:** Follow WHMIS or OSHA respirator regulations found in 29 CFR 1910.134 or European Standard EN 149. Use a NIOSH/MSHA or European Standard EN 149 approved respirator if exposure limits are exceeded or if irritation or other symptoms are experienced. In cases where there is a possibility of the medication becoming airborne, a powered air purifying respirator is recommended.

SPECIFIC ENGINEERING CONTROLS

The following engineering controls should be put in place where cytotoxic medications are being used: A minimum of a Class II biological safety cabinet with HEPA filter exhaust systems that does not allow air to be circulated back into the room should be used while manipulating cytotoxic drugs. The preparation area within the cabinet should be covered with a plastic backed, absorbent material to reduce dispersion and facilitate the clean-up of any spilled medication. Medications should be isolated and locked out in such a manner that only those properly trained have access to the storage location. Puncture proof containers for the disposal of needles, syringes and vials must be provided. Negative pressure rooms that prevent any spilled medication from leaving the room are also recommended.

NOTES

Additional controls
Safe work procedures for handling these materials should be developed and taught to all affected staff. Proper signage informing all employees of the presence of cytotoxic drugs and their hazards must be developed and displayed in highly visible locations. Eating, drinking, smoking, applying makeup and the storage of food should be completely prohibited in the preparation area.

USP: ELV: Industrial use: TWA: 0.001 mg/m³

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL STATE	Solid				
DESCRIPTION	Yellow to light-orange crystalline powder.				
SOLUBILITY	Slightly soluble in alcohol, in chloroform, and in methanol; insoluble in water.				
ODOR	Not available.				
FLAMMABILITY	May be combustible at high temperature				
ODOR THRESHOLD	Not available	pH	8.2	MELTING POINT	(178-184)°C, (352.4-363.2)°F
BOILING POINT	Not available	FREEZING POINT	(178-184)°C, (352.4-363.2)°F	FLASH POINT	Not available
SPECIFIC GRAVITY	Not available	EVAPORATION RATE	Not available	EXPLOSIVE LIMIT	Not available
UPPER FLAMMABLE/ EXPLOSIVE LIMIT(S)	Not available	LOWER FLAMMABLE/ EXPLOSIVE LIMIT(S)	Not available	VAPOR PRESSURE	2.42E-07 mm Hg
VAPOR DENSITY (AIR = 1)	Not available	RELATIVE DENSITY (WATER = 1)	Not available	log P (OCTANOL-WATER)	6.3 (20°C)

AUTO-IGNITION TEMPERATURE

265 °C, 509 °F

DECOMPOSITION TEMPERATURE

Not available

VISCOSITY

Not available

NOTES

The physical data presented above are typical values and should not be construed as a specification.

SECTION 10: STABILITY AND REACTIVITY
REACTIVITY

Not established

STABILITY

Stable under recommended storage conditions

MATERIALS TO AVOID

Strong oxidants

HAZARDOUS DECOMPOSITION PRODUCTS

Toxic fumes of carbon monoxide, carbon dioxide, nitrogen oxides and other gases may occur

HAZARDOUS POLYMERIZATION

Will not occur

POSSIBILITY OF HAZARDOUS REACTION

Not established

CONDITIONS TO AVOID

Moisture, sunlight and extreme temperatures

SECTION 11: TOXICOLOGICAL INFORMATION
ACUTE TOXICITY

 Oral: Rat: LD50: (mg/kg): 2000
 Dermal: Rabbit LD50: (mg/kg): >2500
 Inhalation: Rat: LC50: (mg/L/4hr): Not available

SKIN CORROSION/IRRITATION

 Causes skin irritation.
 525 mg Irritation test; Result: Irritant; Species: Human; Organ: Skin; Severity: Mild

SERIOUS EYE DAMAGE/EYE IRRITATION

Causes serious eye irritation.

RESPIRATORY OR SKIN SENSITIZATION

Due to lack of data the classification is not possible.

GERM CELL MUTAGENICITY

Exposure to cytotoxic drugs has been reported to cause increased frequency of chromosome damage in exposed workers.

CARCINOGENICITY
OSHA TRETINOIN (Retinoic Acid) is not listed.

NTP TRETINOIN (Retinoic Acid) is not listed.

IARC TRETINOIN (Retinoic Acid) is not evaluated.

California Proposition 65 This product contains the following chemical known to the State of California to cause birth defects or other reproductive harm: TRETINOIN (Retinoic Acid).

ADDITIONAL CARCINOGENICITY INFORMATION

Repeated long-term occupational exposure to small amounts of cytotoxic drugs has not been identified to cause cancer. However, many cytotoxic drugs are known to be: Genotoxic, Carcinogenic, Mutagenic.

 30 mg/kg/day Carcinogenicity test
 Result: Increased rate of adenomas and carcinomas.
 Species: Mouse

REPRODUCTIVE TOXICITY

Cytotoxic drugs have also been associated with negative health effects for developing fetuses, including higher incidences of spontaneous abortions, congenital malformations, low birth weight, and infertility.

May damage fertility or the unborn child. This material has caused adverse fetal effects in animal studies.

Suspected toxic for reproduction: The Toolbox profiler DART scheme v.1.0 gives an alert for toxicity to reproduction; CAESAR developmental toxicity model in VEGA (Q)SAR platform predicts that the chemical is Toxicant (EXPERIMENTAL value); Developmental/Reproductive Toxicity library (PG) in VEGA (Q)SAR platform predicts that the chemical is Toxicant (EXPERIMENTAL value); DART database in the Toolbox reports that this substance as Known developmental potential.

SPECIFIC TARGET ORGAN TOXICITY - SINGLE EXPOSURE

Due to lack of data the classification is not possible.

SPECIFIC TARGET ORGAN TOXICITY - REPEATED EXPOSURE

Due to lack of data the classification is not possible.

ASPIRATION HAZARDS

Due to lack of data the classification is not possible.

SIGNS AND SYMPTOMS OF EXPOSURE

Avoid any direct contact with the product. Small amounts: When used and handled according to specifications, the product does not have any harmful effects according to our experience and the information provided to us.

Symptoms related to the physical, chemical, and toxicological characteristics

Rash. Fever. Weakness. Fatigue. Fast heartbeat. Irregular breathing. Shortness of breath. Dry eyes. Dry mouth. Dry skin. Bone pain. Nausea. Vomiting. Mouth sores. Itching. Sweating. Visual disturbances. Hearing problems. Hair loss. Loss of appetite. Flushing. Abdominal pain. Dizziness. Depression.

Delayed and immediate effects of exposure

High blood pressure. Low blood pressure. Blood disorders. Liver damage. Spleen disorders.

Cross sensitivity Persons sensitive to acitretin, etretinate, isotretinoin, or other retinoids may be sensitive to tretinoin also.

Medical conditions aggravated by exposure

Skin disorders. Acute promyelocytic leukemia. Leukocytosis . Respiratory disorders.

POTENTIAL HEALTH EFFECTS

Inhalation May be harmful if inhaled. May cause respiratory tract irritation.

Ingestion Harmful if swallowed.

Skin May be harmful if absorbed through skin. Causes skin irritation. Topical application may cause transitory stinging and a feeling of warmth, and in normal use it produces some erythema, dryness, pruritus, and peeling similar to that of mild sunburn. Sensitive individuals may experience oedema, blistering, and crusting of the skin. Excessive application can cause severe erythema, peeling, and discomfort. Photosensitivity may occur. Temporary hypopigmentation and hyperpigmentation have been reported.

Eyes Causes serious eye irritation

SECTION 12: ECOLOGICAL INFORMATION
TOXICITY

EC50: 48 Hr: Crustacea: Daphnia magna: (mg/L): 0.1 - 3.1

LC50: 96 Hr: Fish: (mg/L): 0.2 - 4.6

EC50: 72 or 96Hr: Algae (or other aqua plants): (mg/L): Not available

PERSISTENCE AND DEGRADABILITY

Biodegradability: 50 - 60 %

Suspected persistent in the environment: The Danish QSAR database contains information indicating that the substance is predicted as non readily biodegradable.

BIOACCUMULATIVE POTENTIAL	Log Pow: 6.3 (20°C) Suspected bioaccumulative: EpiSuite data included in the Toolbox contain at least one experimental log Kow value equal to or higher than 4.5; The Danish QSAR database contains information indicating that the substance is predicted as bioaccumulative (BCF > 2000 L/kg)
MOBILITY IN SOIL	Insoluble in water. Water Solubility: 0.126 mg/L (25°C) Vapor Pressure: 2.42E-07 mm Hg (25°C) Henry's Law Constant: 9.50E-06 atm-m ³ /mole (25°C)
OTHER ADVERSE EFFECTS	Suspected hazardous to the aquatic environment This product is not intended to be released into the environment

SECTION 13: DISPOSAL CONSIDERATIONS

WASTE DISPOSAL	Plastic bags that are at least 2mm thick (if polypropylene) or 4mm thick (if polyethylene) should be used to collect potentially contaminated materials. Bags should be color-coded and labelled with a cytotoxic warning label. All sharps should be placed in puncture proof containers before bagging. All workplaces should have a policy for segregating waste materials resulting from cytotoxic drug preparation and administration. These plans must meet or exceed the government regulations for hazardous waste disposal. Housekeeping staff should wear protective gloves while handling waste containers. Cytotoxic waste must be handled differently than regular garbage and must be disposed according to government regulations. In cases where the waste is to be incinerated, it should be noted that completely sealed (airtight) containers that could build pressure and explode must be avoided. Temperatures of 1,000°C to 1,600°C should be used to render the cytotoxic drugs harmless.
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SECTION 14: TRANSPORT INFORMATION

UNITED STATES & CANADA

UN PROPER SHIPPING NAME	ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.
UN NUMBER	3077
CLASS	9
PACKING GROUP	III

AUSTRALIA

UN PROPER SHIPPING NAME	ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.
UN NUMBER	3077
CLASS	9
PACKING GROUP	III
HAZCHEM	2Z

ENVIRONMENTAL HAZARDS	Not applicable
SPECIAL SHIPPING INFORMATION	Not applicable

SECTION 15: REGULATORY INFORMATION

Chemical Name & CAS	CERCLA 40 CFR Part 302.4	SARA (Title III) 40 CFR Part 372.65	EPA 40 CFR Part 355		Pennsylvania	Right-to-know		California Prop 65
			Appendix A	Appendix B		New Jersey	Massachusetts	
TRETINOIN (Retinoic Acid) 302-79-4	N/L	N/L	N/L	N/L	N/L	N/L	N/L	X

N/L = Not Listed; X = Listed

AUSTRALIAN REGULATIONS

Chemical Name & CAS	Poisons and Therapeutic Goods Regulation	Therapeutic Goods Act	Code of Practices - Illicit Drug Precursors
TRETINOIN (Retinoic Acid) 302-79-4	N/L	Listed as Schedule 4	N/L

SECTION 16: OTHER INFORMATION

REFERENCES

Available upon request

ABBREVIATIONS AND ACRONYMS

CAS – Chemical Abstract Service; **GHS** – Global Harmonized System; **OSHA PEL** – Occupational Safety & Health Administration Permissible Exposure Limits; **TWA** – Time Weighted Average; **HSIS** – Hazardous Substances Information System; **STEL** – Short Term Exposure Limit; **AIHA WEEL** – American Industrial Hygiene Association Workplace Environment Exposure Levels; **LD50** – Lethal Dose, 50%; **IARC** – International Agency for Research on Cancer; **NTP** – National Toxicology Program; **WHMIS** – Workplace Hazardous Materials Information System; **SARA** – Superfund Amendments and Reauthorization Act; **EPA** – Environmental Protection Agency; **CERCLA** – Comprehensive Environmental Response, Compensation, and Liability Act; **HMIS** – Hazardous Materials Information System; **NIOSH** – National Institute for Occupational Safety and Health; **MSHA** – Mine Safety and Health Administration; **ACGIH** – American Conference of Governmental Industrial Hygienists; **IDHL** – Immediately Dangerous to Health or Life; **TLV** – Threshold Limit Value; **HSE** – Health and Safety Executive; **REL** – Recommended Exposure Limit

LAST REVISION

06/2018

SUPERSEDES

11/2015

DISCLAIMER

This document was created in accordance with OSHA, Safe Work Australia and WHMIS regulations. The above information is believed to be correct but does not purport to be all inclusive and shall be used only as a guide. The information in this document is based on the present state of our knowledge and is applicable to the product with regard to appropriate safety precautions. It does not represent any guarantee of the properties of the product. MEDISCA® shall not be held liable for any damage resulting from handling or from contact with the above product. Recipients of the product must take responsibility for observing existing laws and regulations.