

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 626 Tom Miller Road, Plattsburgh, NY, 12901 MEDISCA Pharmaceutique Inc. Tel.: 1.800.665.6334 Fax.: 514.338.1693 4509 Rue Dobrin, St. Laurent, QC, H4R 2L8 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 National Chemical Emergency Centre 44(0)1235239670
RECOMMENDED USES	Pharmaceutical Manufacturing
RESTRICTIONS ON USE	Not applicable

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.

**ADVERSE PHYSIOCHEMICAL,
HUMAN HEALTH AND
ENVIRONMENTAL EFFECTS
PRECAUTIONARY STATEMENT(S)**

Not Available.

Prevention

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

Response

IF SWALLOWED: Immediately call a poison center. Get medical help. Rinse mouth. IF ON SKIN: Wash with plenty of water. If skin irritation occurs, get medical help. 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 help. IF EXPOSED OR CONCERNED: Get medical advice. 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
 $C_{20}H_{28}O_2$
CHEMICAL FAMILY

Retinoid

CAS NUMBER

302-79-4

ALTERNATE CAS NUMBER

Not applicable

MOLECULAR WEIGHT

300.44

COMPOSITION

CHEMICAL NAME	CAS NUMBER	EC NUMBER	% BY WEIGHT
TRETINOIN (Retinoic Acid)	302-79-4	206-129-0	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.

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.

MEDICAL ATTENTION AND
SPECIAL TREATMENT

Get emergency medical help.

SYMPTOMS CAUSED BY
EXPOSURE

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.

SUITABLE & UNSUITABLE
EXTINGUISHING MEDIA

Small fire: dry chemical, CO₂ or water spray. **Large fire:** dry chemical, CO₂, 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.

REFERENCE TO OTHER
SECTIONS

See Section 7 for information on safe handling. See Section 8 for information on personal protection equipment. See Section 13 for disposal information.

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

CONDITIONS FOR SAFE STORAGE

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.

Short term excursions, temperature excursions as experienced during shipping and warehousing, up to 40°C are acceptable.

SECTION 8: EXPOSURE CONTROLS/ PERSONAL PROTECTION

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

	Country	Limit value-8 hours		Limit value-Short Term		IDLH	REL	Advisory	Notes
		ppm	mg/m ³	ppm	mg/m ³				
OSHA	USA	N/L	N/L	N/L	N/L	N/L	N/L	N/A	N/A
ACGIH	USA	N/L	N/L	N/L	N/L	N/L	N/L	N/A	N/A
NIOSH	USA	N/L	N/L	N/L	N/L	N/L	N/L	84:16 cell stimulants and proliferants	Black Box warning for severe birth defects; Special FDA distribution system; FDA Pregnancy Category X
WEEL	USA	N/L	N/L	N/L	N/L	N/L	N/L	N/A	N/A
HSIS	Australia	N/L	N/L	N/L	N/L	N/L	N/L	N/A	N/A
HSE	UK	N/L	N/L	N/L	N/L	N/L	N/L	N/A	N/A
GESTIS	Add Country	N/L	N/L	N/L	N/L	N/L	N/L	N/A	N/A

N/L = Not listed ; N/A = Not Available

PELs are 8-hour TWAs = Limit value - Eight hours

Ceiling or Short-Term TWA = STEL = Limit value - Short term

EXPOSURE GUIDELINES

Cytotoxic: There are no exposure limits set for cytotoxic drugs. Exposure must be kept to a minimum.

PERSONAL PROTECTIVE EQUIPMENT

Eyes: 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:** Wear appropriate gloves to prevent skin exposure. **Clothing:** Wear appropriate protective clothing to minimize contact with skin. **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. **Thermal Hazards:** For products representing a thermal hazard, appropriate Personal Protective Equipment should be used.

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.

BIOLOGICAL MONITORING

Not available

CONTROL BANDING

Not available

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	Odorless				
FLAMMABILITY	May be combustible at high temperature				
AUTO-IGNITION TEMPERATURE	265 °C, 509 °F	BOILING POINT	Not available	DECOMPOSITION TEMPERATURE	Not available
EVAPORATION RATE	Not available	EXPLOSIVE LIMIT	Not available	FLASH POINT	Not available
log P (OCTANOL-WATER)	6.3 (20°C)	LOWER FLAMMABLE/EXPLOSIVE LIMIT(S)	Not available	MELTING/FREEZING POINT	(180-182)°C, (356-359.6)°F
PARTICLE CHARACTERISTICS	Not available	OXIDIZING PROPERTY	Not available	pH	8.2
RELATIVE DENSITY (WATER = 1)	Not available	SPECIFIC GRAVITY	Not available	UPPER FLAMMABLE/EXPLOSIVE LIMIT(S)	Not available
VAPOR DENSITY (AIR = 1)	Not available	VAPOR PRESSURE	< 0.000001 kPa (25 °C)	VISCOSITY	Not available

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

SECTION 10: STABILITY AND REACTIVITY

REACTIVITY	Not established
CHEMICAL STABILITY	Stable under recommended storage conditions
INCOMPATIBLE MATERIALS	Strong oxidizing agents. Acids.
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 SENSITIZATION	Due to lack of data the classification is not possible.
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	<p>OSHA TRETINOIN (Retinoic Acid) is not listed.</p> <p>NTP TRETINOIN (Retinoic Acid) is not listed.</p> <p>IARC TRETINOIN (Retinoic Acid) is not evaluated.</p> <p>California Proposition This product contains the following chemical known to the State of California to cause birth defects or other reproductive harm: TRETINOIN (Retinoic Acid).</p>
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. Mouse: 30 mg/kg/day Carcinogenicity; Result: Increased rate of adenomas and carcinomas.
REPRODUCTIVE TOXICITY	<p>May damage fertility or the unborn child. Retinoids have caused fetal harm resulting in craniofacial, cardiovascular, and central nervous system defects.</p> <p>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.</p> <p>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.</p>
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	Based on available data, the classification criteria are not met.

**SIGNS AND SYMPTOMS OF
EXPOSURE**
ROUTES OF EXPOSURE:

Oral, Dermal, Inhalation, Eye contact

EARLY ONSET SYMPTOMS RELATED TO EXPOSURE:

Not available

DELAYED HEALTH EFFECT FROM 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.

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.

Medical conditions aggravated by exposure:

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

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.

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
ECOTOXICITY

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 bio-accumulative (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-m³/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
DISPOSAL METHODS

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.

SECTION 14: TRANSPORT INFORMATION
UN PROPER SHIPPING NAME

ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.

UN NUMBER

3077

CLASS

9

PACKING GROUP

III

AUSTRALIA
HAZCHEM

2Z

EU
**TRANSPORT IN BULK ACCORDING
TO ANNEX II OF MARPOL 73/78
AND THE IBC CODE**

Not Listed

ENVIRONMENTAL HAZARDS

Not applicable

**SPECIAL SHIPPING
INFORMATION**

Not applicable

SECTION 15: REGULATORY INFORMATION
UNITED STATES REGULATIONS

Chemical Name & CAS	CERCLA 40 CFR Part 302.4	SARA (Title III) 40 CFR	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	Therapeutic Goods Act	Code of Practices - Illicit Drug	Poisons Standard	Work Health and Safety Regulations	Inventory of Industrial Chemicals
TRETINOIN (Retinoic Acid) 302-79-4	N/L	Listed as Schedule 4	N/L	Listed	N/L	N/L

N/L = Not Listed

EU REGULATIONS

Chemical Name & CAS	REACH ANNEX XVII	REACH ANNEX XIV	EC 1005/2009	EC 850/2004	EC 1107/2009	PIC - Prior Informed Consent Regulation	EC 2012/18
TRETINOIN (Retinoic Acid) 302-79-4	N/L	N/L	N/L	N/L	N/L	N/L	N/L

N/L = Not Listed; X = Listed

Any EU regulation not listed above is not applicable to this product.

SUBJECT TO INTERNATIONAL AGREEMENT Not applicable

SECTION 16: OTHER INFORMATION
REFERENCES
ABBREVIATIONS AND ACRONYMS

Available upon request

ACGIH - American Conference of Governmental Industrial Hygienists; **AIHA WEEL** – American Industrial Hygiene Association Workplace Environment Exposure Levels; **CAESAR** – Computer Assisted Evaluation of industrial chemical Substances According to Regulations; **CAS** – Chemical Abstract Service; **CERCLA** – Comprehensive Environmental Response, Compensation, and Liability Act; **EC50** – Effective Concentration, 50%; **EPA** – Environmental Protection Agency; **GHS** – Global Harmonized System; **HMIS** – Hazardous Materials Information System; **HSE** – Health and Safety Executive; **HSIS** – Hazardous Substances Information System; **IARC** – International Agency for Research on Cancer; **IDLH** - Immediately Dangerous to Life or Health; **IRFMN** – Ready Biodegradability Model; **ISS** – Istituto Superiore Sanità; **LC50** – Lethal Concentration, 50%; **LD50** – Lethal Dose, 50%; **MSHA** - Mine Safety and Health Administration; **NIOSH** – National Institute for Occupational Safety and Health; **NTP** – National Toxicology Program; **OSHA PEL** – Occupational Safety & Health Administration Permissible Exposure Limits; **QSAR** – Quantitative Structure-activity relationship; **REL** - Recommended Exposure Limit; **SARA** – Superfund Amendments and Reauthorization Act; **STEL** – Short Term Exposure Limit; **TLV** – Threshold Limit Value; **TWA** – Time Weighted Average; **WHMIS** – Workplace Hazardous Materials Information System

LAST REVISION

04/2024

SUPERSEDES

11/2023

For a list of changes to the SDS since the last version, please communicate with MEDISCA at www.medisca.com

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.

SUPPLEMENTARY INFORMATION

For all country specific requirements not outlined on this Safety Data Sheet, please request Supplementary Page to this Safety Data Sheet.