

Safety Data Sheet

Section 1: Identification

Product identifier

Product Name • Targretin® Capsules

Product Code • NDC 0187-5526-75

Relevant identified uses of the substance or mixture and uses advised against

Recommended use • Finished Pharmaceutical Product; Targretin (bexarotene) capsules are indicated for the treatment of cutaneous manifestations of cutaneous T-cell lymphoma in patients who are refractory to at least one prior systemic therapy.

Restrictions on use • Refer to the product insert and/or prescribing information for restrictions on use and contraindications.

Details of the supplier of the safety data sheet

Manufacturer • Valeant Pharmaceuticals North America, LLC
400 Somerset Corporate Blvd.
Bridgewater, NJ 08807
United States
valeant.com

Telephone (General) • 1-800-321-4576

Emergency telephone number

Manufacturer • 1-800-535-5053 - US - Infotrac

Manufacturer • +1 352-323-3500 - International - Infotrac

This safety data sheet is written to provide health, safety and environmental information for people handling this formulated product in the workplace. It is not intended to provide information relevant to consumer use of the product.

Section 2: Hazard Identification

UN GHS

According to: UN Globally Harmonized System of Classification and Labelling of Chemicals (GHS)

Classification of the substance or mixture

UN GHS • Reproductive Toxicity 1
Acute Toxicity Oral 5
Skin Mild Irritation 3
Eye Mild Irritation 2B

Label elements

UN GHS

DANGER



Hazard statements • May damage fertility or the unborn child.
May be harmful if swallowed

May cause eye irritation
May cause mild skin irritation

Precautionary statements

Prevention • Do not handle until all safety precautions have been read and understood.
Avoid breathing dust, fume, gas, mist, vapours and/or spray.
Wash thoroughly after handling.
Use personal protective equipment as required.

Response • IF exposed or if you feel unwell: Call a POISON CENTER or doctor/physician.
IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

Storage/Disposal • Store in a well-ventilated place. Keep container tightly closed.
Dispose of content and/or container in accordance with local, regional, national, and/or international regulations.

Other hazards

UN GHS • No data available

Section 3 - Composition/Information on Ingredients

Substances

- Material does not meet the criteria of a substance according to United Nations Globally Harmonized System of Classification and Labelling of Chemicals (GHS)

Mixtures

Composition			
Chemical Name	Identifiers	%	Classifications According to Regulation/Directive
1,4 Sorbitan	CAS:27299-12-3 EINECS:248-391-9	N/A	UN GHS: NDA
Bexarotene	CAS:153559-49-0	10%	UN GHS: Repro.1, STOT RE
Butylated hydroxyanisole	CAS:25013-16-5 EINECS:246-563-8	N/A	UN GHS: NDA
Gelatin	CAS:9000-70-8 EINECS:232-554-6	N/A	UN GHS: Skin Irrit. 2; Eye Irrit. 2A
Glycerin	CAS:56-81-5 EINECS:200-289-5	N/A	UN GHS: Skin Irrit. 3; Eye Irrit. 2B
Mannitol	CAS:69-65-8 EINECS:200-711-8	N/A	UN GHS: NDA
Polyethylene glycol #400	CAS:25322-68-3	N/A	UN GHS: NDA
Polysorbate 20	CAS:9005-64-5	N/A	UN GHS: NDA
Povidone	CAS:9003-39-8	N/A	UN GHS: NDA
Sorbitol	CAS:50-70-4 EINECS:200-061-5	N/A	UN GHS: Skin Irrit. 2; Eye Irrit. 2A
Titanium dioxide	CAS:13463-67-7 EINECS:236-675-5	N/A	UN GHS: STOT RE 2; Carc. 2
Water	CAS:7732-18-5 EINECS:231-791-2	N/A	UN GHS: NDA

The exact percentage of composition has been withheld as a trade secret.

Section 4: First-Aid Measures

Description of first aid measures

- Inhalation**
- Normal use of this product does not pose an inhalation hazard. However, during bulk handling should respiratory tract irritation develop, discontinue use and remove to fresh air. Get medical attention if irritation or other symptoms develop or persist.
- Skin**
- No specific treatment is necessary since this material is not likely to be hazardous by contact with the skin or mucous membranes. Immediately flush skin with large amounts of water. Remove contaminated clothing. If irritation (redness, rash, blistering) develops, get medical attention.
- Eye**
- Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first five minutes, then continue rinsing eye. Get medical attention immediately if symptoms occur.
- Ingestion**
- If swallowed, seek medical advice immediately and show this container or label.

Most important symptoms and effects, both acute and delayed

- No data available

Indication of any immediate medical attention and special treatment needed

- Notes to Physician**
- Treat according to accepted protocols. For additional guidance, refer to the current prescribing information.

Section 5: Fire-Fighting Measures

Extinguishing media

- Suitable Extinguishing Media**
- Water spray, carbon dioxide, dry chemical powder or appropriate foam for surrounding fire.

- Unsuitable Extinguishing Media**
- No data available

Special hazards arising from the substance or mixture

- Unusual Fire and Explosion Hazards**
- No data available

- Hazardous Combustion Products**
- No data available.

Advice for firefighters

- As in any fire, wear self-contained breathing apparatus and full protective gear to prevent contact with skin and eyes.

Section 6 - Accidental Release Measures

Personal precautions, protective equipment and emergency procedures

- Personal Precautions**
- No special controls or personal protection required under conditions of intended use. In the event of bulk spills, wear suitable protective eyewear, clothing, protective boots and protective gloves. Evacuate immediate area. Ensure adequate ventilation. Refer to Section 8.
- Emergency Procedures**
- Keep unauthorized personnel away. Clean up spilled tablets and place in sealed container. Avoid breaking tablets or creating dust during clean up.

Environmental precautions

- No data available on the environmental impact of this product.

Methods and material for containment and cleaning up

- Containment/Clean-up Measures**
- LARGE SPILLS: Use HEPA vacuum to clean up spill. If HEPA vacuum is not available, dampen spilled tablets with water prior to cleaning up to prevent dust cloud.

Section 7 - Handling and Storage

Precautions for safe handling

Handling

- Avoid breaking or crushing tablets. Minimize dust generation and accumulation. Use good safety and industrial hygiene practices.

Conditions for safe storage, including any incompatibilities

Storage

- Keep tightly closed. Store at controlled room temperature 2-25°C/36-77°F, to maintain product integrity. Use before date marked on carton and/or container. Protect from light.

Section 8 - Exposure Controls/Personal Protection

Control parameters

Exposure Limits/Guidelines

- Refer to the occupational exposure limits / guidelines for the individual product components.

Exposure Limits/Guidelines					
	Result	ACGIH	Canada Quebec	OSHA	Other Agency Information
Titanium dioxide (13463-67-7)	TWAs	10 mg/m ³ TWA	10 mg/m ³ TWAEV (containing no Asbestos and <1% Crystalline silica, total dust)	15 mg/m ³ TWA (total dust)	Not established
Glycerin (56-81-5)	TWAs	Not established	10 mg/m ³ TWAEV (mist)	15 mg/m ³ TWA (mist, total particulate); 5 mg/m ³ TWA (mist, respirable fraction)	Not established
Polyethylene glycol #400 (25322-68-3)	TWAs	Not established	Not established	Not established	10 mg/m ³ TWA (MW>200, aerosol)

Exposure Control Notations

ACGIH

- Titanium dioxide (13463-67-7): **Carcinogens:** (A4 - Not Classifiable as a Human Carcinogen)

Exposure controls

Engineering Measures/Controls

- NO SPECIAL CONTROLS ARE REQUIRED UNDER CONDITIONS OF INTENDED USE. Local exhaust ventilation should be provided when handling bulk product.

Personal Protective Equipment

Respiratory

- For bulk handling, the personal breathing protection should be determined based upon a risk assessment and in accordance with local regulations. Follow the 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 symptoms are experienced.

Eye/Face

- Wear protective eyewear (goggles, face shield, or safety glasses) when handling bulk product before closed in final packaging.

Hands

- Wear protective gloves when handling bulk product before closed in final packaging.

Skin/Body

- Avoid contact with skin.

General Industrial Hygiene Considerations

- Handle in accordance with good industrial hygiene and safety practice. Wash thoroughly with soap and water after handling.

Environmental Exposure Controls

- No data available

Section 9 - Physical and Chemical Properties

Information on Physical and Chemical Properties

Material Description			
Physical Form	Solid	Appearance/Description	Liquid filled capsule.
Color	White	Odor	Not relevant
General Properties			
Boiling Point	No data available	Melting Point/Freezing Point	No data available
Decomposition Temperature	No data available	pH	Not relevant
Specific Gravity/Relative Density	No data available	Water Solubility	No data available
Viscosity	Not relevant		
Volatility			
Vapor Pressure	Not relevant	Vapor Density	Not relevant
Evaporation Rate	Not relevant		
Flammability			
Flash Point	Not relevant	UEL	Not relevant
LEL	Not relevant	Autoignition	Not relevant
Flammability (solid, gas)	Not relevant		
Environmental			
Octanol/Water Partition coefficient	No data available		

Section 10: Stability and Reactivity

Reactivity

- Stable under normal temperatures and pressures.

Chemical stability

- Hazardous polymerization will not occur.

Possibility of hazardous reactions

- No data available

Conditions to avoid

- Light, heat and humidity.

Incompatible materials

- Strong oxidizing agents.

Hazardous decomposition products

- When heated to decomposition, toxic fumes of nitrous oxides, sulfur oxides, hydrogen chloride and carbon oxides may be emitted.

Section 11 - Toxicological Information

Information on toxicological effects

Components	
Bexarotene (10%)	153559-49-0

Acute Toxicity: Unreported-Mouse TDLo • 100 mg/kg; **Tumorigenic:** Active as anti-cancer agent; **Biochemical:** Enzyme inhibition, induction, or change in blood or tissue levels; **Other enzymes;**
Multi-dose Toxicity: Ingestion/Oral-Rat TDLo • 4.2 mg/kg 14 Day(s)-Intermittent; **Blood:** Changes in serum composition (e.g., TP, bilirubin cholesterol); **Musculoskeletal:** Other changes; **Biochemical:** Metabolism (intermediary); **Lipids, including transport**

GHS Properties	Classification
Respiratory sensitization	UN GHS • Classification criteria not met
Serious eye damage/Irritation	UN GHS • Eye Mild Irritation 2B
Acute toxicity	UN GHS • Acute Toxicity - Oral 5
Aspiration Hazard	UN GHS • Classification criteria not met
Carcinogenicity	UN GHS • Classification criteria not met
Germ Cell Mutagenicity	UN GHS • Classification criteria not met
Skin corrosion/Irritation	UN GHS • Skin Mild Irritation 3
Skin sensitization	UN GHS • Classification criteria not met
STOT-RE	UN GHS • Classification criteria not met
STOT-SE	UN GHS • Classification criteria not met
Toxicity for Reproduction	UN GHS • Toxic to Reproduction 1

Potential Health Effects

Inhalation

- Acute (Immediate)** • Under normal conditions of use, no health effects are expected.
- Chronic (Delayed)** • No data available

Skin

- Acute (Immediate)** • May cause mild irritation. Retinoids as a class have associated with photosensitivity. Mild phototoxicity manifested as sunburn and skin sensitivity to sunlight was observed in patients during treatment.
- Chronic (Delayed)** • No data available

Eye

- Acute (Immediate)** • May cause mild eye irritation with direct contact to eye.
- Chronic (Delayed)** • No data available

Ingestion

- Acute (Immediate)** • May cause mild irritation.
- Chronic (Delayed)** • Targretin capsules induce major lipid abnormalities in most patients.

Carcinogenic Effects			
	CAS	IARC	NTP
Mannitol	69-65-8	Not Listed	Evidence of Carcinogenicity
Titanium dioxide	13463-67-7	Group 2B-Possible Carcinogen	Evidence of Carcinogenicity
Butylated hydroxyanisole	25013-16-5	Group 2B-Possible Carcinogen	Reasonably Anticipated to be Human Carcinogen
Povidone	9003-39-8	Group 3-Not Classifiable	Not Listed

Reproductive Effects

- Pregnancy:** Category X. Targretin capsules are a member of the retinoid class of drugs that is associated with birth defects in humans. Targretin capsules also caused birth defects when administered orally to pregnant rats. Bexarotene caused malformations when administered orally to pregnant rats during days 7-17 of gestation. Developmental abnormalities included incomplete ossification at 4 mg/kg/day and cleft palate, depressed eye bulge/micropthalmia, and small ears at 16 mg/kg/day. The plasma AUC of bexarotene in rats at 4 mg/kg/day is approximately one third the AUC in humans at the recommended daily dose. At doses greater than 10 mg/kg/day, bexarotene caused developmental mortality. The no effect dose for fetal effects in rats was 1 mg/kg/day (producing an AUC approximately one sixth of the AUC at the recommended human daily dose).

Section 12 - Ecological Information

Toxicity

- This material has not been tested for environmental effects.

Persistence and degradability

- No data available

Bioaccumulative potential

- No data available

Mobility in Soil

- No data available

Other adverse effects

Section 13 - Disposal Considerations

Waste treatment methods

Product waste

- Waste characterizations and compliance with applicable laws are the responsibility solely of the waste generator.

Packaging waste

- Dispose of content and/or container in accordance with local, regional, national, and/or international regulations.

Section 14 - Transport Information

	UN number	UN proper shipping name	Transport hazard class (es)	Packing group	Environmental hazards
DOT	Not Applicable	Not Regulated	Not Applicable	Not Applicable	
TDG	Not Applicable	Not Regulated	Not Applicable	Not Applicable	
IMO/IMDG	Not Applicable	Not Regulated	Not Applicable	Not Applicable	
IATA/ICAO	Not Applicable	Not Regulated	Not Applicable	Not Applicable	

Special precautions for user • No data available

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code • No data available

Section 15 - Regulatory Information

Safety, health and environmental regulations/legislation specific for the substance or mixture

SARA Hazard Classifications • No data available

Inventory				
Component	CAS	Canada DSL	EU EINECS	TSCA
1,4 Sorbitan	27299-12-3	No	Yes	No
Bexarotene	153559-49-0	No	No	No
Gelatin	9000-70-8	Yes	Yes	Yes

Sorbitol	50-70-4	Yes	Yes	Yes
Glycerin	56-81-5	Yes	Yes	Yes
Mannitol	69-65-8	Yes	Yes	Yes
Butylated hydroxyanisole	25013-16-5	Yes	Yes	Yes
Polyethylene glycol #400	25322-68-3	Yes	No	Yes
Polysorbate 20	9005-64-5	Yes	No	Yes
Povidone	9003-39-8	Yes	No	Yes
Titanium dioxide	13463-67-7	Yes	Yes	Yes

Canada

Labor

Canada - WHMIS - Classifications of Substances

• Povidone	9003-39-8	Uncontrolled product according to WHMIS classification criteria (listed under Povidone)
• Sorbitol	50-70-4	Not Listed
• Mannitol	69-65-8	Uncontrolled product according to WHMIS classification criteria
• Gelatin	9000-70-8	Not Listed
• Polysorbate 20	9005-64-5	Uncontrolled product according to WHMIS classification criteria
• Titanium dioxide	13463-67-7	D2A (In certain cases, this classification does not apply. For more information, consult the section Substance Specific Issues - Titanium dioxide, mixture containing on Health Canada's WHMIS Division website.)
• Glycerin	56-81-5	Uncontrolled product according to WHMIS classification criteria
• Butylated hydroxyanisole	25013-16-5	Not Listed
• Bexarotene	153559-49-0	Not Listed
• Polyethylene glycol #400	25322-68-3	Not Listed
• 1,4 Sorbitan	27299-12-3	Not Listed

Canada - WHMIS - Ingredient Disclosure List

• Povidone	9003-39-8	Not Listed
• Sorbitol	50-70-4	Not Listed
• Mannitol	69-65-8	Not Listed
• Gelatin	9000-70-8	Not Listed
• Polysorbate 20	9005-64-5	Not Listed
• Titanium dioxide	13463-67-7	Not Listed
• Glycerin	56-81-5	Not Listed
• Butylated hydroxyanisole	25013-16-5	1 %
• Bexarotene	153559-49-0	Not Listed
• Polyethylene glycol #400	25322-68-3	Not Listed
• 1,4 Sorbitan	27299-12-3	Not Listed

United States - California

Environment

U.S. - California - Proposition 65 - Carcinogens List

• Povidone	9003-39-8	Not Listed
• Sorbitol	50-70-4	Not Listed
• Mannitol	69-65-8	Not Listed
• Gelatin	9000-70-8	Not Listed
• Polysorbate 20	9005-64-5	Not Listed
• Titanium dioxide	13463-67-7	carcinogen, 9/2/2011 (airborne, unbound particles of respirable size)
• Glycerin	56-81-5	Not Listed
• Butylated hydroxyanisole	25013-16-5	carcinogen, 1/1/1990
• Bexarotene	153559-49-0	Not Listed
• Polyethylene glycol #400	25322-68-3	Not Listed
• 1,4 Sorbitan	27299-12-3	Not Listed

U.S. - California - Proposition 65 - Developmental Toxicity

• Povidone	9003-39-8	Not Listed
• Sorbitol	50-70-4	Not Listed
• Mannitol	69-65-8	Not Listed
• Gelatin	9000-70-8	Not Listed
• Polysorbate 20	9005-64-5	Not Listed
• Titanium dioxide	13463-67-7	Not Listed
• Glycerin	56-81-5	Not Listed
• Butylated hydroxyanisole	25013-16-5	Not Listed
• Bexarotene	153559-49-0	Not Listed
• Polyethylene glycol #400	25322-68-3	Not Listed
• 1,4 Sorbitan	27299-12-3	Not Listed

U.S. - California - Proposition 65 - No Significant Risk Levels (NSRL)

• Povidone	9003-39-8	Not Listed
• Sorbitol	50-70-4	Not Listed
• Mannitol	69-65-8	Not Listed
• Gelatin	9000-70-8	Not Listed
• Polysorbate 20	9005-64-5	Not Listed
• Titanium dioxide	13463-67-7	Not Listed
• Glycerin	56-81-5	Not Listed
• Butylated hydroxyanisole	25013-16-5	4000 µg/day NSRL
• Bexarotene	153559-49-0	Not Listed
• Polyethylene glycol #400	25322-68-3	Not Listed
• 1,4 Sorbitan	27299-12-3	Not Listed

U.S. - California - Proposition 65 - Reproductive Toxicity - Female

• Povidone	9003-39-8	Not Listed
• Sorbitol	50-70-4	Not Listed
• Mannitol	69-65-8	Not Listed
• Gelatin	9000-70-8	Not Listed
• Polysorbate 20	9005-64-5	Not Listed
• Titanium dioxide	13463-67-7	Not Listed
• Glycerin	56-81-5	Not Listed
• Butylated hydroxyanisole	25013-16-5	Not Listed

• Bexarotene	153559-49-0	Not Listed
• Polyethylene glycol #400	25322-68-3	Not Listed
• 1,4 Sorbitan	27299-12-3	Not Listed

U.S. - California - Proposition 65 - Reproductive Toxicity - Male

• Povidone	9003-39-8	Not Listed
• Sorbitol	50-70-4	Not Listed
• Mannitol	69-65-8	Not Listed
• Gelatin	9000-70-8	Not Listed
• Polysorbate 20	9005-64-5	Not Listed
• Titanium dioxide	13463-67-7	Not Listed
• Glycerin	56-81-5	Not Listed
• Butylated hydroxyanisole	25013-16-5	Not Listed
• Bexarotene	153559-49-0	Not Listed
• Polyethylene glycol #400	25322-68-3	Not Listed
• 1,4 Sorbitan	27299-12-3	Not Listed

Section 16 - Other Information

Revision Date	• 04/December/2015
Last Revision Date	• 04/December/2015
Preparation Date	• 04/December/2015
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