MATERIAL SAFETY DATA SHEET
Soriatane® (Acitretin) Capsules

SECTION 1. MATERIAL IDENTIFICATION AND COMPANY

MATERIAL IDENTIFICATION

Generic Name: **Soriatane® (Acitretin) Capsules**

NOTE: This MSDS for **Soriatane® (Acitretin) Capsules** is written to address potential worker health and safety issues associated with the handling of this product as a capsule, i.e., during the transportation, distribution, and use by medical personnel. If formulating this product, consult the MSDSs for each ingredient.

COMPANY

Stiefel Laboratories, Inc.
3160 Porter Drive
Palo Alto, CA 94304
In case of emergency, contact: (650) 843-2800

SECTION 2. PRODUCT COMPOSITION

Ingredient	CAS #	EINECS No.	% Composition	EU R and S Phrases
Acitretin	55079-83-9	259-474-4	Approx. 45%	61-36/38-50/53
Microcrystalline cellulose	9004-34-6	232-674-9	Approx. 55%	None applicable

Each capsule contains acitretin, microcrystalline cellulose, and small quantities (<1%) of sodium ascorbate, gelatin, black monogramming ink and maltodextrin (a mixture of polysaccharides).

Gelatin capsule shells contain gelatin and small quantities (<1%) of iron oxide (yellow, black, and red), and titanium dioxide. They may also contain small quantities (<1%) of benzyl alcohol, carboxymethylcellulose sodium, edetate calcium disodium.

MATERIAL SAFETY DATA SHEET
Soriatane® (Acitretin) Capsules

SECTION 3. HAZARD IDENTIFICATION

Appearance: Gelatin Capsule

Signal Word: CAUTION

Hazard Overview: Material intended for uses as a human pharmaceutical. As a capsule, material not considered hazardous under U.S. Hazard Communication Standard [29 CFR 1910.1200]. **This product only presents an occupational hazard or risk if the contents of capsules are spilled or accidentally broken or crushed**. The active pharmaceutical ingredient in the capsule is acitretin. **Acitretin is considered a human teratogen based on human experience and laboratory animal studies. Women of child bearing age should avoid exposure if contents are released. Women of childbearing potential should also avoid ingestion of alcohol (ethanol) containing products (e.g., food, prescription and nonprescription medications) for 2 months after acitretin exposure. Clinical evidence has shown that concurrent ingestion of acitretin and ethanol has been associated with the formation of etretinate, which has a significantly longer elimination half-life than acitretin of at least 3 years. Because the longer elimination half-life of etretinate would increase the duration of teratogenic (causing birth defects) potential for a female of childbearing potential, ethanol must not be ingested. This allows for elimination of acitretin.** Acitretin may also cause hypervitaminosis A with symptoms of dry lips, dry mucous membranes, skin changes, itchiness, and severe headache. Other potentially serious adverse effects associated with acitretin include hepatotoxicity, hypertriglyceridemia and lowered HDL, pancreatitis, ophthalmologic effects, hyperostosis, depression and/or other psychiatric symptoms (aggression, suicidal ideation), and pseudotumor cerebri (benign intracranial hypertension).

A person should not donate blood during and for at least 3 years following acitretin exposure because women of childbearing potential must not receive blood from someone being treated with Soriatane.

Statement of Known Hazard: Under normal handling conditions, no acute or chronic effects are expected. If material is spilled or released, overexposure to contents has the potential to affect the developing fetus. Overexposure may also induce a hypervitaminosis A syndrome that is characterized by dry lips, dry mucous membranes, skin changes, itchiness, and severe headache.

EU Indicator of Danger: Under normal handling conditions, this material should not present a risk or hazard. If material is spilled or released, it is potentially toxic (T) if overexposure occurred

EU Risk Phrases: Under normal handling conditions, no EU Risk phrases apply. If a spill occurred and there was potential for exposure the following Risk phrases may apply.
R 61 May cause harm to the unborn child
R 36/38 Irritating to the eyes and skin
R 53 May cause long-term adverse effects in the aquatic environment.

SORIATANE is indicated for the treatment of severe psoriasis in adults. Due to the risk of severe birth defects, in females of reproductive potential SORIATANE should be reserved for non-pregnant patients with severe psoriasis who are unresponsive to other therapies or whose clinical condition contraindicates the use of other treatments.

Common side effects include: chapped lips; peeling fingertips, palms, and soles; itching; scaling skin all over; weak nails; sticky or fragile skin; runny or dry nose; nosebleeds; dry mouth; joint pain; tight muscles; hair loss; dry eyes; and rise in blood fats (lipids).

Less frequent, but potentially serious side effects include bad headaches, nausea, vomiting, blurred vision. These symptoms can be signs of increased brain pressure that can lead to blindness or even death. Other potentially serious side effects include decreased vision in the dark (night blindness); depression, aggressive feelings, or suicidal thoughts; yellowing of your skin or the whites of your eyes, loss of appetite or dark urine; aches or pains in your bones, joints, muscles or back, trouble moving; loss of feeling in your hands or feet; frequent urination, great thirst or hunger. Shortness of breath, dizziness, chest pain, weakness, trouble speaking, or swelling of a leg may be signs of a heart attack, blood clots, or stroke. Additionally, acitretin can cause severe birth defects.

SECTION 4. FIRST AID MEASURES

Eye Contact
Flush eyes thoroughly with water and notify supervisor.

Skin Contact
Wash skin thoroughly with soap and water and notify supervisor.

Inhalation
Immediately move to fresh air. If signs of toxicity occur, notify medical personnel.

Ingestion
Drink 1 to 2 glasses of water to dilute. If signs of toxicity occur, notify medical personnel.

Note to Physician
Medical conditions aggravated by exposure: **Women of childbearing potential must be counseled by a knowledgeable physician regarding birth defects and contraception (birth control measures) following exposure to acitretin. A person should not donate blood during and for at least 3 years following acitretin exposure because women of childbearing potential must not receive blood from someone being treated with Soriatane.**

Other medical conditions that may be aggravated by acitretin exposure include preexisting liver, kidney, cardiovascular, or metabolic (diabetes, hyperlipidemia) disease. Acitretin may be hepatotoxic and has been associated with increased liver function tests and changes in liver biopsy status. Acitretin may cause hypertriglyceridemia, elevations in total cholesterol, and/or decreased high-density lipoprotein (HDL) levels. Nursing mothers should avoid acitretin exposure prior to or during nursing since acitretin excretion in human milk has been documented.

SECTION 5. FIRE PROTECTION

Flash Point / Explosivity
As a capsule, the product is not flammable or explosive.

Extinguishing Media
In case of a fire, use water fog, halon, dry chemical fire extinguisher, foam, or CO_2.

Fire Fighting Procedures
Wear full structural fire fighting protective clothing and NIOSH/MSHA-approved positive pressure, self-contained breathing apparatus. Decontaminate after use.

SECTION 6. SPILL AND RELEASE MEASURES

If capsules are spilled and contents are released, the following precautions should be followed.

Procedures to be Followed in Case of Spill or Breakage of Capsules

If in solid or dried form, do not raise dust. Surround spill or powder with absorbents and place a damp cloth or towel over the area to minimize powder from entering the air. Add excess liquid to allow for the material to enter solution. Capture remaining liquid onto spill absorbents. Place spill materials into a leak-proof container suitable for disposal. Decontaminate area a second time. Dispose of material in a manner that is compliant with federal, state and local laws.

If in liquid form, surround spill using spill pillows or other absorbents. Capture remaining liquid onto spill absorbents. Place spill materials into a leak-proof container suitable for disposal. Decontaminate area a second time. Dispose of material in a manner that is compliant with federal, state and local laws.

Wear appropriate personal protective equipment when cleaning up a spill or breakage of capsules, including at a minimum, gloves, overgarment (e.g., lab coat), and safety glasses with side shields. For large spills, wear Tyvek or other protective overgarment and at least a half face air purifying respirator with NIOSH-approval for dusts and mists if inhalation exposure is likely.

SECTION 7. HANDLING AND STORAGE

Handling
Avoid contact with skin, eyes or clothing.

Storage
Store in tightly closed containers.

SECTION 8. EXPOSURE CONTROL/PERSONAL PROTECTION

Occupational Exposure Limits
None established for product or the active ingredient. The excipient, microcrystalline cellulose is considered a "nuisance dust" with an OSHA Permissible Exposure Limit of 15 mg/m^3 as an 8-hour time-weighted-average (TWA) for total dust and 5 mg/m^3 as an 8-hour TWA for the respirable fraction. The ACGIH Threshold Limit Value for microcrystalline cellulose is 10 mg/m^3 as an 8-hour TWA.

Eye Protection
Should not be needed during normal handling of capsules. Wear safety glasses with side shields if eye contact is likely, e.g., during clean up of large spill. Base the choice of protection on the job activity and potential for contact with eyes and face.

Respiratory Protection
Should not be needed during normal handling of product. Wear a half face air purifying respirator with NIOSH-approval for dusts and mists if inhalation exposure is likely, e.g., during clean up of large spill. Base the choice of respirator on the job activity, potential for inhalation exposure, or on air monitoring results.

Skin Protection
Health care workers should wear disposable gloves if administering product to a patient to avoid unnecessary or repeated skin contact. Wear disposable gloves, lab coat, or other protective over garment if skin contact is likely, e.g., during cleanup of a large spill. Base the choice of skin protection on the job activity and potential for contact.

Other
Wash hands, face and other potentially exposed areas immediately after handling material (especially before eating, drinking, or smoking). Decontaminate all protective equipment after use.

SECTION 9. PHYSICAL/CHEMICAL PROPERTIES

Appearance, Color, Odor:	Capsule.
Boiling Point:	Not applicable/mixture.
Melting Point:	Not applicable/mixture.
Vapor Pressure:	No data available.
Solubility in Water:	Readily disintegrates in water.
Evaporation Rate:	No data available.
Specific Gravity:	No data available.
Vapor Density:	No data available.

SECTION 10. STABILITY AND REACTIVITY

Stability:
Chemically stable; stability of excipients not guaranteed beyond expiration date on package.

Incompatibility:
No data available.

Hazardous Decomposition Products:
No data available.

Hazardous Polymerization:
Will not occur.

SECTION 11. TOXICOLOGICAL INFORMATION

The active ingredient of this product is acitretin. The following is the available toxicology data on this material. Consult the Patient Package Insert for further information.

Vitamin A and related analogues (e.g., retinoids), such as the primary ingredient in this capsule, acitretin, are well-known teratogens. Major human fetal abnormalities associated with acitretin and/or etretinate administration have been reported including meningomyelocele, meningoencephalocele, multiple synostoses, facial dysmorphia, syndactyly, absence of terminal phalanges, malformations of hip, ankle and forearm, low-set ears, high palate, decreased cranial volume, cardiovascular malformation and alterations of the skull and cervical vertebrae.

When used clinically in patients at the recommended dose, acitretin can induce a hypervitaminosis A syndrome that is characterized by dry lips, dry mucous membranes, skin changes, itchiness, and severe headache. Other adverse effects potentially include joint and muscle pain, changes in lipid metabolism (e.g., increased serum triglycerides, increased serum cholesterol, and decreased high-density lipoproteins), possible night-blindness, blurred vision, hair thinning, and nausea and/or vomiting.

Overdosage. Symptoms of overdose are identical to acute hypervitaminosis A, e.g., headache and vertigo. In the event of acute overdosage, Soriatane must be withdrawn at once. **All females of childbearing potential who have incurred an overdose of Soriatane must have a pregnancy test at the time of overdose and receive counseling regarding birth defects and contraceptive use for at least 3 years' duration after the overdose.**

The following is a summary of non-clinical studies on the active ingredient:

Acute toxicity – Not considered very acutely toxic. The acute oral LD_{50} in rats and mice was greater than 4 and 8 g/kg, respectively. Acitretin is considered to be irritating to the skin and eyes.

Chronic toxicity – Chronic toxicity studies in dogs administered up to 50 mg/kg/day of acitretin evidenced testicular changes (e.g., spermatogenic arrest) at the highest dose.

Reproductive toxicity (fertility impairment) – Negative for fertility impairment in rats administered doses of up to 3 mg/kg/day. Changes in sperm morphology were observed at these doses.

Developmental toxicity (birth defects) – Acitretin has been shown to be embryotoxic and/or teratogenic in rabbits, mice, and rats at oral doses of 0.6, 3 and 15 mg/kg/day, respectively. These doses are approximately 0.2, 0.3 and 3 times the maximum recommended therapeutic dose, respectively, based on a mg/m^2 comparison.

Genotoxicity – Negative in several short-term screening tests for genetic damage, including the Ames bacterial cell mutagenicity test, a mammalian mutagenicity test, and several tests assessing the potential for acitretin induced chromosome damage.

Carcinogenicity – Negative in a long-term cancer study in rats administered doses up to 2 mg/kg/day for a period of 104 weeks.

SECTION 12. ENVIRONMENTAL INFORMATION

Persistence and Degradability
No data available.

Aquatic Toxicity
No data available.

Because of its effects in mammalian systems (teratogenicity), it is assumed that this class of compounds may have similar effects on aquatic species.

SECTION 13. WASTE DISPOSAL METHODS

DO NOT DISPOSE OF DOWN THE DRAIN. Dispose of waste materials according to prescribed Federal, state, and local regulations, e.g., appropriately permitted chemical waste incinerator. Rinse water resulting from spill cleanups should be discharged in an environmentally safe manner, e.g., to an appropriately permitted wastewater treatment facility.

SECTION 14. TRANSPORTATION INFORMATION

DOT Hazard Class
Not regulated

Proper Shipping Name
Not regulated.

UN Number
Not applicable.

SECTION 15. LABELING/REGULATORY INFORMATION

US OSHA: This MSDS complies with the requirements under 29 CFR 1910.1200

If shipped in bulk containers, the following label should be considered

Material intended for uses as a human pharmaceutical. As a capsule, material not considered hazardous under U.S. Hazard Communication Standard [29 CFR 1910.1200]. **This product only presents an occupational hazard or risk if the contents of capsules are spilled or accidentally broken or crushed**. The active pharmaceutical ingredient in the capsule is acitretin. Acitretin is considered a human teratogen based on human experience and laboratory animal studies. Women of child bearing age should avoid exposure if contents are released. Acitretin may also cause hypervitaminosis A with symptoms of dry lips, dry mucous membranes, skin changes, itchiness, and severe headache.

EU Indicators of Danger, Hazard Symbol and Risk Phrases
Not regulated as a capsule

Canada – WHMIS Classifications
Drugs are exempt.

California Proposition 65
Acitretin is listed as a developmental toxicant.

TSCA
Drug products are exempt under TSCA.

MATERIAL SAFETY DATA SHEET
Soriatane® (Acitretin) Capsules

SECTION 16. OTHER INFORMATION

No additional information

Abbreviations

ACGIH:	American Conference of Governmental Industrial Hygienists
CAS#:	Chemical Abstract Services Number
CFR	Code of Federal Regulations
DOT:	Department of Transportation
EU:	European Union
IARC:	International Agency for Research on Cancer
IATA:	International Air Transport Association
OSHA:	Occupational Safety and Health Administration
NTP:	National Toxicology Program

The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections which pertain to their particular conditions.

No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained form the use thereof, or the hazards connected with the use of the material.