ALLERGAN

MATERIAL SAFETY DATA SHEET

NFPA Rating: Health: 1 Flammability: 0 Reactivity: 0 Special: 0

TELEPHONE CONTACTS:
Product Technical and Medical Information: (800) 433-8871
Transportation Emergency 24-Hour Response (CHEMTREC): (800) 424-9300

SECTION 1: PRODUCT IDENTIFICATION

Compound Name:	**FLUOROPLEX® (Fluorouracil) 1% Topical Cream**
Chemical Class:	Topical Antineoplastic
Manufacturer's Name:	Allergan, Inc.
Address:	2525 Dupont Drive Irvine, CA 92612
Revision Date:	June 14, 2001 (Supercedes January 25, 1993)

SECTION 2: COMPOSITION/HAZARDOUS INGREDIENTS

Chemical Name	CAS Number	Percent (By Weight)	Exposure Limits in Air (8 hr. TWA) OSHA PEL	ACGIH TLV
5-Fluorouracil	51-21-8	1.0	N/E	N/E

SECTION 3: HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW: FLUOROPLEX® (Fluorouracil) 1% Topical Cream has been shown to produce adverse reproductive effects in rats and mice. Use of Fluoroplex® by women who are, or may become, pregnant is not recommended.

Potential Health Effects:

EYE CONTACT: Contact with the eyes may result in moderate to severe irritation (burning or stinging), and may result in severe eye injury. Do not allow contact with the eyes.

SKIN CONTACT: Contact with the skin may result in irritation, redness and inflammation. In severe cases, erosion of the dermal layer of skin may occur. Exposure to sunlight may intensify skin reactions.

INHALATION: The product is non-volatile and inhalation is not likely to occur.

INGESTION: If ingested, may cause irritation, burning and gastric upset, resulting in nausea, vomiting and diarrhea.

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: The therapeutic use of **FLUOROPLEX® (Fluorouracil) 1% Topical Cream** is not recommended for women who are, or may become pregnant. This product should not be used by anyone allergic to any of its components.

CHRONIC EFFECTS: Prolonged or repeated contact with the skin may result in irritation and erythema. On keratotic skin, scaling, tenderness, erosion, ulceration and necrosis may occur, followed by re-epithelization of the affected skin. Prolonged contact may result in hyperpigmentation of the skin. Exposure to sunlight or other UV radiation sources may intensify skin reactions. Allergic contact dermatitis has been reported from use of this product.

Fluorouracil may cause fetal harm when administered to a pregnant woman. Fluorouracil administered parenterally has been shown to be teratogenic in mice, rats and hamsters, and embryolethal in monkeys. Fluorouracil is contraindicated in women who are or may become pregnant.

No ingredient in this product is regulated or listed as a carcinogen by OSHA, IARC, or NTP.

SECTION 4: FIRST AID MEASURES

Eye Contact: If contact occurs or irritation develops, flush eyes with plenty of water for at least 15 minutes. Obtain medical attention if irritation or other symptoms persist.

Skin Contact: If unintentional contact occurs, wash skin thoroughly with soap and water. Wash hands with soap and water after contact. If redness or irritation develops as a result of unintentional contact, consult a physician

Thoroughly launder contaminated clothing before reuse.

Inhalation: Inhalation is not likely to occur. If symptoms occur, move to fresh air and obtain medical attention. Treat symptomatically.

Ingestion: If ingested, induce emesis and perform gastric lavage Treatment includes supportive and symptomatic therapy. Consult a physician or poison control center immediately if ingestion has occurred.

SECTION 5: FIRE FIGHTING MEASURES

Flash Point and Method: Greater than 200°F (Seta Flash Cup)

Flammable Limits: Not applicable

Autoignition Temperature: No data for this product

Fire-Extinguishing Materials: Material is non-flammable. Use extinguishing media suitable for materials supporting combustion such as water fog, CO_2, foam or dry chemical.

Fire fighting Procedures: Use self-contained breathing apparatus in enclosed or confined spaces or as otherwise needed.

Unusual Fire and Explosion Hazards: None known

SECTION 6: ACCIDENTAL RELEASE MEASURES

Take up with absorbent material and remove product. Flush spill area with water. Use appropriate personal protective equipment for spill clean up.

SECTION 7: HANDLING AND STORAGE

Handling: Avoid unintentional contact with skin surfaces. Do not allow contact with eyes or mucous membranes. Wash thoroughly after handling. Observe all precautions contained on product label and package insert.

Storage: Store in a cool, dry location out of direct sunlight. Keep container closed when not in use.

SECTION 8: EXPOSURE CONTROLS AND PERSONAL PROTECTION

Engineering Controls: None necessary for normal product handling.

Respiratory Protection: None necessary for normal product handling. For spill clean up, use NIOSH approved respirator (R-95 or equivalent).

Eye Protection: None required for normal product handling. Wear safety glasses or chemical goggles during spill clean up or if potential exists for product misting or spray.

Protective Clothing: None required for normal product handling. Where unintended contact may occur, use impervious PVC or nitrile-based chemical resistant gloves.

Hygienic Work Practices: Wash hands thoroughly after handling. No eating, drinking or smoking in area.

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

Vapor Density (Air = 1): No data for this product

Boiling Point: Not Determined

Solubility in Water: Slightly soluble

Specific Gravity: Approximately 1.0

pH: 8.5

Vapor Pressure (mm Hg at 20° C): No data for this product

Appearance and Odor: Light colored opaque cream with slight odor

SECTION 10: STABILITY AND REACTIVITY

General: This product is stable and hazardous polymerization will not occur.

Incompatible Materials and Conditions to Avoid: Store away from oxidizers and heat. Store below 25 ^{O}C.

Hazardous Decomposition: None known

SECTION 11: TOXICOLOGICAL INFORMATION

Oral LD_{50} (5-fluorouracil): 230 mg/kg (rats); 115 mg/kg (mouse); 18.9 mg/kg (rabbit)

Oral (Mutidose): 5-fluorouracil was administered to dogs at dose levels of 10.0, 5.0, and 2.3 mg/kg/day on successive days except weekends for a total of ten doses. The dog on the 10.0 mg/kg/day regimen died after the third day of treatment. No signs of gross toxicity were noted after the third dose of the compound. In general, 5-fluorouracil at these dosages caused severe reticulopenia, leukopenia and thrombopenia. The bone marrow of the animal that died was almost devoid of hematopoietic elements, and lesions of the intestinal epithelium were observed. It is reported that granulocytopenia is the most dangerous side-effect of 5-fluorouracil in humans.

Dermal: The toxic dose levels and toxic effects of systemic and topical 5-fluorouracil treatment were determined in mice, rabbits, cats, monkeys and dogs. Topical application to the intact and abraded skin of rabbits at 10 times the proposed human dose (BID for 30 days) produced no discernable bone marrow changes, decrease in body weight, alopecia, dermatitis or stomatitis. Local erythema occurred during treatment; this disappeared upon cessation of treatment.

When applied to normal intact human skin, a 1% mixture of 5-fluorouracil in propylene glycol did not produce detectable effects on non-keratotic skin after twice daily treatment for 14 days. Thirty-seven patients were monitored with routine hematologic tests while using 1% 5-fluorouracil solution or 5% ointment. Systemic toxicity from absorption through the skin was not detected after topical application of 5-fluorouracil.

Carcinogenisis, Mutagenisis and Reproduction: In three *in vitro* cell transformation assays, fluorouracil produced morphological transformation of cells. Morphological transformation was also produced in one of these *in vitro* assays by a metabolite of fluorouracil and the transformed cells produced malignant tumors when injected into immunosuppressed syngeneic mice. Fluorouracil has been shown to exert mutagenic activity in the yeast cells, **Bacillus subtilis,** and **Drosophila** assays. In addition, fluorouracil has produced chromosome damage at concentrations of 1.0 and 2.0 mcg/mL in an *in vitro* hamster fibroblast assay and increases in micronuclei formation in the bone marrow of mice at intraperitoneal doses within the human therapeutic dose range of 12-15 mg/kg/day. Patients receiving cumulative doses of 0.24-1.0 g of fluorouracil parenterally have shown an increase in numerical and structural chromosome aberrations in peripheral blood lymphocytes. Fluorouracil has been shown to impair fertility after parenteral administration in rats. In mice, single-dose intravenous and intraperitoneal injections of fluorouracil have been reported to kill differentiated spermatogonia and spermatocytes at a dose of 500 mg/kg and produce abnormalities in spermatids at 50 mg/kg. Fluorouracil was negative in the dominant lethal mutation assay performed in mice.

SECTION 12: ECOLOGICAL INFORMATION

No ecological information is available for the product.

SECTION 13: DISPOSAL CONSIDERATIONS

For small quantities of **FLUOROPLEX® (Fluorouracil) 1% Topical Cream**, discard as ordinary trash. For large quantities, contact Allergan for information on disposal options.

SECTION 14: TRANSPORT INFORMATION

Not a hazardous material for DOT, IATA, IMO or TDG shipment.

SECTION 15: REGULATORY INFORMATION

TSCA (Toxic Substances Control Act):
As defined by U.S. Code Title 15, Chapter 53 (TSCA), Section 2602 and TSCA Regulations at 40CFR, Subchapter R, Part 710, this drug product is exempt from regulations under TSCA..

CERCLA (Comprehensive Environmental Response, Compensation, and Liability Act:
This product contains no components subject to reporting or notification requirements.

SARA Title III (Superfund Amendments and Reauthorization Act):
311/312 Hazard Categories: Immediate Health, Chronic Health
313 Reportable Ingredients: None

WHMIS (Workplace Hazardous Materials Information System - Canada):
Not Regulated (Product is regulated by the Food and Drugs Act)

SECTION 16: OTHER INFORMATION

Revision Summary: MSDS revised June 14, 2001 (Supercedes January 25, 1993)

The preceding information is based on available data and is believed to be correct. However, no warranty is expressed or to be implied regarding the accuracy of this information, the results to be obtained from the use thereof or the hazards connected with the use of the material. Since the information contained herein may be applied under conditions beyond our control and with which we may be unfamiliar, Allergan does not assume any responsibility for the results of its use. This information is furnished upon the condition that the persons receiving it shall make their own determinations of the effects, properties, and protections which pertain to their particular conditions.