

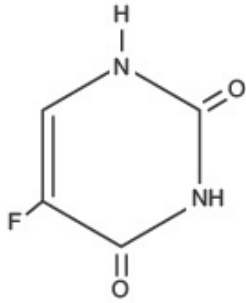
FLUOROPLEX- fluorouracil cream
Aqua Pharmaceuticals, LLC

FLUOROPLEX (fluorouracil) 1% Topical Cream

DESCRIPTION

FLUOROPLEX[®] (fluorouracil) 1% Topical Cream is an antineoplastic/antimetabolite product for dermatological use. Fluorouracil has the empirical formula C₄H₃FN₂O₂ and a molecular weight of 130.08. It is sparingly soluble in water and slightly soluble in alcohol. The pH is approximately 8.5.

Structural Formula:



Fluorouracil

Chemical Name:

2,4(1H,3H)-Pyrimidinedione, 5-fluoro-

FLUOROPLEX[®] 1% Topical Cream contains:

Active Ingredient: fluorouracil 1.0%

Inactive Ingredients: benzyl alcohol, emulsifying wax, isopropyl myristate, mineral oil, purified water, and sodium hydroxide.

CLINICAL PHARMACOLOGY

There is evidence that fluorouracil (or its metabolites) blocks the methylation reaction of deoxyuridylic acid to thymidylic acid. In this fashion, fluorouracil interferes with the synthesis of deoxyribonucleic acid (DNA) and to a lesser extent inhibits the formation of ribonucleic acid (RNA).

INDICATIONS AND USAGE

FLUOROPLEX[®] Cream is indicated for the topical treatment of multiple actinic (solar) keratoses.

CONTRAINDICATIONS

Fluorouracil is contraindicated in women who are or may become pregnant.

This product should not be used by patients who are allergic to any of its components.

WARNINGS

There exists the potential for a delayed hypersensitivity reaction to fluorouracil. Patch testing to prove hypersensitivity may be inconclusive¹.

If an occlusive dressing is used, there may be an increase in the incidence of inflammatory reactions in the adjacent normal skin.

The patient should avoid prolonged exposure to sunlight or other forms of ultraviolet irradiation during treatment with FLUOROPLEX[®] Cream, as the intensity of the reaction may be increased.

PRECAUTIONS

General: There is a possibility of increased absorption through ulcerated or inflamed skin.

Information for patients: The medication should be applied with care near the eyes, nose, and mouth. Excessive reaction in these areas may occur due to irritation from accumulation of drug. FLUOROPLEX[®] Cream is applied with the fingers, and the hands should be washed immediately afterward. The reaction to FLUOROPLEX[®] Cream in treated areas may be unsightly during therapy, and, in some cases, for several weeks following cessation of therapy.

Laboratory Tests: To rule out the presence of a frank neoplasm, a biopsy should be made of those areas failing to respond to treatment or recurring after treatment.

Carcinogenesis, mutagenesis, impairment of fertility: Adequate long-term studies in animals to evaluate carcinogenic potential have not been conducted with fluorouracil. 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.

Pregnancy: Teratogenic Effects: Pregnancy Category X: 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. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

Nursing mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, and because there is some systemic absorption of fluorouracil after topical administration (see **PRECAUTIONS: General**), mothers should not nurse their infants while receiving this drug.

Pediatric use: Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

Pain, pruritus, burning, irritation, inflammation, allergic contact dermatitis and telangiectasia have been reported. Occasionally, hyperpigmentation and scarring have also been reported.

OVERDOSAGE

Ordinarily, overdosage will not cause acute problems. If FLUOROPLEX[®] Cream accidentally comes in contact with the eye(s), flush the eyes(s) with water or normal saline. If FLUOROPLEX[®] Cream is accidentally ingested, induce emesis and gastric lavage. Administer symptomatic and supportive care as needed.

DOSAGE AND ADMINISTRATION

The patient should be instructed to apply sufficient medication to cover the entire face or other affected areas.

Apply medication twice daily with fingertips and wash hands afterwards. A treatment period of 2-6 weeks is usually required.

Increasing the frequency of application and a longer period of administration with FLUOROPLEX[®] Cream may be required on areas other than the head and neck.

When FLUOROPLEX® Cream is applied to keratotic skin, a response occurs with the following sequence: erythema, usually followed by scaling, tenderness, erosion, ulceration, necrosis and re-epithelization. When the inflammatory reaction reaches the erosion, ulceration and necrosis stages, the use of the drug should be terminated. Responses may sometimes occur in areas which appear clinically normal. These may be sites of subclinical actinic (solar) keratosis which the medication is affecting.

HOW SUPPLIED

FLUOROPLEX® (fluorouracil) 1% Topical Cream is available in 30 g tubes (NDC 16110-812-30)

NOTE: Avoid freezing. Store at 15° - 30°C (59° - 86°F) in tight containers.

Rx Only

REFERENCE

1. Epstein E. Testing for 5-fluorouracil allergy: patch and intradermal tests. Contact Dermatitis 1984; 10:311.

Revised March 2012

Manufactured for:

Aqua Pharmaceuticals

West Chester, PA 19380, U.S.A.

By:

Contract Pharmaceuticals Limited

Mississauga

Ontario, Canada

L5N 6L6

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Printed in U.S.A.

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Patient Information FLUOROPLEX® (FLOOR-oh-plex) (fluorouracil) 1% Topical Cream
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Important: FLUOROPLEX Cream is for use on skin only (topical). Apply with care near the eyes, nose and mouth.

What is FLUOROPLEX Cream?

FLUOROPLEX Cream is a prescription medicine used on the skin to treat multiple actinic (solar) keratosis. It is not known if FLUOROPLEX Cream is safe and effective in children.

Who should not use FLUOROPLEX Cream?

Do not use FLUOROPLEX Cream if:

- you are pregnant or may become pregnant. FLUOROPLEX Cream may harm your unborn baby. Stop using FLUOROPLEX Cream and tell your healthcare provider right away if you become pregnant while using FLUOROPLEX Cream.
- you are allergic to any of the ingredients in FLUOROPLEX Cream. See the end of this leaflet for a list of ingredients in FLUOROPLEX Cream.

Before using FLUOROPLEX Cream, tell your healthcare provider about all of your medical conditions, including if you:

- are breastfeeding or plan to breastfeed. It is not known if FLUOROPLEX Cream passes into your breast milk. You should not breastfeed during treatment with FLUOROPLEX Cream.

How should I use FLUOROPLEX® Topical Cream?

- Use FLUOROPLEX Cream exactly as your healthcare provider tells you. Your healthcare provider will tell you where to apply FLUOROPLEX Cream, how often and how long to apply it.
- FLUOROPLEX Cream is usually applied 2 times a day for 2 to 6 weeks.

- Use your fingertips to apply enough FLUOROPLEX Cream to cover the areas to be treated on your face or other affected areas, as instructed by your healthcare provider.
- Skin reactions are expected when you use FLUOROPLEX Cream. These skin reactions begin with redness, usually followed by dryness or tenderness and crusting of your skin. Before you see any healing of your skin, these skin reactions continue to progress. Stop using FLUOROPLEX Cream when you see raw areas (erosion and ulcers) and shedding of dead skin (sloughing). Be sure to follow your healthcare provider's instructions about when to stop using FLUOROPLEX Cream.
- If your skin reaction bothers you or is severe, or if you are not sure what to do, call your healthcare provider for instructions.
- Avoid letting FLUOROPLEX Cream build up in the skin folds around your eyes, nose or mouth.
- Wash your hands right away after you apply FLUOROPLEX Cream. If you accidentally get FLUOROPLEX Cream in your eyes, flush your eyes with water or normal saline.

What should I avoid while using FLUOROPLEX Cream?

- Avoid covering the treated areas with an airtight dressing, unless your healthcare provider tells you to.
- Avoid sunlight and ultraviolet lights, such as sun lamps and tanning machines. FLUOROPLEX Cream can make your skin sensitive to light. You could get a severe sunburn.

What are the possible side effects of FLUOROPLEX Cream?

- Skin reactions including possible allergic reactions (allergic contact dermatitis). You may get skin reactions such as:
 - pain
 - itching
 - burning
 - irritation
 - redness and swelling
 - small blood vessels that can be seen under the skin
 - darkening of the skin
 - scarring

Tell your healthcare provider if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of FLUOROPLEX Cream. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store FLUOROPLEX Cream?

- Do not freeze FLUOROPLEX Cream.
- Store FLUOROPLEX Cream between 59°F to 86°F (15°C to 30°C) in tight containers.

Keep FLUOROPLEX Cream and all medicines out of the reach of children.

General Information about the safe and effective use of FLUOROPLEX Cream.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use FLUOROPLEX Cream for a condition for which it was not prescribed. Do not give FLUOROPLEX Cream to other people, even if they have the same symptoms you have. It may harm them. You can ask your pharmacist or healthcare provider for information about FLUOROPLEX Cream that is written for the health professionals.

What are the ingredients in FLUOROPLEX Cream?

Active ingredient: fluorouracil

Inactive ingredients: benzyl alcohol, emulsifying wax, isopropyl myristate, mineral oil, purified water, and sodium hydroxide

® Marks owned by Aqua Pharmaceuticals

Manufactured by: Aqua Pharmaceuticals, an Almirall Company, Exton, PA 19341 U.S.A.

Made in Germany

For more information, call 1-866-665-2782.

This Patient Information has been approved by the U.S. Food and Drug Administration

Issued: July 2016

PRINCIPAL DISPLAY PANEL - 30 g Tube Label

NDC 16110-812-30

30 grams

Fluoroplex®

(fluorouracil) 1%
Topical Cream

RX ONLY

CONTAINS:

Active: fluorouracil 1.0%

Inactives: benzyl alcohol; emulsifying wax; mineral oil; isopropyl myristate; sodium hydroxide; and purified water.

DOSAGE: Refer to accompanying literature for complete prescribing information.

Avoid freezing.

Store at 15° - 30°C (59° - 86°F).

SEE CRIMP FOR LOT NO. AND EXPIRATION DATE

Manufactured by: Almirall Hermal GmbH, 21465 Reinbek, Germany

Distributed by: Aqua Pharmaceuticals, an Almirall Company Exton, PA 19341, U.S.A.

Fluoroplex is a registered trademark of Aqua Pharmaceuticals, LLC

AQUA PHARMACEUTICALS



PRINCIPAL DISPLAY PANEL - 30 g Carton Label

NDC 16110-812-30

30 grams

Fluoroplex[®]

(fluorouracil) 1%
Topical Cream

Contains:

Active: fluorouracil 1.0%

Inactives: benzyl alcohol; emulsifying wax; mineral oil; isopropyl myristate; sodium hydroxide; and purified water.

Rx Only

Dosage: Refer to accompanying literature for complete prescribing information.

Avoid freezing.

Store at 15° - 30°C (59° - 86°F).

Manufactured by: Almirall Hermal GmbH, 21465 Reinbek, Germany

Distributed by: Aqua Pharmaceuticals, an Almirall Company Exton, PA 19341, U.S.A.

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AQUA PHARMACEUTICALS

an Almirall company



FLUOROPLEX

fluorouracil cream

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:16 110 -8 12
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
FLUOROURACIL (UNII: U3P01618RT) (FLUOROURACIL - UNII:U3P01618RT)	FLUOROURACIL	10 mg in 1 g

Inactive Ingredients

Ingredient Name	Strength
BENZYL ALCOHOL (UNII: LKG8494WBH)	
ISOPROPYL MYRISTATE (UNII: 0RE8K4LNJS)	
MINERAL OIL (UNII: T5L8T28FGP)	
WATER (UNII: 059QF0K00R)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:16 110-8 12-30	1 in 1 CARTON	12/03/1993	
1		30 g in 1 TUBE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA016988	12/03/1993	

Labeler - Aqua Pharmaceuticals, LLC (605425912)**Establishment**

Name	Address	ID/FEI	Business Operations
Almirall Hermal GmbH		312540746	ANALYSIS(16 110-8 12) , MANUFACTURE(16 110-8 12)

Establishment

Name	Address	ID/FEI	Business Operations
Contract Pharmaceuticals Limited Canada		248761249	MANUFACTURE(16 110-8 12)

Revised: 7/2017

Aqua Pharmaceuticals, LLC