AUSTRALIAN PRODUCT INFORMATION

FLUOROURACIL VIATRIS

Fluorouracil cream

1 NAME OF THE MEDICINE

Fluorouracil

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains fluorouracil 5% w/w as the active ingredient.

Excipients with known effect: hydroxybenzoates.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

Cream

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Solar and senile keratoses, Bowen's disease.

4.2 DOSE AND METHOD OF ADMINISTRATION

FLUOROURACIL VIATRIS should only be used under medical supervision.

FLUOROURACIL VIATRIS is well tolerated. The healthy skin surrounding the area being treated may occasionally become reddened, but soon resumes its normal colour on cessation of treatment.

In cases of senile and solar keratoses a thin layer of the cream is applied to the affected areas once or twice daily, generally without a dressing. In the treatment of other conditions (including keratosis palmaris) a fresh occlusive dressing should be applied daily. Treatment should be continued up to the erosion stage. Duration of therapy is usually 3-4 weeks, but it may prove necessary to exceed this on occasion. When FLUOROURACIL VIATRIS is applied to the skin, the following usually happens: a redness of the affected area (generally within 3 to 5 days) followed by blistering, peeling, and cracking (within 11 to 14 days) with occasional open sores and some discomfort. Although the skin seems to be worse, it is a sign that the medication is working. The treated skin will flake away. Some redness of the skin will continue for some time after the drug is stopped.

Limitation of Treatment Area

The total area of skin being treated with FLUOROURACIL VIATRIS at any time should not exceed 500 sq cm (approx. 23 x 23 cm). Larger areas should be treated a section at a time.

4.3 CONTRAINDICATIONS

Fluorouracil is contraindicated in women who are or may become pregnant during therapy (see Section 4.6 FERTILITY, PREGNANCY AND LACTATION).

Known hypersensitivity to fluorouracil or any of its excipients.

Fluorouracil should not be used in patients with dihydropyrimidine dehydrogenase (DPD) enzyme deficiency. A large percentage of fluorouracil is catabolised by the enzyme dihydropyrimidine dehydrogenase. DPD enzyme deficiency can result in shunting of fluorouracil to the anabolic pathway, leading to cytotoxic activity and potential toxicities.

Rarely, life-threatening toxicities such as stomatitis, diarrhoea, neutropenia, and neurotoxicity have been reported with intravenous administration of fluorouracil in patients with DPD enzyme deficiency.

A case of life-threatening systemic toxicity has been reported with the topical use of fluorouracil 5% in a patient with DPD enzyme deficiency. Symptoms included severe abdominal pain, bloody diarrhoea, vomiting, fever, and chills. Physical examination revealed stomatitis, erythematous skin rash, neutropenia, thrombocytopenia, inflammation of the oesophagus, stomach, and small bowel. Although this case was observed with 5% fluorouracil cream, it is unknown whether patients with profound DPD enzyme deficiency would develop systemic toxicity with lower concentrations of topically applied fluorouracil.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

The normal pattern of response includes: early and severe inflammatory phases (typically characterised by erythema, which may become intense and blotchy), a necrotic phase (characterised by skin erosion) and finally healing (when epithelialisation occurs). The clinical manifestation of response usually occurs in the second week of fluorouracil treatment. However, these treatment effects sometimes are more severe and include pain, blistering and ulceration.

Fluorouracil is highly irritant, and so should not be allowed to come in contact with mucous membranes (eyes, nose or mouth) due to the possibility of irritation, local inflammation and ulceration. There is a possibility of increased absorption through ulcerated or inflamed skin.

Treatment of perioral area or nasolabial fold should be avoided, or treated carefully. Because of its irritant nature, care should be taken to ensure that fluorouracil does not come into contact with normal skin. Fluorouracil should be applied with a non-metal applicator or rubber glove. Should a glove not be worn and the hands come in contact with fluorouracil during application they should be washed thoroughly after applying fluorouracil.

Exposure to UV-radiation, (e.g. natural sunlight or tanning salon) should be avoided. Fluorouracil therapy is not advisable in persons who work outdoors for prolonged periods in the sun. Excessive sun exposure may produce a diffuse phototoxic response in the areas of application; therefore exposure should be minimised during and immediately following treatment with fluorouracil because the intensity of the reaction may be increased.

While treatment is in progress, avoid cosmetics on treated areas and other topical medication applied to the same area, unless otherwise directed.

Occlusion of the skin with resultant hydration has been shown to increase percutaneous penetration of several topical preparations. If any occlusive dressing is to be used, there may be an increase in the severity of inflammatory reactions in the adjacent normal skin. A porous gauze dressing may be applied for cosmetic reasons without increase in reaction.

The excipients stearyl alcohol and propylene glycol may cause local skin irritations (e.g. contact dermatitis); the excipients methyl hydroxybenzoate and propyl hydroxybenzoate may cause allergic reactions (possibly delayed).

Information for patients: Fluorouracil may be fatal if ingested by pets. Avoid allowing pets to contact the FLUOROURACIL VIATRIS container or the skin where FLUOROURACIL VIATRIS has been applied. Store FLUOROURACIL VIATRIS out of reach of pets. Safely discard or clean any cloth or applicator that may retain FLUOROURACIL VIATRIS and avoid leaving any residues of FLUOROURACIL VIATRIS on your hands, clothing, carpeting or furniture.

Use in the Elderly

No data available.

Paediatric Use

Safety and effectiveness in children have not been established.

Effects on Laboratory Tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Although no significant medicine interactions with fluorouracil have been reported, potential medicine interactions are possible, caution should be taken with medicines that may have an effect on the DPD enzyme.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on Fertility

No data available.

Use in Pregnancy – Pregnancy Category D

Category D. Drugs which have caused, are suspected to have caused, or may be expected to cause, an increased incidence of human fetal malformations or irreversible damage. These drugs may also have adverse pharmacological effects. Accompanying texts should be consulted for further details.

Studies in animals have shown that fluorouracil is teratogenic. The potential risk for humans is unknown, hence fluorouracil is contraindicated in pregnancy or where pregnancy cannot be excluded (see Section 4.3 CONTRAINDICATIONS).

Use in Lactation

It is not known whether fluorouracil is excreted in human milk. Because there is some systemic absorption of fluorouracil after topical administration, because many medicines are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants, fluorouracil use should be avoided in nursing mothers.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The most frequently encountered reactions are often related to an extension of the pharmacological activity of the medicine. These include pain, pruritus, hyperpigmentation, burning, crusting, allergic contact dermatitis, erosions, erythema, hyperpigmentation, irritation, photosensitivity, scarring, rash, soreness and ulceration at the site of application. Leukocytosis is the most frequent haematological adverse effect.

Application site haemorrhage has also been reported (frequency unknown).

The patient should be advised of the temporary unsightly appearance and local discomfort to be expected during treatment with this drug (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE). Patients with chloasma and rosacea and other inflammatory dermatoses may encounter accentuation of their condition and should first be treated with appropriate therapy before using the medication. While absorption of fluorouracil through healthy skin is negligible, absorption is considerably increased when it is applied to diseased skin.

Although a causal relationship is remote, other adverse reactions which have been reported infrequently are:

Nervous System Disorders: Dizziness, emotional upset, insomnia, irritability, headache.

Gastrointestinal Disorders: Nausea.

Skin and Subcutaneous Tissue Disorders: Alopecia, blistering, bullous pemphigoid, discomfort, ichthyosis, scaling, suppuration, swelling, telangiectasia, tenderness, urticarial, skin rash.

Special Senses: Conjunctival reaction, corneal reaction, lacrimation, nasal irritation.

Miscellaneous: Herpes simplex.

Reporting Suspected Adverse Effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

If fluorouracil is accidentally ingested, signs of fluorouracil overdosage may include nausea, vomiting and diarrhoea. Stomatitis and blood dyscrasias may occur in severe cases. Appropriate measures should be taken for the prevention of systemic infection and daily white cell counts should be performed.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of Action

When the preparation is applied to keratotic and preneoplastic lesions it produces the following pattern of response: first erythema, then, usually, vesiculation, erosion, ulceration, necrosis and epithelialisation.

Clinical Trials

A study was performed to prove the therapeutic equivalence of the test product; Fluoruracil AMEDA (fluorouracil 5% cream) and the reference product; Efudex (fluorouracil 5% Cream) which is sold in USA and has been shown to be equivalent to the Australian fluorouracil 5% cream (Efudix). The study type was a randomised, double-blind, placebo-controlled, three-arm parallel assignment, multicentre therapeutic equivalence study with clinical endpoints. The primary objectives were to demonstrate therapeutic equivalence between the afore-mentioned products and to demonstrate superiority over vehicle (placebo) when treating multiple actinic or solar keratosis lesions (AKs) in an adult population. The secondary objective was to compare the adverse event profile of the test and reference products.

A total of 278 adults (mITT population) that had between 5 and 10 clinically typical, visible, discrete, non-hyperkeratotic, non-hypertrophic AK lesions of at least 4 mm on the face and/or bald scalp were assigned to the test, reference or placebo treatment. Subjects were instructed to apply a thin layer of the product to the treatment area on the face and/or bald scalp twice daily (morning and evening) for 2 weeks. 28 days after the treatment ended, final assessment occurred to review the primary efficacy endpoint: the proportion of subjects with 100% clearance of all AK lesions in the treatment area (i.e., complete cure). The results for the test and reference product were 39.1% and 37.2% respectively for the mITT population and 39.2% and 37.8%

respectively in the PP population. The difference in proportion between products was 1.5% with an associated adjusted 90% CI of -10.9% to 13.8%, which is well within the equivalence limits of -20% to 20%.

Both the test and reference products were shown to be superior to placebo, and the safety profile of the test product was not clinically different to that of the reference product, with both treatments well tolerated by subjects.

5.2 PHARMACOKINETIC PROPERTIES

No data available.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Methyl hydroxybenzoate, polysorbate 60, propylene glycol, propyl hydroxybenzoate, purified water, stearyl alcohol and white soft paraffin.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C. Protect from heat.

6.5 NATURE AND CONTENTS OF CONTAINER

Tube, aluminium, 20 g.
Pack size: 1 tube per carton.

Australian Register of Therapeutic Goods (ARTG)

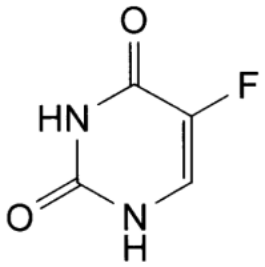
AUST R 384710 – FLUOROURACIL VIATRIS fluorouracil 5%w/w cream tube

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking it to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical Structure



CAS Number

51-21-8

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 (Prescription Only Medicine)

8 SPONSOR

Accord Healthcare

Level 24, 570 Bourke Street

Melbourne VIC 3000

Australia

Phone: 1800 134 988

9 DATE OF FIRST APPROVAL

23/05/2023

10 DATE OF REVISION

9/10/2025

Summary Table of Changes

Section Changed	Summary of New Information
All	New PI

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