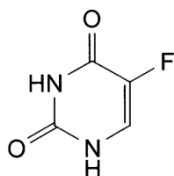


PRODUCT INFORMATION

EFUDIX®

NAME OF THE MEDICINE

Fluorouracil



CAS number: 51-21-8

DESCRIPTION

Efudix is a homogenous, opaque, white cream containing fluorouracil 5% w/w. Efudix also contains the excipients methyl hydroxybenzoate, soft white paraffin, polysorbate 60, propyl hydroxybenzoate, propylene glycol, stearyl alcohol and water – purified.

PHARMACOLOGY

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.

INDICATIONS

Solar and senile keratoses, Bowen's disease.

CONTRAINDICATIONS

Efudix is contraindicated in women who are or may become pregnant during therapy (see *Use in Pregnancy*).

Efudix 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.

Known hypersensitivity to fluorouracil or any of its excipients.

PRECAUTIONS

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 Efudix treatment. However, these treatment effects sometimes are more severe and include pain, blistering and ulceration.

Efudix 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 Efudix does not come into contact with normal skin. Efudix should be applied with a non-metal applicator or rubber glove. Should a glove not be worn and the hands come in contact with Efudix during application they should be washed thoroughly after applying Efudix.

Exposure to UV-radiation, (e.g. natural sunlight or tanning salon) should be avoided. Efudix 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 Efudix 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).

Use in Pregnancy

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 Efudix is contraindicated in pregnancy or where pregnancy cannot be excluded (see **Contraindications**).

Use in Lactation

It is not known whether Efudix 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, Efudix use should be avoided in nursing mothers.

Paediatric use

Safety and effectiveness in children have not been established.

INTERACTIONS WITH OTHER MEDICINES

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

ADVERSE 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.

The patient should be advised of the temporary unsightly appearance and local discomfort to be expected during treatment with this drug (see **Precautions**). 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 Efudix 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.

DOSAGE AND ADMINISTRATION

Efudix should only be used under medical supervision.

Efudix 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 Efudix 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 Efudix at any time should not exceed 500 sq cm (approx. 23 x 23 cm). Larger areas should be treated a section at a time.

OVERDOSAGE

Contact the Poisons Information Centre on 13 11 26 for advice on the management of overdosage.

If Efudix 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.

PRESENTATION AND STORAGE CONDITIONS

Fluorouracil 5% w/w cream: 20 g aluminium tube.
Store below 30°C. Protect from heat.

NAME AND ADDRESS OF THE SPONSOR

iNova Pharmaceuticals (Australia) Pty Ltd
Level 10, 12 Help Street,
Chatswood, NSW 2067

POISON SCHEDULE OF THE MEDICINE

Prescription Only Medicine

**DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS
(THE ARTG)**

23 August 1991

DATE OF MOST RECENT AMENDMENT

14 June 2016

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