

EFUDIX

Fluorouracil

Presentation

Cream, 5% w/w; white, opaque.

Uses

Actions

EFUDIX is a competitive antagonist for uracil in the formation of RNA and inhibits the incorporation of uracil into RNA. DNA may be inhibited indirectly because of its dependence for synthesis on RNA.

When applied topically to keratoses and preneoplastic skin lesions, EFUDIX produced the following pattern of response: erythema, usually followed by scaling, tenderness, erosion, ulceration, necrosis and re-epithelialisation. Responses may sometimes occur in areas which appear clinically normal. These may be sites of subclinical actinic (solar) keratoses which the medication is affecting.

Pharmacokinetics

Little is absorbed when EFUDIX is applied to healthy skin but up to 20% of a dose applied to diseased skin may be excreted in the urine over 24 hours. It is also absorbed to a small extent through serous membranes. EFUDIX is converted to active nucleotide metabolites within the target cells. EFUDIX is excreted unchanged in the urine, or inactivated in the liver or excreted as respiratory carbon dioxide (with the production of urea).

Indications

EFUDIX is used for the topical treatment of superficial pre-malignant and malignant skin lesions; keratoses including senile, actinic and arsenical forms; keratoacanthoma; Bowen's disease; superficial basal-cell carcinoma. Deep, penetrating or nodular basal cell and squamous cell carcinomas do not usually respond to EFUDIX therapy. It should be used only as a palliative therapy in such cases where no other form of treatment is possible.

Dosage and Administration

EFUDIX cream is for topical application and should not be diluted.

Pre-malignant Conditions

The cream should be applied thinly to the affected area once or twice daily; an occlusive dressing is not essential.

Malignant Conditions

The cream should be applied once or twice daily under an occlusive dressing where this is practicable.

The cream should not harm healthy skin. Treatment should be continued until there is marked inflammatory response from the treated area, preferably with some erosion in the case of pre-malignant conditions. Severe discomfort may be alleviated by the use of topical steroid cream. The usual duration of treatment for an initial course of therapy is three to four weeks, but this may be prolonged. Lesions on the face usually respond more quickly than those on the trunk or lower limbs whilst lesions on the hands and forearms respond more slowly.

Healing may not be complete until one or two months after therapy is stopped.

Limitation of Treatment Area

The total area of skin being treated with EFUDIX cream at any time should not exceed 500 square centimeters. Larger areas should be treated a section at a time.

Elderly: Many of the conditions for which EFUDIX is indicated are common in the elderly. No special precautions are necessary.

Children: EFUDIX is not recommended for use on children.

Contraindications

EFUDIX is contraindicated in patients with known hypersensitivity to EFUDIX or parabens or any of the other excipients.

Use in Pregnancy: EFUDIX has been shown to be teratogenic. EFUDIX should not normally be administered to patients who are pregnant. It should also be regarded as contraindicated in mothers who are breast-feeding.

DPD Enzyme Deficiency

EFUDIX should not be used in patients with dihydropyrimidine dehydrogenase (DPD) enzyme deficiency. A large percentage of fluorouracil is catabolized by the enzyme dihydropyrimidine dehydrogenase (DPD). 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 esophagus, 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.

Warnings and Precautions

Hypersensitivity reactions may occur in susceptible individuals.

Use of Occlusive Dressing

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

Prolonged Exposure to Sunlight

EFUDIX therapy is not advisable in persons who work outdoors for prolonged periods in the sun. Excessive exposure to sunlight or other forms of UV irradiation during treatment may produce a diffuse phototoxic response in the areas of application.

Irritant Nature

EFUDIX is highly irritant and so should not be allowed to come in contact with mucous membranes, the eyes or normal skin. The perioral area or nasolabial fold should be avoided or treated carefully.

Excessive reaction in these areas may occur due to irritation from accumulation of medicine. The preparations should preferably be applied with a nonmetal spatula, cotton bud or suitable glove. The hands should be carefully washed immediately after each application.

Unightly Appearance

The patient should be advised of the temporary unightly appearance and local discomfort to be expected during treatment and, in some cases, for several weeks after cessation of therapy.

Presence of Frank Neoplasm

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

Patients with Chloasma, Rosacea and Other Inflammatory Dermatoses

These patients may encounter accentuation of their condition and should first be treated with appropriate therapy before using the medication.

Adverse Effects

EFUDIX is generally well tolerated, though pain, pruritus, burning, irritation, inflammation and hyperpigmentation have been noted at the site of application. Less common effects are scarring, soreness, tenderness, allergic contact dermatitis, photosensitivity, suppuration, scaling and swelling reactions.

These side effects on healthy skin surrounding the area being treated are usually transient. Pre-existing subclinical lesions may become apparent.

Exposure to sunlight may increase the intensity of the reaction.

Interactions

Not known.

Overdosage

If EFUDIX is accidentally ingested, signs of fluorouracil overdosage may include nausea, vomiting and diarrhea. 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.

Pharmaceutical Precautions

Storage: EFUDIX cream should be stored at or below 30°C.

Medicine Classification

Prescription Medicine.

Package Quantities

Cream, 5%, 20g.

Further Information

Excipients: EFUDIX contains methyl and propyl parahydroxybenzoate, propylene glycol, polysorbate, stearyl alcohol.

Trademark: EFUDIX is a trademark.

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