PRESCRIBING INFORMATION

EFUDIX® | FLUOROURACIL 5% CREAM

(fluorouracil)

Please refer to Summary of Product Characteristics (SmPC) before prescribing.

Indications:

Fluorouracil 5% cream 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 fluorouracil 5% cream therapy. It should be used only as a palliative therapy in such cases where no other form of treatment is possible.

Presentation:

This medicine is a white, opaque cream containing 5% w/w fluorouracil.

Dosage and administration:

Adults: Fluorouracil 5% cream is for topical application.

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 a marked inflammatory response from the treated area, preferably with some erosion in the case of pre-malignant conditions. 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.

Elderly: No special precautions are necessary.

Paediatric population: Fluorouracil 5% cream is not recommended for use in children.

Method of application:

The hands should be washed carefully after applying this medicine. Also, care should be taken to avoid contact with mucous membranes or the eyes when applying the cream.

The total area of skin being treated with this medicine at any one time should not exceed 500 cm^2 (approx 23 x 23 cm). Larger areas should be treated a section at a time.

Contraindications:

Hypersensitivity to any of the ingredients including parabens. Co-administration with antiviral nucleoside drugs (e.g. brivudine and analogues). Pregnancy, breast-feeding.

Warning and 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 fluorouracil 5% cream treatment. However, these treatment effects can sometimes be more severe and include pain, blistering and ulceration. Occlusive dressing may increase inflammatory reactions of the skin.

Instruct patients not to smoke or go near naked flames - risk of severe burns. Fabric (clothing, bedding, dressings etc) that has been in contact with this product burns more easily and is a serious fire hazard. Washing clothing and bedding may reduce product build-up but not totally remove it.

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

Pre-existing subclinical lesions may become apparent following fluorouracil 5% cream use.

Any severe skin discomfort during treatment with fluorouracil 5% cream may be alleviated by the use of an appropriate topical steroid cream.

When used according to the approved prescribing information this medicine should have minimal effect on healthy skin.

Significant systemic drug toxicity is unlikely via percutaneous absorption of fluorouracil when this medicine is administered as per the approved prescribing information. However, the likelihood of this is increased if the product is used on skin areas in which the barrier function is impaired (e.g. cuts), if the product is applied under an occlusive dressing, and/or in individuals with deficiency in dihydropyrimidine dehydrogenase (DPD). DPD is a key enzyme involved in metabolising and eliminating fluorouracil. Determination of DPD activity may be considered where systemic drug toxicity is confirmed or suspected. There have been reports of increased toxicity in patients who have reduced activity of the enzyme dihydropyrimidine dehydrogenase. In the event of suspected systemic drug toxicity, fluorouracil 5% cream treatment should be stopped.

An interval of at least four weeks should elapse between treatment with brivudine, sorivudine or analogues and subsequent administration of fluorouracil 5% cream.
The excipients stearyl alcohol and propylene glycol may cause local skin irritations (e.g. contact dermatitis); the excipients methyl parahydroxybenzoate and propyl parahydroxybenzoate may cause allergic reactions (possibly delayed).

Interaction with other medicinal products:

Although no significant drug interactions with fluorouracil 5% cream have been reported, potential drug interactions are possible and indicated as follows.
Brivudine, sorivudine and analogues are potent inhibitors of DPD, a fluorouracil metabolising enzyme. For this reason, concomitant administration of these drugs with fluorouracil 5% cream is contraindicated.

Pregnancy and lactation:

Due to the genotoxic potential of fluorouracil, women of childbearing potential should use effective contraceptive measures while being treated with fluorouracil and for 6 months following completion of treatment.
Men are recommended to use effective contraceptive measures and to not father a child while receiving fluorouracil and for 3 months following completion of treatment.
There is no adequate data from the use of topical fluorouracil in pregnant women. Studies in animals have shown that fluorouracil is teratogenic. The potential risk for humans is unknown, hence fluorouracil 5% cream should not be used during pregnancy.
Women of childbearing potential should not become pregnant during topical fluorouracil therapy and should use an effective method of contraception during treatment with fluorouracil therapy. If a pregnancy occurs during treatment the patient should be advised about the risk for the child of adverse effects associated with the treatment and genetic counselling is recommended.
No information is available on the excretion of fluorouracil into breast milk. Studies in animals have shown the fluorouracil is teratogenic. A risk to the suckling child cannot be excluded, so fluorouracil 5% cream should not be used in nursing mothers. If use during breastfeeding is absolutely necessary, breastfeeding must be discontinued.
No clinical data in humans are available on the effects of topical fluorouracil on fertility. Experiments in various species revealed an impairment of the fertility and reproductive performance of systemic 5-fluorouracil (5-FU). The reduced systemic exposure to 5-FU following its topical administration will reduce the potential toxicity. The use of topical 5-fluorouracil may impair female and male fertility. Topical fluorouracil is not recommended in men attempting to father a child.

Effects on ability to drive and use machines:

It is unlikely that treatment will have any effect on the ability to drive and use machines when used according to the dosage instructions.

Undesirable effects:

Very rare: Hypersensitivity and allergic reactions; pruritus; urticaria; rash; erythemas including erythema multiforme; dermal and epidermal conditions; skin and subcutaneous skin ulcerations; dermatitis and eczema conditions; blisters and alopecia. Exposure to sunlight may increase the intensity of the reaction. Haematological disorders, diarrhoea haemorrhagic, diarrhoea, vomiting, abdominal pain, stomatitis, pyrexia, chills and mucosal inflammation.
Frequency not known: Dysgeusia, headache, dizziness, conjunctival irritation, keratitis, increased lacrimation, nausea, application site haemorrhage.
Adverse reactions associated with exacerbations of normal pattern of response which are related to pharmacological activity of fluorouracil on the skin are the most frequently reported reactions.
Allergic type skin reactions and reactions related to systemic drug toxicity are very rarely reported.
For complete information, consult the Summary of Product Characteristics.

Legal Category: POM **Marketing Authorisation Number**: PL 46302/0128
MAH: Mylan Products Limited, 20 Station Close, Potters Bar, Herts, EN6 1TL, UK.
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The SmPC for this product, including adverse reactions, precautions, contra-indications, and method of use can be found at:
http://www.mhra.gov.uk/Safetyinformation/Medicinesinformation/SPCandPILs/index.htm and from Viatris Medical Information, Building 4, Trident Place, Hatfield Business Park, Mosquito Way, Hatfield, Hertfordshire, AL10 9UL, phone no. 01707 853000, Email: info.uk@viatris.com

Please continue to report suspected adverse drug reactions with any medicine or vaccine to the MHRA through the Yellow Card Scheme. It is easiest and quickest to report adverse drug reactions online via the Yellow Card website: http://www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Alternatively, you can report via some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) or by calling the Commission on Human Medicines (CHM) free phone line: 0800-731-6789. Adverse reactions/events should also be reported to MAH at e-mail address: pv.uk@viatris.com.