Tretilone Cream

(Fluocinolone acetonide +
Hydroquinone + Tretinoin)

ٹریٹیلون کریم

(فلوسینولون ایسٹونائڈ +
ہائیڈروکینون + ٹریٹینائن)

COMPOSITION:

Each gram contains:

Fluocinolone acetonide 0.1mg
Hydroquinone 40mg
Tretinoin 0.5mg

(Innovator's specifications)

DESCRIPTION:

Tretilone cream contains fluocinolone acetonide, USP, hydroquinone, USP, and tretinoin, USP, in a hydrophilic cream base for topical application.

Fluocinolone acetonide is a synthetic fluorinated corticosteroid for topical dermatological use and is classified therapeutically as an anti-inflammatory. It is a white crystalline powder that is odorless and stable in light.

Hydroquinone is classified therapeutically as a depigmenting agent. It is prepared from the reduction of p-benzoquinone with sodium bisulfite. It occurs as fine white needles that darken on exposure to air.

Tretinoin is all-trans-retinoic acid formed from the oxidation of the aldehyde group of retinene to a carboxyl group. It occurs as yellow to light-orange crystals or crystalline powder with a characteristic odor of ensilage. It is highly reactive to light and moisture. Tretinoin is classified therapeutically as a keratolytic.

MECHANISM OF ACTION:

One of the components in Tretilone cream, hydroquinone, is a depigmenting agent, and may interrupt one or more steps in the tyrosine-tyrosinase pathway of melanin synthesis. However, the mechanism of action of the active ingredients in Tretilone cream in the treatment of melasma is unknown.

INDICATIONS:

Tretilone creamis indicated for the short-term treatment of moderate to severe melasma of the face, in the presence of measures for sun avoidance, including the use of sunscreens.

Limitations of Use:

Tretilone creamis NOT indicated for the maintenance treatment of melasma. After achieving control with it, some patients may be managed with other treatments instead of triple therapy with Tretilone cream. Melasma usually recurs upon discontinuation of Tretilone cream.The safety and efficacy Tretilone creamin patients of Fitzpatrick Skin Types V and VI have not been studied. Excessive bleaching resulting in undesirable cosmetic effect in patients with darker skin cannot be excluded.

The safety and efficacy of Tretilone cream in the treatment of hyperpigmentation conditions other than melasma of the face have not been studied.

Because pregnant and lactating women were excluded from, and women of childbearing potential had to use birth control measures in the clinical trials, the safety and efficacy of Tretilone cream in pregnant women and nursing mothers have not been established.

DOSAGE & ADMINISTRATION:

Apply a thin film of Tretilone cream to the affected area once daily, at least 30 minutes before bedtime. Gently wash the face and neck with a mild cleanser. Rinse and pat the skin dry.

Apply Tretilone cream to the hyperpigmented areas of melasma including about 1/2 inch of normal appearing skin surrounding each lesion.

Rub lightly and uniformly into the skin. Therapy should be discontinued when control is achieved. During the day, use a sunscreen of SPF 30, and wear protective clothing. Avoid sunlight exposure. Patients may use moisturizers and/or cosmetics during the day.

Tretilone cream is for topical use only. It is not for oral, ophthalmic, or intravaginal use.

PHARMACOKINETICS:

Percutaneous absorption of unchanged tretinoin, hydroquinone and fluocinolone acetonide into the systemic circulation of two groups of healthy volunteers (Total N=59) was found to be minimal following 8 weeks of daily application of 1g (Group I, n=45) or 6g (Group II, n=14) of Tretilone cream.

For tretinoin quantifiable plasma concentrations were obtained in 57.78% (26 out of 45) of Group I and 57.14% (8 out of 14) of Group II subjects. The exposure to tretinoin as reflected by the C_{max} values ranged from 2.01 to 5.34 ng/mL (Group I) and 2.0 to 4.99 ng/mL (Group II). Thus, daily application of Tretilone cream resulted in a minimal increase of normal endogenous levels of tretinoin. The circulating tretinoin levels represent only a portion of total tretinoin-associated retinoids, which would include metabolites of tretinoin and that sequestered into peripheral tissues.

For hydroquinone, quantifiable plasma concentrations were obtained in 18% (8 out of 44) Group I subjects. The exposure to hydroquinone, as reflected by the C_{max} values, ranged from 25.55 to 86.52 ng/mL. All Group II subjects (6g dose) had post-dose plasma hydroquinone concentrations below the quantitation limit. For fluocinolone acetonide, Groups I and II subjects had all post-dose plasma concentrations below quantitation limit.

WARNINGS &PRECAUTIONS:

Hypersensitivity

Tretilone cream contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening asthmatic episodes in susceptible individuals. If anaphylaxis, asthma or other clinically significant hypersensitivity reactions occur, institute appropriate therapy and discontinue Tretilone cream. Allergic contact dermatitis may also occur.

Exogenous Ochronosis

Tretilone cream contains hydroquinone, which may produce exogenous ochronosis, a gradual blue-black darkening of the skin, the occurrence of which should prompt discontinuation of therapy. The majority of patients developing this condition are Black, but it may also occur in Caucasians and Hispanics.

Effects on Endocrine System

Tretilone cream contains the corticosteroid fluocinolone acetonide. Systemic absorption of topical corticosteroids can produce reversible hypothalamic pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. Manifestations of Cushing's syndrome, hyperglycemia, and glucosuria can also be produced by systemic absorption of topical corticosteroid while on treatment. If HPA axis suppression is noted, the use of Tretilone cream should be discontinued. Recovery of HPA axis function generally occurs upon discontinuation of topical corticosteroids.

The ACTH or cosyntropin stimulation test may be helpful in evaluating patients for HPA axis suppression.

Cutaneous Reactions

Cutaneous hypersensitivity to the active ingredients of Tretilone cream has been reported in the literature. In a patch test study to determine sensitization potential in 221 healthy volunteers, three volunteers developed sensitivity reactions to Tretilone cream or its components. Tretilone cream contains hydroquinone and tretinoin that may cause mild to moderate irritation. Local irritation, such as skin reddening, peeling, mild burning sensation, dryness, and pruritus may be expected at the site of application. Transient skin reddening or mild burning sensation does not preclude treatment. If a reaction suggests hypersensitivity or chemical irritation, the use of the medication should be discontinued.

Information for Patients

Exposure to sunlight, sunlamp, or ultraviolet light should be avoided. Patients who are consistently exposed to sunlight or skin irritants either through their work environment or habits should exercise particular caution.

Sunscreen and protective covering (such as the use of a hat) over the treated areas should be used. Sunscreen use is an essential aspect of melasma therapy, as even minimal sunlight sustains melanocytic activity.

Weather extremes, such as heat or cold, may be irritating to patients treated with Tretilone cream. Because of the drying effect of this medication, a moisturizer may be applied to the face in the morning after washing.

Application of Tretilone cream should be kept away from the eyes, nose, or angles of the mouth, because the mucosa is much more sensitive than the skin to the irritant effect. If local irritation persists or becomes severe, application of the medication should be discontinued, and the health care provider consulted.

Allergic contact dermatitis, blistering, crusting, and severe burning or swelling of the skin and irritation of the mucous membranes of the eyes, nose, and mouth require medical attention. If the medication is applied excessively, marked redness, peeling, or discomfort may occur. This medication is to be used as directed by the health care provider and should not be used for any disorder other than that for which it is prescribed.

Laboratory Tests

The following tests may be helpful in evaluating patients for HPA axis suppression:

- ACTH or cosyntropin stimulation test
- A.M. plasma cortisol test
- Urinary free cortisol test

Pregnancy

Teratogenic Effects: Pregnancy Category C.

There are no adequate and well-controlled studies in pregnant women. Tretilone cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Tretilone cream contains the teratogen, tretinoin, which may cause embryo-fetal death, altered fetal growth, congenital malformations, and potential neurologic deficits.

Nursing Mothers

Corticosteroids, when systemically administered, appear in human milk. It is not known whether topical application of Tretilone cream could result in sufficient systemic absorption to produce detectable quantities of fluocinolone acetonide, hydroquinone, or tretinoin in human milk. Because many drugs are secreted in human milk, caution should be exercised when Tretilone cream is administered to a nursing woman. Care should be taken to avoid contact between the infant being nursed and Tretilone cream.

SIDE EFFECTS:

The following local adverse reactions have been reported infrequently with topical corticosteroids. They may occur more frequently with the use of occlusive dressings, especially with higher potency corticosteroids. These reactions are listed in an approximate decreasing order of occurrence: burning, itching, irritation, dryness, folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, skin atrophy, striae, and miliaria.

Tretilone cream contains hydroquinone, which may produce exogenous ochronosis, a gradual blue-black darkening of the skin, whose occurrence should prompt discontinuation of therapy. Cutaneous hypersensitivity to the active ingredients of Tretilone cream has been reported in the literature.

DRUG INTERACTIONS:

Patients should avoid medicated or abrasive soaps and cleansers, soaps and cosmetics with drying effects, products with high concentration of alcohol and astringent, and other irritants or keratolytic drugs while on Tretilone cream treatment. Patients are cautioned on concomitant use of medications that are known to be photosensitizing.

CONTRAINDICATIONS:

Tretilone cream is contraindicated in individuals with a history of hypersensitivity, allergy, or intolerance to this product or any of its components.

STORAGE & INSTRUCTIONS:

Do not store or transport above 25°C. Do not freeze. Protect from heat, sunlight and moisture. Keep away from the reach of the children.

To be sold on the prescription of a registered medical practitioner only.

FOR EXTERNAL USE ONLY.

HOW SUPPLIED:

Tretilone Cream: 15g

خوراک وطریقہ استعمال:

ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔

ہدایات:

دوا کو ۲۵ ڈگری سینٹی گریڈ درجہ حرارت سے زیادہ پر محفوظ اور منتقل نہ کریں۔
دھوپ، گرمی، نمی اور منجمد ہونے سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔
صرف مستند ڈاکٹر کے نسخے پر فروخت کریں۔ صرف بیرونی استعمال کے لئے ہے۔

Manufactured by:
PHARMASOL
PRIVATE LIMITED
Plot # 549,Sundar Industrial Estate,
Lahore, Pakistan.