LUMACIP PLUS Cream (Fluocinolone acetonide 0.01% + Hydroquinone 4% + Tretinoin 0.05%)

**Composition**

LUMACIP PLUS Cream
Each gram contains:
- Fluocinolone acetonide IP....................... 0.01% w/w
- Hydroquinone USP............................. 4% w/w
- Tretinoin Ph. Eur............................... 0.05% w/w

**Dosage Form**

Cream

**Description**

LUMACIP PLUS Cream contains fluocinolone acetonide, hydroquinone, and tretinoin, 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.

Hydroquinone is classified therapeutically as a depigmenting agent. It is prepared from the reduction of p-benzoquinone with sodium bisulphite.

Tretinoin is all-trans-retinoic acid, which is formed from the oxidation of the aldehyde group of retinene to a carboxyl group. Tretinoin is classified therapeutically as a keratolytic.

**Pharmacology**

**Pharmacodynamics**

Hydroquinone is a depigmenting agent. It is a hydroxylphenolic chemical and inhibits the conversion of 3,4-dihydroxyphenylalanine (DOPA) to melanin by inhibiting the tyrosinase enzyme. The other mechanisms proposed are as follows:

- Inhibition of DNA/RNA synthesis
- Degradation of melanosomes
- Destruction of melanocytes

Tretinoin accelerates desquamation, and removes pre-formed melanin. The role of retinoids is likely to be due to its promotion of keratinocyte proliferation and acceleration of epidermal turnover. Tretinoin induces dispersion of pigment granules inside the keratinocyte and accelerates the turnover of epidermal cells, facilitating the elimination of dispersed pigment.
Fluocinolone acetonide, a corticosteroid, inhibits the tyrosinase activity, affects the secretory function of melanocytes and has an anti-metabolic effect on the keratinocytes. Corticosteroids also inhibit the various mediators of inflammation and, hence, also inhibit the stimulatory impulses for melanocytes. However, the mechanism of action of the active ingredients in the triple combination cream (fluocinolone acetonide 0.01%, hydroquinone 4%, tretinoin 0.05%) in the treatment of melasma is unknown.

**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 6 g (Group II, n=14) of the triple combination cream (fluocinolone acetonide 0.01%, hydroquinone 4%, tretinoin 0.05%).

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 $C_{\text{max}}$ 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 the triple combination cream resulted in a minimal increase of the normal endogenous levels of tretinoin. The circulating tretinoin levels represent only a portion of the total tretinoin-associated retinoids, which would include metabolites of tretinoin and those that sequestered into the 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 $C_{\text{max}}$ values, ranged from 25.55 to 86.52 ng/mL. All Group II subjects (6 g dose) had post-dose plasma hydroquinone concentrations below the quantitation limit. For fluocinolone acetonide, all subjects in Groups I and II had post-dose plasma concentrations below the quantitation limit.

**Indications**

LUMACIP PLUS Cream is 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. LUMACIP PLUS Cream, is NOT indicated for the maintenance treatment of melasma. After achieving control with LUMACIP PLUS cream, some patients may be managed with other treatments. Melasma usually recurs upon discontinuation of LUMACIP PLUS cream.

**Dosage And Administration**

Apply a thin film of LUMACIP PLUS 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 a thin film of the cream to the hyperpigmented areas of melasma, including about half-inch of the normal-appearing skin surrounding each lesion. Rub lightly and uniformly into the skin.

Application of LUMACIP PLUS 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 cream’s 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. 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.
Contraindications

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

Warnings And Precautions

- **Hypersensitivity**

  LUMACIP PLUS 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 LUMACIP PLUS Cream. Allergic contact dermatitis may also occur.

- **Exogenous Ochronosis**

  LUMACIP PLUS 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**

  LUMACIP PLUS 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 LUMACIP PLUS 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 the triple combination cream (fluocinolone acetonide 0.01%, hydroquinone 4%, tretinoin 0.05%) 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 the cream or its components. LUMACIP PLUS 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. Patients should avoid medicated or abrasive soaps and cleansers, soaps and cosmetics with drying effects, products with high concentrations of alcohol and astringents, and other irritants or keratolytic drugs while on LUMACIP PLUS Cream treatment. Patients are cautioned on concomitant use of medications that are known to be photosensitizing.

- **Drug interactions**

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

- **Pregnancy**
Pregnancy Category C: Teratogenic Effects
LUMACIP PLUS Cream contains the teratogen, tretinoin, which may cause embryo-foetal death, altered foetal growth, congenital malformations and potential neurologic deficits. There are no adequate and well-controlled studies in pregnant women. The potential developmental effects of tretinoin are serious, but the risk from topical administration is small. Exposure during the period for organogenesis in the first trimester is, theoretically, more likely to produce adverse outcomes than in later pregnancy.
There are no adequate and well-controlled studies in pregnant women. LUMACIP PLUS Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Lactation
Corticosteroids, when systemically administered, appear in human milk. It is not known whether the topical application of LUMACIP PLUS 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 LUMACIP PLUS Cream is administered to a nursing mother. Care should be taken to avoid contact between the infant being nursed and LUMACIP PLUS Cream.

Paediatric use
Safety and effectiveness of LUMACIP PLUS Cream in paediatric patients have not been established.

Geriatric Use
Clinical studies of this triple combination cream (fluocinolone acetonide 0.01%, hydroquinone 4%, tretinoin 0.05%) did not include sufficient number of subjects aged 65 years and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function and of concomitant disease or other drug therapy.

Undesirable Effects
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.
In the controlled clinical trials, adverse events were monitored in 161 patients who used the triple combination cream (fluocinolone acetonide 0.01%, hydroquinone 4%, tretinoin 0.05%) once daily during an 8-week treatment period. There were 102 (63%) patients who experienced at least one treatment-related adverse event during these studies. The most frequently reported events were erythema, desquamation, burning, dryness and pruritus at the site of application. The majority of these events were mild-to-moderate in severity. From the controlled clinical studies, adverse events reported by at least 1% of patients and judged by the investigators to be reasonably related to treatment with the triple combination cream (fluocinolone acetonide 0.01%, hydroquinone 4%, tretinoin 0.05%) are summarized (in decreasing order of frequency) as follows:

<table>
<thead>
<tr>
<th>Incidence and Frequency of Treatment-related Adverse Events with the triple combination cream (fluocinolone acetonide 0.01%, hydroquinone 4%, tretinoin 0.05%) in at least 1% or more of Patients (N=161)</th>
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<tbody>
<tr>
<td><strong>Adverse Event</strong></td>
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<tr>
<td>Adverse Reaction</td>
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<td>Erythema</td>
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<td>Desquamation</td>
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<td>Burning</td>
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<td>Dryness</td>
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<td>Pruritus</td>
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<td>Acne</td>
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<td>Paraesthesia</td>
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<td>Telangiectasia</td>
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<td>Pigmentary changes</td>
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<td>Papules</td>
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<td>Acne-like rash</td>
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<td>Rosacea</td>
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<td>Dry mouth</td>
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<td>Rash</td>
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<td>Vesicles</td>
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In an open-label, long-term safety study, patients who had undergone cumulative treatment of melasma with the triple combination cream (fluocinolone acetonide 0.01%, hydroquinone 4%, tretinoin 0.05%) for 6 months showed a similar pattern of adverse events as in the 8-week studies. 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.

**Overdosage**

If the medication is applied excessively, marked redness, peeling or discomfort may occur.

**Storage And Handling Instructions**

Store below 25° C
Protect from light. Do not freeze
Packaging Information

LUMACIP PLUS Cream...............................Tube of 15g
Last updated: December 2011
Last reviewed: May 2016

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