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| **Approved** **Order of Ministry of Healthcare of Ukraine****01.08.2017 No. 887** **Registration certificate No. UA/0081/02/01****AMENDED****Order of Ministry of****Healthcare of Ukraine****02.12.2021 No. 2690** |

INSTRUCTION

**for medical use**

**PHORCAL®**

***Composition:***

*active substance:* calcitriol;

1 g of ointment contains 3 µg of calcitriol;

*excipients:* white soft paraffin, mineral oil light, alpha-Tocopherol.

**Pharmaceutical form.** Ointment.

*Basic physical and chemical properties:* white or almost white uniform ointment.

**Pharmacotherapeutic group.**

Antipsoriatic drugs for local use. АТС code D05A X03.

***Pharmacological properties.***

*Pharmacodynamics.*

Mechanism of action.

Calcitriol inhibits proliferation and stimulates keratinocyte differentiation.

Also calcitriol reduces adhesion and accelerates the exfoliation of horny cells. Calcitriol inhibits the proliferation of T-lymphocytes and normalizes the production of various factors of the inflammatory process.

*Pharmacokinetics.*

Absorption.

When applying locally, the absorption of calcitriol is approximately 10%.

After absorption, both calcitriol in unchanged form and its metabolites are detected in the blood plasma. The effect of metabolites on calcium homeostasis is insignificant. In most patients, circulating levels of exogenous calcitriol are below detection levels (2 μg/ml).

*Distribution.*

In clinical trials, there was no significant increase in plasma levels of calcitriol after treatment of a significant body surface area of up to 6000 cm2 (35% of the skin surface).

***Indications.***

Plaque psoriasis of mild and moderate severity (local treatment of skin manifestations) with lesion up to 35% of the skin surface.

***Contraindications.***

- Hypersensitivity to the active substance or to any of the drug components;

- hypercalcaemia and other pathological conditions characterized by calcium dysmetabolism;

- systemic therapy of calcium homeostasis;

- liver and kidney dysfunction.

***Drug interactions and other kinds of interactions.***

Synchronous usage of calcitriol with betamethasone has shown higher efficacy of this combination for local treatment of psoriasis than separate usage of these drugs.

Prescription of Phorcal® ointment in combination with UV irradiation has a faster therapeutic effect. Thiazide diuretics increase the risk of hypercalcaemia.

Caution should be exercised when using Phorcal® ointment synchronously with oral active metabolites of vitamin D (calcitriol, alfacalcidol), high doses of vitamin D and preparations of calcium because of possible potential action and increasing of risk of development of hypercalcaemia.

There is no experience of simultaneous use of calcitriol and other medications for the treatment of psoriasis.

Information on the interaction of systemic drugs after the use of an ointment with calcitriol is limited.

It is not recommended to apply Phorcal® ointment synchronously with salicylic acid and preparations containing salicylic acid.

As calcitriol ointment may cause light irritation, its synchronous use with peeling agents, astringent or irritating substances may increase the irritating effect.

***Special warnings and precautions for use.***

Ointment is recommended for use on the face with caution, since there is a risk of irritation in this area. Avoid getting ointment into the eyes. After applying the ointment on the affected area, wash your hands to avoid accidental use in uninfected areas. In case of accidental contact of the ointment with mucous membrane of the eyes, mouth or nose, wash it thoroughly with warm water. Daily application of the ointment should not exceed 35% of the skin surface. Do not apply more than 30 g of ointment per day, as a certain amount of calcitriol penetrates through the skin, and excessive use of the ointment can cause systemic side effects associated with hypercalcaemia.

Because of the potential effect on calcium metabolism, do not add the substances that enhance the ointment penetration, or apply bandage on the skin coated with the drug.

At long-term administration one should periodically monitor the level of calcium in the blood serum, because the systemic effect of the drug can occur.

Pre-clinical studies have shown that the use of calcitriol ointment enhances the sensitivity of the skin to ultraviolet radiation (UVR). Therefore, patients who use the Phorcal® ointment should avoid excessive action of the sunlight (both natural and artificial) on the affected skin. Furthermore, we recommend to limit the use of phototherapy in patients receiving treatment with Phorcal® ointment.

There is no information on the use of calcitriol with other clinical implications of psoriasis (another than plaque psoriasis), including *Psoriasis guttata acuta*, pustular psoriasis, *Psoriasis erythrodermica*, progressive plaque psoriasis.

Usually the drug is well tolerated. Some patients may develop side effects, which are usually localized at the application site and are characterized by mild to moderate flow, they disappear on their own. In case of severe irritation at the ointment application site or allergic reactions, contact dermatitis, the patient should consult a doctor and, if necessary, stop the treatment.

The drug contains propylene glycol, which can cause skin irritation.

*Pregnancy and lactation.*

*Pregnancy.*

It is not recommended to administer the drug during pregnancy due to the lack of sufficient data regarding the drug application in pregnant women.

*Lactation.*

Calcitriol was found in the milk of nursing females. It is not known whether calcitriol penetrates into breast milk, so if it is necessary to use the Phorcal® ointment during lactation, one should decide on termination of breast-feeding.

*Effects on ability to drive and operate machinery.*

No effect.

***Administration and dosage.***

For external use only. Apply thin layer of the ointment to the affected areas of skin 2 times a day (in the morning and in the evening). Daily application of the ointment should not exceed 35% of the skin surface. Do not apply more than 30 g of ointment per day. The average duration of treatment is 6 weeks. On the recommendation of the physician a long-term treatment is possible. The clinical experience of using ointment for more than 6 weeks is limited.

*Children.*

Because of the absence of data regarding the application of calcitriol ointment to children, the drug is contraindicated in this age group of patients.

***Overdose.***

In the local application at the recommended doses the drug overdose is unlikely, but long-term treatment and excessive application of ointment (over 100 g per week) may cause hypercalcaemia and hypercalciuria. In the case of hypercalcaemia and hypercalciuria it is necessary to stop drug administration until the calcium levels in serum and urine come back to normal. In case of accidental ingestion, anorexia, nausea, vomiting, constipation, hypotension, depression, sometimes drowsiness and coma may occur.

*Treatment:* symptomatic therapy.

***Side effects.***

*Immune system:* hypersensitivity reactions, including allergic reactions.

*Skin and its appendages:* itching, discomfort, burning, skin irritation (can be expressed in the form of pustules, papules or vesicles), erythema (redness), dry skin, psoriasis (worsening), swelling of the skin, contact dermatitis. Dermatitis may occur on the face, particularly around the mouth, which usually resolves after discontinuation of the drug administration.

*Metabolism:* hypercalcaemia.

*Kidneys and the urinary system:* hypercalciuria, urolithiasis.

***Shelf-life.*** 3 years.

**Storage.**

Store below 25°С in original package and in a dark place.

Keep it out of reach of children.

**Package.**

30 g, 100 g in tubes, 1 tube in a carton box.

**Conditions of supply.**

On prescription.

**Manufacturer.**

KUSUM HEALTHCARE PVT. LTD.

**Manufacturer’s location and address of the place of business.**

SP 289 (A), RIICO Indl. Area, Chopanki, Bhiwadi (Raj.), India.

**Last revision date.**