

EpiCeram®
Topical therapeutic Skin Barrier Emulsion

PEDIAPHARM INC.

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Summary Product Information:

EpiCeram Skin Barrier Emulsion is a steroid-free, fragrance - free, ceramide- dominant formulation.

Indications:

EpiCeram Skin Barrier Emulsion is to be used to treat dry skin conditions and to manage and relieve the burning and itching associated with various types of dermatoses, including atopic dermatitis. EpiCeram Skin Barrier Emulsion helps to relieve dry, waxy skin by maintaining a moist wound and skin environment, which is beneficial to the healing process.

Contraindications

EpiCeram Skin Barrier Emulsion is contraindicated in persons with known hypersensitivity to any of the components of the formulation.

Warnings

EpiCeram Skin Barrier Emulsion does not contain a sunscreen and should always be used in conjunction with a sunscreen in sun exposed areas. In radiation dermatitis and/or in conjunction with ongoing radiation therapy, apply following radiation therapy. Do not apply within 4 hours prior to radiation therapy. Apply twice daily or as indicated by the radiation therapist. After application, a temporary tingling sensation may occur (10 to 15 minutes). Keep this and similar products out of the reach of children. Follow directions for use. If condition does not improve within 10 to 14 days, consult a physician.

Precautions and Observations

For the treatment of any dermal wound, consult a physician.

- Use EpiCeram Skin Barrier Emulsion only as directed.
- EpiCeram Skin Barrier Emulsion is non-toxic; however it is for external use only and should not be ingested or taken internally.

- If clinical signs of infection are present, appropriate treatment should be initiated. If clinically indicated, use of EpiCeram Skin Barrier Emulsion may be continued during the anti-infective therapy.
- If the condition does not improve within 10-14 days, consult a physician.
- EpiCeram Skin Barrier Emulsion does not contain a sunscreen and should always be used in conjunction with a sun screen in sun exposed areas.
- In radiation dermatitis and/or in conjunction with ongoing radiation therapy, apply following radiation therapy.
- Do not apply within 4 hours prior to radiation therapy. Apply twice daily or as indicated by the radiation therapist.
- Following the application of EpiCeram Skin Barrier Emulsion a temporary tingling sensation may occur (10-15 minutes).
- Keep this and other similar products out of the reach of children.

Mode of action and clinical pharmacology

The stratum corneum is a multilayered tissue composed of flattened anucleated corneocytes embedded in a lipid-enriched extracellular matrix is derived from lipid sheets extruded from the lamellar bodies. Lamellar bodies fuse with the plasma membrane of the granular cell and discharge lipids and enzymes into the extracellular space. Enzymatic processing of the extracellular lipids is required to generate the mature lamellae. The corneocytes with the extracellular lipid surroundings provide the mechanical protection and water regulation of the skin barrier. In patients with atopic dermatitis, this lipid barrier is markedly reduced.

EpiCeram is a ceramide-dominant, physiologic, lipid-based emulsion that provides an optimal **3:1:1 ratio of ceramides, cholesterol and free fatty acids** to replenish the skin barrier in atopic skin.

EpiCeram normalizes the skin barrier through multiple proposed mechanisms:

- Creation of a barrier to prevent transepidermal water loss
- Bulk replenishment of physiologic lipids
- Enrichment of high quality of ceramides
- Delivery of an optimal ratio of ceramides, cholesterol, and free fatty acids
- Formulation is buffered at pH 5.5

In a study designed to assess the efficacy of EpiCeram® in correcting the lipid-biochemical abnormalities in atopic dermatitis (AD), EpiCeram reduced clinical disease severity after 14 and 28 days of therapy (*Efficacy of a lipid-based barrier repair formulation in moderate-to-severe paediatric atopic dermatitis, Sugarman, JL, J Drugs in Dermatol. 2009;8(12):1106-1111*).

The study, a five-center, investigator-blinded, randomized trial, compared EpiCeram® to fluticasone propionate cream (Cutivate®) in 121 patients with moderate-to-severe AD. Primary outcome measures were: 1) Reduction in disease severity, assessed as SCORAD scores; 2) improvement in pruritus; and 3) changes in sleep habits.

Results showed that EpiCeram reduced clinical disease severity, decreased pruritus, and improved sleep habits both 14 and 28 days after initiation of therapy. The EpiCeram-treated group did not differ significantly from the fluticasone-treated group by 28 days in terms of SCORAD, pruritus, and sleep habit scores.

SCORAD scores decreased 37% and 51% from the baseline at 14 and 28 days respectively (Table 1; $p < 0.001$). Subjective pruritus and sleep habits scores decreased in parallel, and to a comparable extent (Table 1). Both the patients/family self-assessment and IGA scores also demonstrated parallel, highly significant improvement at 14 and 28 days.

Based upon changes in SCORAD and IGA scores, there was no statistical difference between the ceramide-dominant, barrier formulation and fluticasone propionate at 28 days (Table 2). Both agents demonstrated significant improvements in pruritus, sleep habits, and patient/family assessment scores at both 14 and 28 days, changes that did not differ significantly from one another. Fluticasone propionate-treated subjects demonstrated significantly faster improvement in SCORAD and IGA scores at 14 days ($p < 0.05$) (Table 2). Thus, with the exception of SCORAD and IGA scores at day 14, the ceramide-dominant barrier formulation and fluticasone propionate cream demonstrated comparable efficacy for moderate-to-severe atopic dermatitis.

Table 1

CLINICAL ENDPOINTS FOLLOWING TREATMENT WITH EPICERAM

	Time	Mean	Change (%)¹	Significance
SCORAD (0 to 72)	Baseline	37.2	--	--
	Day 14	23.6	37	<0.001
	Day 28	18.5	51	<0.001
PRURITUS²	Baseline	6.1	--	--
	Day 14	3.9	39	<0.001

	Day 28	2.8	52	<0.001
SLEEP HABITS²	Baseline	4.1	--	--
	Day 14	2.2	42	<0.001
	Day 28	1.4	62	<0.001

¹ Reduction from baseline; ² Ten-point scale where 0=none.

Table 2

STATISTICAL COMPARISONS OF RESPONSES TO EPICERAM AND FLUTICASONE

	Mean Reduction from Baseline	
SCORAD (0 to 72)	EpiCeram (%)	Fluticasone (%)
Day 14	13.6 (36.6)	18.5 (57.6)
Anova p-value: 0.021; Rank sum p-value: 0.081		
Day 28	18.7 (50.7)	22.2 (66.7)
Anova p-value: 0.134; Rank sum p-value: 0.363		

SCORAD: 0 = no evidence of disease

Instructions for Use

Apply in a thin layer to the affected skin areas 2 times per day (or as needed) and massage gently into the skin. If the skin is broken, cover EpiCeram Skin Barrier Emulsion with a dressing of choice.

Information to be provided to the patients using EpiCeram:

- Patients should use EpiCeram as directed by the physician. EpiCeram is for external topical use only; patients should wash their hands after application.
- Patients should not use EpiCeram for any disorder other than that for which it is prescribed.
- EpiCeram is recommended to be used b.i.d. in atopic dermatitis on targeted area as directed by your physician; it can be used as a prophylactic on areas prone to repeated atopic dermatitis.
- Should EpiCeram be prescribed along with steroids or a topical immunomodulator, it is recommended to apply EpiCeram on affected areas of the skin just a few minutes before

to allow proper penetration. To ensure efficacy of EpiCeram in combination therapy, it should never be mixed with any other product.

- EpiCeram should not be mixed on skin with an emollient or moisturizer
- Prior to applying EpiCeram after a shower or bath, make sure that the skin is completely dry

Ingredients

Capric Acid, Cholesterol, Citric Acid, Conjugated Linoleic Acid, Dimethicone, Disodium EDTA, E. Cerifera (Candelilla) Wax, Food Starch, Modified Corn Syrup Solids, Glycerin, Glyceryl Stearate, Hydroxypropyl Bispalmitamide MEA (Ceramide), Palmitic Acid, PEG-100 Stearate, Petrolatum, Phenoxyethanol, Potassium Hydroxide, Purified Water, Sorbic Acid, Squalane, Xanthan Gum.

Supplied: EpiCeram Skin Barrier Emulsion is available in 50 g tube.

Store at 15°C to 30°C (59° F to 86°F). Do not freeze.

Marketed in Canada by:

Pediapharm, Inc.

Verdun, QC H3E 1A2

Customer service: 1-877-630-5674

Website: www.epiceram.ca