

Lumivoid

Depigmenting Cream

8086354-9093

INGREDIENTS

Aqua, Glyceryl Stearate (and) PEG 100 Stearate, Cetearyl Alcohol (and) Ceteareth-20, Glycerin, Steareth-2, Garcinia Indica Seed Butter, Caprylyl / Capric Triglyceride, Zinc oxide (and) Triethoxycaprylylsilane, Dicaprylyl Carbonate, Propylene Glycol, Cetearyl Alcohol, Steareth-21, Cetyl Alcohol, Polyacrylamide (and) C13-14 Isoparaffin (and) Laureth-7, Polysorbate 20, Propanediol (and) Aqua (and) Boerhavia Diffusa Root Extract, Dimethicone, Dimethicone/Vinyl Dimethicone Crosspolymer (and) Silica, Olea Europaea (Olive) Oil, Isopropyl Palmitate (and) Pentaerythrityl Tetraisoostearate, Aqua (and) Glycerin (and) Polysorbate 20 (and) Niacinamide (and) Linoleic acid (and) Linolenic acid (and) Tocopheryl acetate (and) Retinyl Palmitate (and) Lecithin (and) Ascorbyl Glucoside (and) Xanthan Gum (and) Phenoxyethanol (and) Methylisothiazolinone (and) Caprylyl Glycol (and) Decylene Glycol (and) Pentaerythrityl Tetra-di-t-butyl Hydroxyhydrocinnamate (and) Aminomethyl Propanol (Cosmevit DCx™), Aqua (and) Vaccinium Myrtillus Fruit Extract (and) Saccharum Officinarium (Sugar Cane) Extract (and) Citrus Aurantium Dulcis (Orange) Fruit Extract (and) Citrus Limon (Lemon) Fruit Extract (and) Acer Saccharum (Sugar Maple) Extract, Lactic acid, Phenoxyethanol (and) Methylisothiazolinone, Xanthan Gum, Tetrahydrodiferuloylmethane (SabiWhite®), Fragrance, Titanium Dioxide, Pentaerythrityl Tetra-di-t-butyl Hydroxyhydrocinnamate, Sodium Metabisulfite, Glycyrrhiza Glabra (Licorice) Root Extract, Tocopheryl Acetate, Disodium EDTA, Tetrahydropiperine (Cosmoperine®).

SabiWhite® and Cosmoperine® is a registered trademark of Sami-Sabinsa Group Limited, India.

CosmeVit DCx™ is a trademark of Sami-Sabinsa Group Limited, India.

INDICATION

It is a cosmetic product used to lighten skin tone and provide protection against UV radiation and skin conditioning.

DIRECTIONS FOR USE

- Cleanse face with water. Pat dry gently.
- Take a small quantity of Lumivoid cream on to your finger tip and apply over skin in a gentle circular motion.
- Replace cap tightly after use.
- Apply twice daily or as recommended by the physician.

PREGNANCY AND BREAST FEEDING

No data is known about the use of this product during pregnancy and breast feeding. Consult physician before using this product during pregnancy and breast feeding.

CONTRAINDICATIONS

No specific data found but do not use in case of wounded, cut or bruised skin. Do not use in cases of known hypersensitivity (especially allergic reaction) to any of the ingredients of this product.

WARNINGS AND PRECAUTIONS

Depigmentation and skin lightening products, which have been in use for ages in Asian countries where skin complexion is a major esthetic criterion, Hydroquinone and derivatives thereof, retinoids, alpha- and beta-hydroxy acids, ascorbic acid, divalent ion chelators, kojic acid, azelaic acid, as well as diverse herbal extracts are described in terms of their efficacy and safety.

Contents of Lumivoid are as per safe limits. However, below points should be considered for all the contents.

Retinoic Acid (Retinyl) or Tretinoin/ Retinol and Retinaldehyde

In the 1990s, retinol was widely used in anti-aging cosmetics. The concentration used generally ranges from 0.04% to 0.07% retinol equivalent. Furthermore, retinoids are known to induce the production of pro-inflammatory cytokines and are therefore irritating molecules. Lastly the "Photomutagenicity" of retinol requires certain precautions to be taken in case of exposure to the sun.

It directly intervenes in the melanogenesis process by inhibiting tyrosinase induction and dispersing the pigments in the keratinocytes on the one hand, and is capable of accelerating epidermal turnover on the other hand. The undesirable effects observed are erythema and desquamation.

The presence of retinoids in cosmetics can lead to burning, tingling, dryness, exfoliation, and desquamation. In 2015, the ANSM contra-indicated their use during pregnancy because of their strong teratogenic potency. In addition, the presence of retinoic acid and its salts in cosmetics has been prohibited in countries, including EU member states plus Iceland, Liechtenstein and Norway.

Hydroquinone.

The use of hydroquinone has lately been banned in all European countries because of concerns regarding its possible association with carcinogenesis. Several other countries have limited the amount of hydroquinone allowed in cosmetic products. Its glycosylated counterpart, arbutin, may under some environmental conditions, carry similar cancer risks. In fact, in acidic conditions, this substance easily hydrolyzes into hydroquinone.

However, the SCCS (Scientific Committee on Consumer Safety) considers the occurrence of arbutin in a concentration up to 7% in face creams as safe, provided that the concentration of hydroquinone in the cosmetics remains below 1 ppm. Other substances that are still authorized should be used cautiously.

Alpha Hydroxy Acids (AHAs)

Lumivoid contains ACB Fruit Mix (a blend of natural alpha hydroxy acids). Products containing AHAs are marketed for a variety of purposes, such as smoothing fine lines and surface wrinkles, improving skin texture and tone, unblocking and cleansing pores, and improving skin condition in general. Sometimes AHAs are used in cosmetics for other purposes, such as to adjust the pH (the degree of acidity or alkalinity). Various AHAs and lactic acid have keratolytic activity which may cause irritation. AHA-containing products cause exfoliation, or shedding of the surface skin.

The extent of exfoliation depends on the type and concentration of the AHA, its pH, and other ingredients in the product. Some products containing AHAs have been marketed for uses, such as treating acne, removing scars, and lightening discolorations. FDA received a total of 114 adverse dermatologic experience

reports for AHA-containing skin care products between 1992 and February 2004, with the maximum number in 1994.

The reported adverse experiences included burning, dermatitis or rash, swelling, pigmentary changes, blisters or welts, skin peeling, itching, irritation or tenderness, chemical burns, and increased sunburn.

These studies confirmed previous industry studies indicating that applying AHAs to the skin results in increased UV sensitivity. After four weeks of AHA application, volunteers' sensitivity to skin reddening produced by UV increased by 18 percent. Similarly, the volunteers' sensitivity to UV-induced cellular damage doubled, on average, with considerable differences among individuals. However, the studies also indicated that this increase in sensitivity is reversible and does not last long after discontinuing the use of the AHA cream. One week after the treatments were halted, researchers found no significant differences in UV sensitivity among the various skin sites.

The studies did not identify exactly how AHAs bring about the increase UV sensitivity, although the effects did not appear to involve dramatic increases in UV-induced damage to DNA in the skin.

FDA recommends that the labeling of a cosmetic product that contains an AHA as an ingredient and that is typically applied to the skin or mucous membrane, such as the lips, bear a statement that conveys the following information:

Sunburn Alert : This product contains an alpha hydroxy acid (AHA) that may increase your skin's sensitivity to the sun and particularly the possibility of sunburn. Use a sunscreen, wear protective clothing, and limit sun exposure while using this product and for a week afterwards.

Care should also be taken after AHA treatment: the skin should be neutralized after the application of AHA, as it might cause burning and erythema. For this reason, their concentration should not exceed 10% (m/m) in the finished product, with a final pH of the formulation not lower than 3.5. Moreover, corticosteroid-containing creams, diverted from their prime usage (e.g., anti-inflammatory), lead to severe adverse effects, ranging from irreversible stretch marks and epidermal thinning to neuropathy and steroid addiction.

Based on industry-sponsored studies, the Cosmetic Ingredient Review (CIR) Expert Panel - the industry's self-regulatory body for reviewing the safety of cosmetic ingredients concluded that products containing the AHAs (glycolic and lactic acid) are safe for use by consumers if: The AHA concentration is 10 percent or less.

The final product has a pH of 3.5 or greater. The final product is formulated in such a way that it protects the skin from increased sun sensitivity or its package directions tell consumers to use daily protection from the sun.

DRUG INTERACTIONS

No clinically significant drug interactions are known. If your doctor has directed you to use this product, or if you use any prescription product on the skin, tell your doctor or pharmacist of all prescription and non prescription/herbal products you may use, including other skin care products (Refer warning & precaution section).

SAFETY DATA

1. Ocular Irritation assay of Lumivoid Cream

Lumivoid was evaluated with the Irritation Assay System in order to predict its potential to cause ocular irritation. The proprietary Ocular Irritation® assay is a standardized and quantitative *in vitro* test which utilizes changes of relevant macromolecules to predict the acute ocular irritation of chemicals and chemical formulations. This method mimics an acute ocular irritation test. The irritancy potential of a test sample is expressed as an Irritation Draize Equivalent (IDE) score. This score is defined by comparing the increase in optical density (OD₅₀₀) produced by the test material to a standard curve that is constructed by measuring the increase in OD405 produced by a set of calibration substances. The predicted *in vivo* classification, based on this scoring system, is shown in Table 1. Test samples producing an IDE score of less than or equal to 12.5 are to be considered UN GHS/EU CLP non-irritants. Test samples that produce IDE score greater than 12.5 are to be classified as UN GHS/EU CLP irritants.

Table 1. Prediction Model of the Ocular Irritation® Assay

Irritation Score	Degree of Ocular Irritancy	UN GHS/EU CLP Classification
0-12.5	Minimal	Non-irritant (No Category)
> 12.5-30.0	Mild	Irritant(Category 1/ Category 2)
> 30.0-51.0	Moderate	
> 51.0	Severe	

The results of this analysis provided a predicted *in vivo* classification for the test sample. Three batches of the cream were compared for their irritancy potential by the Ocular Irritation® assay system. Standard volume dependent dose-response studies of Lumivoid Cream were performed with the Ocular Irritation® test method. Sample volumes (50 µl and 100 µl) of neat sample were applied to the synthetic bio barrier for analysis. The three batches of Lumivoid Cream were comparable in their activity. The results classified all the three batches of Lumivoid Cream as a Mild Irritant. In summary, the Irritation® test method classified Lumivoid as a Mild Irritant for the ocular irritation potential.

2. Dermal Irritation® assay of Lumivoid Cream

Lumivoid was evaluated with the Irritation® Assay System in order to predict its potential to cause dermal irritation. The proprietary Dermal Irritation® assay is standardized and quantitative *in vitro* acute dermal tests which utilize changes of relevant macromolecules to detect, rank and predict acute dermal irritancy of chemicals and chemical formulations.

The Dermal Irritation® assay is based on the principle that chemicals that cause dermal irritation are known to induce alterations in the structure of keratin, collagen and other dermal proteins. The Dermal Irritation Assay System is an *in vitro* test that mimics these biochemical phenomena. The assay system consists of two components; the first component is a membrane substrate that has been modified by covalently cross linking a mixture of keratin and collagen with an indicator dye. The second component is a reagent solution consisting of a highly organized globulin/protein macromolecular matrix. Reaction of the test sample with these proteins and macromolecular complexes promotes conformational changes that may be readily detected by their change in absorbance at 450 nm.

The extent of dye release and protein denaturation may be quantified by measuring the changes in optical density of the reagent solution at 450 nm (OD₄₅₀).

Comparison of these optical density measurements to those produced by standard chemical irritants permits calculation of a Human Irritancy Equivalent (HIE) score that has been shown to be directly related to the potential dermal irritancy of the test material Table 2.

Table 2. Relationship between Human Irritancy Equivalent (HIE) Score and Irritancy Classification for the Dermal Irritation® Test Method.

Human Irritancy Equivalent (HIE) Score	Predicted Dermal Irritancy
0.0 - 0.90	Non-Irritant
0.90 - 1.20	Non-Irritant/ Irritant
1.20 – 5.0	Irritant

The results of this analysis provided a predicted *in vivo* classification for the test sample. Three batches of the cream were compared for their irritancy potential by the Dermal Irritation® assay system. In summary, the Irritation® test method classified Lumivoid as a UV-induced Mild to Moderate irritant for Dermal irritation potential.

UNDESIRABLE EFFECTS

Occasional hypersensitivity or irritant reactions may occur. Burning, tingling, dryness, exfoliation, desquamation, skin shedding, dermatitis or rash, swelling, pigmentary changes, blisters or welts, and increased sunburn may occur. (Refer warning and precaution section)

KEY INGREDIENTS

SabiWhite®

SabiWhite® (INCI:Tetrahydrodiferuloylmethane) is a color free natural extract derived from *Curcuma longa* (Turmeric) roots. This color free curcumin sourced from turmeric is known to slow down melanogenesis (formation of melanin) by inhibiting the action of tyrosinase, an enzyme that participates in melanin formation. Laboratory studies revealed that SabiWhite® is an effective skin lightening agent with multifunctional topical benefits. SabiWhite® offers effective topical antioxidant protection. Its antioxidant action is of a comprehensive "bioprotectant" nature, efficiently preventing the formation of free radicals, while quenching pre-formed ones as well. This dual action protects skin cells from damage by UV radiation and the resultant inflammation and injury with far reaching beneficial effects on overall health and wellbeing. Curcuminoids are reported to protect normal human keratinocytes from hypoxanthine/xanthine oxidase injury in *in-vitro* studies. This study suggests that curcuminoids and therefore SabiWhite® offers protection to the skin. Preliminary *in vitro* studies indicate that SabiWhite® efficiently inhibits tyrosinase, the rate-limiting enzyme in the synthesis of melanin. SabiWhite® is clinically proven to be safe, effective and comparable to Hydroquinone.

Glycyrrhiza Glabra (Licorice) Root Extract

Licorice contains Glabridin, a unique molecule which is known for its skin lightening properties by inhibiting the enzyme tyrosinase and melanin synthesis. Licorice possesses potent and effective anti-inflammatory and antioxidant properties to give smooth glowing skin. Glabridin has been studied for its inhibitory effect on pigmentation and is reported that glabridin inhibited tyrosinase activity of melanocytes without cytotoxicity.

The anti-inflammatory properties of glabridin were attributed to inhibition of superoxide anion production and cyclooxygenase activity. Studies have shown that it can provide a considerable skin brightening effect, while remaining non-toxic to the melanin forming cells.

CosmeVit DCx™

Powerhouse of skin nutrients that provides a holistic approach to manage a healthy and glowing skin with a multifaceted approach to skin lightening, skin moisturizing and skin protection. It is composed of :

- Retinol (Vitamin A) Palmitate is effective as an antioxidant, skin-cell regulator and helps skin repair
- Vitamin E Acetate is a stable form of Vitamin E, acts as a cell membrane protectant
- Niacinamide - Manages hyper pigmentation and moisture balance
- Vitamin F-Linoleic acid and Linolenic acids well recognized to promote skin vitality.
- Ascorbyl Glucoside-Stabilized form of Vitamin C with antioxidant benefits.

Propanediol (and) Aqua (and) Boerhavia Diffusa Root Extract [Melavoid] Melavoid is obtained from the roots of punarnava (*Boerhaavia diffusa L.*), standardized in boeravinones. Melavoid a skin lightening active ingredient, works on the initial mechanisms of pigmentation, decreasing skin tone and spots. An *in silico* screening demonstrated that boeravinone B, a component of *Boerhaavia diffusa*, is the suitable active to act as a natural agonist of PPAR-γ.

In vitro efficacy of Melavoid in human melanocytes NHEM (Normal Human Epidermal Melanocytes) was assessed and demonstrated. In this study, 63% of tyrosinase expression reduction and 55% of tyrosinase activity decrease was shown. In the same culture, melanin synthesis reduction was specifically evaluated. At the same time, it was observed that Melavoid maintains melanocytes viability (unlike kojic acid) by reducing their number of dendrites, thus preventing an accumulation of pigment in the epidermis. Melavoid decreases the amount of melanin by 34% without affecting melanocyte viability.

In vivo efficacy tests performed in a panel of Asian volunteers.

56 days of treatment with, Melavoid versus placebo in evaluation of normal skin without spots Melavoid produces a maximum ITA (Individual Typological Angle) increment up to 28%, diminishing skin pigmentation intensity. In evaluation of spotted skin, Melavoid is an intelligent pigmentant; its activity is higher in areas with spots and thus evens skin color.

Aqua (and) Vaccinium Myrtillus Fruit Extract (and) Saccharum Officinarium (Sugar Cane) Extract (and) Citrus Aurantium Dulcis (Orange) Fruit Extract (and) Citrus Limon (Lemon) Fruit Extract (and) Acer Saccharum (Sugar Maple) Extract [ACB Fruit Mix]

An ideal combination of natural fruit acids (AHAs) from sugar cane, sugar maple, orange, and lemon. It is well recognized for its exfoliant property.

Cosmoperine®

Cosmoperine® is obtained from black pepper and standardized to contain

minimum 98.5% Tetrahydropiperine. It is a patented and proven dermal penetration enhancer.

Zinc oxide (and) Triethoxy caprylyl silane

Zinc oxide (and) Triethoxy caprylyl silane is surface treated Zinc Oxide offering the best balance between highest broad-band UV protection and transparency. It is an effective and stable physical sunscreen.

Dimethicone

Dimethicone is a silicon-based polymer used as an effective skin conditioning agent and skin protectant. It has a non-greasy, non-occlusive and non-stinging effect on the skin. This medication is used as a moisturizer to treat or prevent dry, rough, scaly, itchy skin and minor skin irritations.

Olea Europaea (Olive) Oil

It is obtained from the *Olea europaea* used to moisturize the dry skin. Olive oil also possesses antioxidant properties.

Dimethicone / Vinyl Dimethicone Crosspolymer (and) Silica

Dimethicone/Vinyl Dimethicone Crosspolymer (and) Silica shows good sebum absorption properties.

Glycerin and Propylene glycol are used as humectant in Lumivoid Cream which prevents loss of moisture, thereby retaining the skin's natural moisture. Garcinia Indica Seed Butter, Caprylic/Capric Triglyceride (CCTG), Dicaprylyl Carbonate, Cetearyl Alcohol, Cetyl alcohol and with Isopropyl palmitate/ Pentaerythrityl Tetraisoostearate are used as emollient in Lumivoid Cream, which provides skin softening and smoothing properties.

UNDERSTANDING THE BASICS OF SKIN

- Skin is the body's largest organ and has 3 layers.
- The top layer is called the epidermis. It protects the underlying skin layers from the outside environment
- The second layer is the dermis. It contains cells that provide strength, support, and flexibility to the skin
- The last layer is the hypodermis. It contains the fat cells or adipose tissue that insulates the body and helps it helps to conserve heat.

Functions of the Skin

- First line of defence
- Protection from dehydration, pathogens, and injury
- Regulates body temperature

WHAT IS HYPERPIGMENTATION ?

- Hyperpigmentation is a common, usually harmless condition in which patches of skin become darker in color than the normal surrounding skin.
- Excess production of melanin causes hyperpigmentation. Melanin is a pigment that gives skin its color and it is produced by skin cells called melanocytes. Several different conditions or factors can alter the production of melanin in the body.

Causes of Hyperpigmentation

- Overexposure to the sun
- Injury or inflammation to the skin due to acne, eczema, or psoriasis can cause increased pigment production, resulting in dark spots
- Due to pregnancy or oral contraceptives

What is Melasma ?

- Melasma is a dark or brown discoloration commonly seen over cheeks, forehead, nose, and upper lip. Melasma can affect anyone, but is more common in women, especially pregnant women.

Treatment of Hyperpigmentation

- Treatment options are available either with topical drug-based or dermatological procedures.
- It's important to highlight that topical treatments do not work overnight because it takes time and consistent use to produce a noticeable improvement in the skin tone.

WHAT IS Lumivoid ?

- Lumivoid Cream is a composite of scientifically-validated nutrients that helps to brighten the skin, minimize pigmentation problems naturally, lighten the skin tone, protect from sun exposure.

• *In vitro* evaluation of Lumivoid Cream substantiates the skin lightening efficacy further.

EXPIRY DATE : Do not use later than the date of expiry

STORAGE AND HANDLING INSTRUCTIONS

STORE AT A TEMPERATURE NOT EXCEEDING 30° C. DO NOT FREEZE.

For external use only and protect from sun exposure. Avoid contact with eyes. Keep away from children

PACKAGING INFORMATION : 5 gm, 15 gm and 30 gm lami tube.

Mfg. Lic. No. HIM/COS/13/189



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IN/LUMIVOID/5,15, 30 GM/MAR-2023/04/PI

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PRODUCT NAME	ITEM / PACK	DESIGN STYLE	CODE	DIMENSIONS (MM)	ART WORK SIZE	DATE	COUNTRY : Domestic P2P	NO. OF COLORS : 4	PANTONE SHADE NOS.:	SUBSTRATE : Front -Back	REMARK :	LOCAION : Helios Pharma		SUPERSEDES A/W NO. :		
												Activities	Signature	Department	Date	
Lumivoid	Insert	Front -Back	8086354-9093	150 x 270 mm	S/S	18-03-2023										

This colour proof is not colour binding. Follow Pantone shade reference for actual colour matching.