
TRADENAME (methyl aminolevulinate) Cream, 16.8%

For Topical Use Only.

Not for Ophthalmic, Oral, or Intravaginal Use

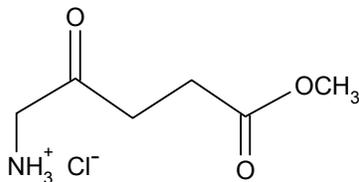
Must be dispensed to and applied by a physician.

DESCRIPTION

TRADENAME[®] Cream is an oil in water emulsion. TRADENAME[®] Cream contains methyl aminolevulinate hydrochloride equivalent to 168 mg/g of methyl aminolevulinate.

Methyl aminolevulinate hydrochloride is a white to slightly yellow powder that is freely soluble in water and methanol, soluble in ethanol and practically insoluble in most organic solvents.

The chemical formula for methyl aminolevulinate HCl is C₆H₁₁NO₃•HCl (MW=181.62) and it has the following structural formula:



TRADENAME[®] Cream contains glyceryl monostearate, cetostearyl alcohol, polyoxyl stearate, cholesterol and oleyl alcohol as emulsifying agents. It also contains glycerin, white petrolatum, isopropyl myristate, refined peanut oil, refined almond oil as emollients, edetate disodium as a chelating agent and methylparaben and propylparaben as preservatives.

CLINICAL PHARMACOLOGY

Mechanism of Action

Photosensitization following application of TRADENAME Cream occurs through the metabolic conversion of methyl aminolevulinate (prodrug) to photoactive porphyrins (PAP), which accumulates in the skin lesions to which TRADENAME Cream has been applied. When exposed to light of appropriate wavelength and energy, the accumulated photoactive porphyrins produce a photodynamic reaction, resulting in a cytotoxic process dependent upon the simultaneous presence of oxygen. The absorption of light results in an excited state of porphyrin molecules, and subsequent spin transfer from photoactive porphyrins to molecular oxygen generates singlet oxygen, which can further react to form superoxide and hydroxyl radicals. Photosensitization of actinic (solar) keratosis lesions using TRADENAME Cream, plus illumination with a CureLight BroadBand Model CureLight 01 (a red light of 570 to 670 nm wavelength) at 75 J/cm², is the basis for TRADENAME photodynamic therapy (PDT).

Pharmacokinetics

The time-course of PAPs after application of TRADENAME Cream has been monitored by means of fluorescence. After application of TRADENAME Cream to actinic keratosis lesions in 8 patients, fluorescence was measured at several time points over 28 hours. Three hours after the application of TRADENAME Cream the fluorescence in the treated lesions was significantly greater than that seen in both treated and untreated normal skin, and after application of vehicle cream (not containing methyl aminolevulinate) to normal skin. After application of TRADENAME Cream for 28 hours and subsequent illumination with red light of 570 to 670 nm wavelength at a total light dose of 75 J/cm², complete photobleaching (photodegradation) of Protoporphyrin IX occurred with levels of Protoporphyrin IX returning to pre-treatment values within 1 hour after illumination. However, the fate of other photoactive porphyrins are unknown.

The clinical dose of methyl aminolevulinate cream and duration of application were derived from a study in which three different strengths of the cream (16, 80 and 160 mg/g methyl aminolevulinate, as hydrochloride), each applied for 3 hours or 18 hours, were tested in 16 patients.

CLINICAL STUDIES

TRADENAME Cream plus illumination with the CureLight BroadBand Model CureLight 01 (a red light of 570 to 670 nm wavelength) at 75 J/cm² has been studied in 130 patients with non-hyperkeratotic actinic keratoses in two clinical trials. These trials were not identical; however, both were randomized, multicenter, and double-blinded with patients randomized to TRADENAME-PDT and Vehicle-PDT study arms that required two treatment sessions (7 days apart). One study was conducted in the U.S. and patients were randomized 1:1 TRADENAME to Vehicle and one study was conducted in Australia with patients randomized 4:1 TRADENAME to Vehicle. In both studies treatment consisted of a multi-step process that was repeated after 7 days consisting of 1) Lesion preparation (debridement with sharp curette) to roughen the surface of the lesion. 2) TRADENAME or Vehicle Cream application to lesions with occlusion with an adhesive, non-absorbent dressing, 3) Waiting at least 2.5 hours, but no more than 4 hours to allow for conversion of the methyl aminolevulinate, 4) Removal of cream with gauze and saline, 5) Red light Dosimetry and Illumination with the CureLight BroadBand Model CureLight 01 (a red light of 570 to 670 nm wavelength).

Study patients had previously untreated facial and scalp actinic keratoses (AKs) that were slightly palpable (better felt than seen). Hyperkeratotic actinic keratoses were excluded. In the U.S. study 100% of patients had 4 to 10 lesions at baseline. However, in the Australian study, 63% (70/111) of patients had less than 4 lesions at baseline, 31% (34/111) of the enrolled patients had 4 to 10 lesions, and 6% (7/111) had more than 10 lesions at baseline (a maximum of 6 treatment fields were allowed in this study).

A "Cleared" AK lesion was defined as being not visible and not palpable as assessed 3 months after the second treatment session. Patients with all treated lesions cleared at 3 months were defined as Complete Responders.

The percentage of patients in whom 75% or more of the treated lesions were clear and the percent of patients in whom 100% of the treated lesions were clear 3 months after the second TRADENAME-PDT treatment session are shown in Table 1 for each of the two studies.

Patient Response	Australian Study		U. S. Study	
	TRADENAME -PDT	Vehicle PDT	TRADENAME -PDT	Vehicle PDT
Patients with at least 75% of AK Lesions Cleared	76/88 (86%)	4/23 (17%)	35/42 (83%)	12/38 (32%)
Complete Responders (All Lesions clinically cleared at 3 months)	71/88 (81%)	3/23 (13%)	33/42 (79%)	8/38 (21%)

Patients with 4 or more lesions had lower success rates than those with less than 4 lesions when treated with PDT using TRADENAME Cream (see Table 2).

Baseline Lesion Count	Australian Study		U.S. Study	
	TRADENAME -PDT	Vehicle PDT	TRADENAME -PDT	Vehicle PDT
Below 4	49/55 (89%)	3/15 (20%)	N/A	N/A
4 – 10	18/27 (67%)	0/7	33/42 (79%)	8/38 (21%)
More than 10	4/6 (67%)	0/1	N/A	N/A
Total	71/88 (81%)	3/23 (13%)	33/42 (79%)	8/38 (21%)

Lesions that were slightly palpable (Grade 1) had a better success rate than lesions that were visible and palpable (Grade 2) – See Table 3.

Lesion Grade	Australian Study		U.S. Study	
	TRADENAME -PDT	Vehicle PDT	TRADENAME -PDT	Vehicle PDT
Lesion Grade 1 (slightly palpable AK: better felt than seen)	198/209 (95%)	12/35 (34%)	172/196 (88%)	72/162 (44%)
Lesion Grade 2 (visible and palpable AK: easily seen and	119/151 (79%)	9/39 (23%)	49/64 (77%)	20/80 (25%)

felt)				
Total	317/360 (88%)	21/74 (28%)	221/260 (85%)	92/242 (38%)

Response rate by lesion location is presented in Table 4.

Lesion Location	Australian Study		U.S. Study	
	TRADENAME -PDT	Vehicle PDT	TRADENAME -PDT	Vehicle PDT
Face	251/273 (92%)	15/62 (24%)	195/226 (86%)	73/204 (36%)
Scalp	66/87 (76%)	6/12 (50%)	26/34 (76%)	19/38 (50%)
Total	317/360 (88%)	21/74 (28%)	221/260 (85%)	92/242 (38%)

The overall treatment effect as evidenced by the high vehicle response rate may include the contribution of lesion preparation, i.e. curettage. Adequate lesion preparation is an important component for AK therapy with TRADENAME Cream.

Information regarding further treatments for residual or new AK lesions performed after 3 months is not available.

INDICATIONS AND USAGE

TRADENAME Cream in combination with 570 to 670 nm wavelength red light illumination using the CureLight BroadBand Model CureLight 01 lamp is indicated for treatment of non-hyperkeratotic actinic keratoses of the face and scalp in immunocompetent patients when used in conjunction with lesion preparation (debridement using a sharp dermal curette) in the physician's office when other therapies are unacceptable or considered medically less appropriate.

CONTRAINDICATIONS

TRADENAME Cream is contraindicated in patients with cutaneous photosensitivity, or known allergies to porphyrins, and in patients with known sensitivities to any of the components of TRADENAME Cream, which includes peanut and almond oil (See WARNINGS regarding sensitivity to TRADENAME Cream).

This product contains refined peanut oil (See PRECAUTIONS).

WARNINGS

TRADENAME Cream is intended for topical use in the physician's office by trained physicians only. Do not apply to the eyes or to mucous membranes.

TRADENAME Cream has demonstrated a high rate of contact sensitization (allergenicity) (See ADVERSE REACTIONS). Care should be taken by the physician applying TRADENAME Cream to avoid inadvertent skin contact. Nitrile gloves should be worn when applying and removing the cream. Vinyl and latex gloves do not provide adequate protection when using this product.

TRADENAME Cream when used with CureLight BroadBand Model CureLight 01 lamp must be used with appropriate protective sleeves obtained from the product manufacturer to decrease the risk of blood-borne transmitted diseases (hepatitis, HIV, etc.). Change the disposable covers for the device (probe and horseshoe positioning device) between patients. Universal Precautions should be used with this treatment.

PRECAUTIONS

The safety and efficacy have not been established for the treatment of cutaneous malignancies and for skin lesions other than non-hyperkeratotic face and scalp actinic keratoses using PDT with TRADENAME Cream. Thick (hyperkeratotic) actinic keratoses should not be treated with TRADENAME Cream. The safety and efficacy of TRADENAME Cream has not been established in patients with immunosuppression, porphyria or pigmented actinic keratoses.

General

TRADENAME Cream Application

During the time period between the application of TRADENAME (methyl aminolevulinate) Cream and exposure to red light illumination, the treatment site will become photosensitive. After TRADENAME Cream application, patients should avoid exposure of the photosensitive treatment sites to sunlight or bright indoor light (e.g., examination lamps, operating room lamps, tanning beds, or lights at close proximity) during the period prior to red light treatment. Exposure to light may result in a stinging and/or burning sensation and may cause erythema and/or edema of the lesions. Before exposure to sunlight, patients should, therefore, protect treated lesions from the sun by wearing a wide-brimmed hat or similar head covering of light-opaque material. Sunscreens will not protect against photosensitivity reactions caused by visible light. The treated site should be protected from extreme cold with adequate clothing or remaining indoors between application of TRADENAME and PDT light treatment.

After illumination of TRADENAME Cream, the area treated should be kept covered and away from light for at least 48 hours.

Because of the potential for skin to become photosensitized, the TRADENAME Cream should be used by a trained physician to apply drug only to non-hyperkeratotic actinic keratoses and perilesional skin within 5 mm of the lesion. Redness, swelling, burning, and stinging are expected as a result of therapy; however, if these symptoms increase in severity and persist longer than 3 weeks, the patient should contact their doctor.

TRADENAME Cream has not been studied for more than two treatment sessions. Information regarding further treatments for residual or new AK lesions performed after 3 months is not available.

Photosensitivity and Device Precautions

The patient, operator and other persons present should wear protective goggles that sufficiently screen out light with wavelengths from 570 to 670 nm during red light treatment.

If for any reason the patient cannot have the red light treatment after application of TRADENAME Cream, the cream should be rinsed off, and the patient should protect the treated area from sunlight, prolonged or intense light for two days. Prolonged exposure for greater than 4 hours to TRADENAME Cream should be avoided.

Coagulation defects

TRADENAME Cream has not been tested on patients with inherited or acquired coagulation defects.

Hypersensitivity

TRADENAME Cream is formulated with refined peanut and almond oil.

TRADENAME (methyl aminolevulinate) Cream has not been tested in patients who are allergic to peanuts. TRADENAME (methyl aminolevulinate) Cream has demonstrated a high rate of contact sensitization (allergenicity).

Information for Patients

The physician should provide and discuss the attached Patient Package Insert with each patient.

Drug Interactions

There have been no studies of the interaction of TRADENAME Cream with any other drugs, including local anesthetics. It is possible that concomitant use of other known photosensitizing agents might increase the photosensitivity reaction of actinic keratoses treated with TRADENAME Cream.

Carcinogenesis, Mutagenesis, Impairment to Fertility

Long-term studies to evaluate the carcinogenic potential of TRADENAME Cream have not been performed.

Methyl aminolevulinate was negative for genetic toxicity in the Ames assay, and the chromosomal aberration assay in Chinese hamster ovary cells, tested with and without metabolic activation and in the presence and absence of light. Methyl aminolevulinate was also negative in the *in vivo* micronucleus assay in the rat. In contrast, at least one report in the literature has noted genotoxic effects in cultured rat hepatocytes after aminolevulinate (ALA) exposure with PpIX formation. Other studies have documented oxidative DNA damage *in vivo* and *in vitro* as a result of ALA exposure.

No animal fertility studies have been conducted.

Pregnancy

Teratogenic effects: Pregnancy Category C: Animal reproduction studies have not been conducted with TRADENAME Cream. It is also not known whether TRADENAME Cream can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity.

TRADENAME Cream should be given to a pregnant woman only if clearly needed.

Nursing Mothers

The amount of methyl aminolevulinate secreted into human breast milk following topical administration of TRADENAME Cream is not known. Because many drugs are secreted in human milk, caution should be exercised when TRADENAME Cream is administered to a nursing mother. If TRADENAME Cream is used in a nursing mother, a decision should be made whether or not to stop nursing.

Pediatric Use

It is not recommended that TRADENAME Cream be used in pediatric patients. Actinic keratosis is rarely found in pediatric patients.

Geriatric Use

Seventy percent (269 among 383) of the patients treated with TRADENAME Cream in all clinical studies of actinic keratosis were 65 years of age or older. No overall differences in safety and efficacy were observed between patients aged 65 years and older and those who were younger.

ADVERSE REACTIONS

Dermal Safety Studies

Provocative studies to evaluate irritancy and sensitization have demonstrated that TRADENAME Cream is an irritant and sensitizer. A provocative cumulative irritancy and sensitization (allergenicity) study of TRADENAME Cream with a cross-sensitization challenge with ALA was performed in 156 subjects. Only 98 of the 156 subjects tested entered the challenge phase. Fifty-two percent of the subjects (30/58), who agreed to challenge with TRADENAME Cream, were positive (sensitized). Forty subjects refused challenge with TRADENAME Cream and 60 withdrew. At least 58 of the 60 subjects who withdrew from the study discontinued due to irritation/sensitization.

Ninety-eight subjects agreed to challenge with ALA. Two percent of the ALA challenged subjects (2/98) were scored as equivocal reactions and 2% in the paraffin vehicle group were scored as positive.

Adverse Events

In vehicle-controlled phase 3 studies of actinic keratosis, 88% of patients treated with TRADENAME Cream reported one or more adverse events.

Burning was the most frequent complaint, reported by 50% of patients (ranging from mild, to severe) and 9% of those patients reported severe burning sensation. Pain in the skin was reported by 21% of patients and 7% had severe pain. Local erythema lasting up to two weeks and edema up to one week after treatment were reported by 31% and 6% of patients.

Symptoms and signs of local phototoxicity were observed in 88% of patients treated with TRADENAME Cream in all clinical studies of TRADENAME-PDT for actinic keratoses.

Percentage of patients with local adverse reactions based on occurrence per patient in vehicle controlled phase 3 studies.		
Events	TRADENAME-PDT (n=130)	Vehicle PDT* (n=61)
	n (%) of patients with AEs	n (%) of patients with AEs
Burning sensation skin	65 (50.0%)	9 (14.8%)
Erythema	60 (46.2%)	12 (19.7%)
Skin pain	27 (20.8%)	6 (9.8%)
Stinging skin	25 (19.2%)	2 (3.3%)
Crusting	20 (15.4%)	6 (9.8%)
Edema skin	20 (15.4%)	1 (1.6%)
Skin peeling	14 (10.8%)	2 (3.3%)
Blisters	14 (10.8%)	2 (3.3%)
Bleeding skin	11 (8.5%)	2 (3.3%)
Pruritus/Itching	17 (13.1%)	2 (3.3%)
Skin ulceration	7 (5.4%)	0 (0%)
Skin infection	3 (2.3%)	1 (1.6%)
Skin hyper-pigmentation	1 (0.8%)	0 (0%)

The majority of patients in all the clinical trials had local pain or discomfort upon illumination. There were 4 (1.0%) withdrawals/discontinuations among 383 patients treated with TRADENAME Cream in all the clinical trials of actinic keratosis, all of which were due to the adverse event of local pain on illumination.

There have been reported instances of patients treated with TRADENAME Cream (2 out of 130) who have developed squamous cell and basal cell carcinoma at the site of treatment. The relationship to treatment with TRADENAME Cream is unknown.

Serious erythema and facial edema have been described in European post-marketing reports.

OVERDOSAGE

TRADENAME Cream Overdose

TRADENAME Cream overdose has not been reported. If the patient for any reason cannot have the red light treatment during the prescribed period after application (the 3 hour timespan), the cream should be rinsed off, and the patient should protect the exposed area from sunlight, prolonged or intense light for two days.

Red Light Overdose

There is no information on overdose of red light following TRADENAME Cream application.

In case of red light overexposure and skin burn occurs, the patient should be treated according to standard of practice guidelines for treatment of cutaneous burns.

DOSAGE AND ADMINISTRATION

Photodynamic therapy for non-hyperkeratotic actinic keratoses with TRADENAME Cream is a multi-stage process as described below: Two treatment sessions 7 days apart should be conducted. Not more than one gram (half a tube) of TRADENAME Cream should be applied per treatment session.

One TRADENAME-PDT session consists of:



1) Lesion debriding –

Before applying TRADENAME Cream, the surface of the lesions should be prepared with a small dermal curette to remove scales and crusts and roughen the surface of the lesion. This is to facilitate access of the cream and light to all parts of the lesion.

Figure 1 A Lesion debriding



Only nitrile gloves should be worn during this and subsequent steps and Universal Precautions should be taken. Vinyl and latex gloves do not provide adequate protection when using this product.

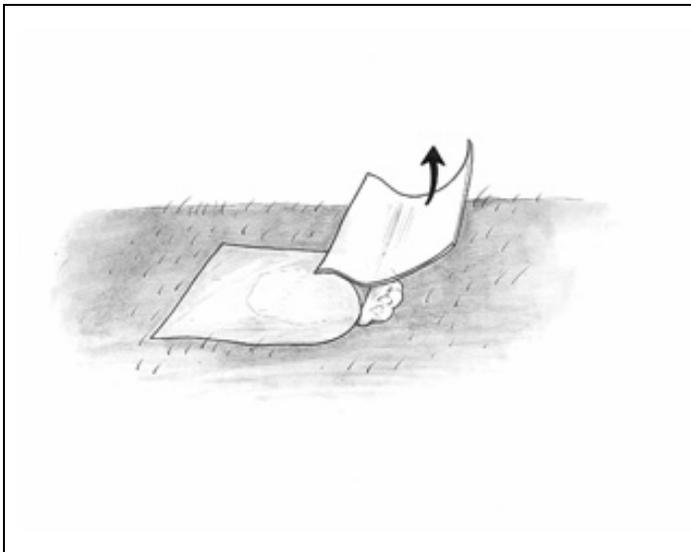
Figure 1B Lesion debriding



2) Application of TRADENAME Cream –

Using a spatula, apply a layer of TRADENAME Cream about 1 mm thick to the lesion and the surrounding 5 mm of normal skin. Do not apply more than one g of TRADENAME Cream for each patient per treatment session.

Figure 2: Cream application

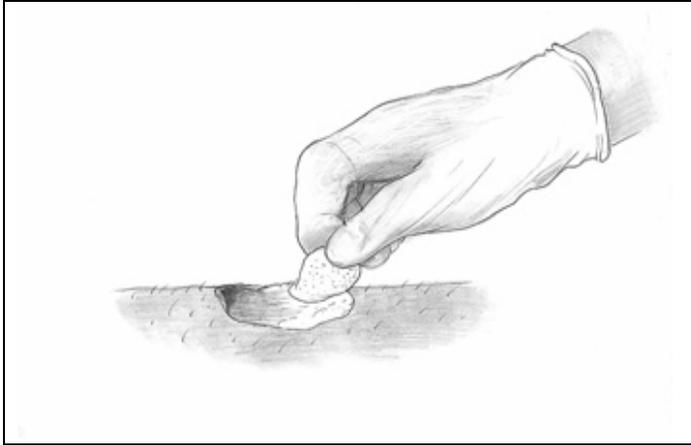


The area to which the cream has been applied should then be covered with an occlusive, non-absorbent dressing for 3 hours. Multiple lesions may be treated during the same treatment session. Each treatment field is limited to a diameter of 55mm. Only nitrile gloves should be worn by the qualified healthcare provider in order to avoid skin contact with the cream. This product is not intended for application by patients or unqualified medical personnel.

Figure 3: Occlusive dressing application

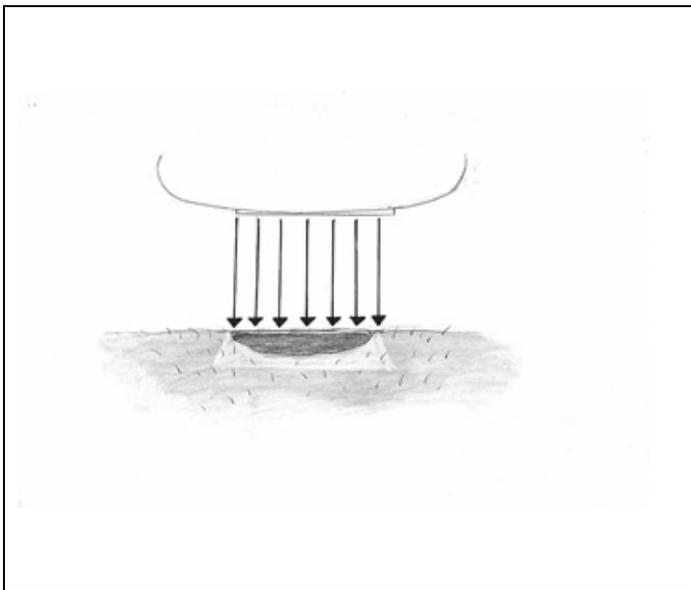
3) Wait for 3 hours - (at least 2.5 hours, but no more than 4 hours).

After Cream application, patients should avoid exposure of the photosensitive treatment sites to sunlight or bright indoor light (e.g., examination lamps, operating room lamps, tanning beds, or lights at close proximity) during the period prior to red light treatment. Exposure to light may result in a stinging and/or burning sensation and may cause erythema and/or edema of the lesions. Patients should protect treated areas from the sun by wearing a wide-brimmed hat or similar head covering of light-opaque material. Sunscreens will not protect against photosensitivity reactions caused by visible light. It has not been determined if perspiration can spread the TRADENAME Cream outside the treatment site to the eyes or surrounding skin. The treated site should be protected from extreme cold with adequate clothing or remaining indoors between application of TRADENAME Cream and PDT light treatment.



4) Removal of Dressing and Rinse Off Excess Cream - Following removal of the occlusive dressing, clean the area with saline and gauze. Nitrile gloves should be worn at this step by the trained physician.

Figure 4: Cream removal



5) Illumination of TRADENAME Treated Lesion - It is important to ensure that the correct light dose is administered. The light intensity at the lesion surface should not be higher than 200 mW/cm^2 . Patient and operator should adhere to safety instructions and Universal Precautions provided with the lamp. The patient and operator should wear protective goggles during illumination. Patients should be advised that transient stinging and/or burning at the target lesion sites may occur during the period of light exposure.

Figure 5: Illumination

The CureLight BroadBand Model CureLight 01 lamp is approved for the use in TRADENAME-PDT. The lamp should be carefully calibrated so that dosing is accurate and immediately thereafter the lesion should be exposed to red light with a continuous spectrum of 570 to 670 nm and a total light dose of 75 J/cm^2 . To avoid direct contact between lamp parts and patient skin, always use disposable protective plastic sleeves on the positioning device and on the light measuring probe. Following each patient treatment, the disposable protective plastic sleeves should be removed from the positioning device and from the light measuring probe and discarded.

If red light treatment is interrupted or stopped for any reason, it may be restarted. If the patient for any reason cannot have the red light treatment during the prescribed period after application (the 3 hour timespan), the cream should be rinsed off and the patient should protect the exposed area from sunlight, prolonged or intense light for two days. TRADENAME Cream is not intended for use with any device other than the approved lamp: CureLight BroadBand Model CureLight 01.

Use of TRADENAME Cream without subsequent red light illumination is not recommended.

No more than 1 g (half a tube) of product should be used for each of the two weekly treatment sessions. Multiple lesions may be treated during the same treatment session using a total of 1 g of TRADENAME Cream. Lesion response should be assessed 3 months after the last treatment session.

This product is not intended for application by patients or unqualified medical personnel, therefore, this product is only dispensed to physicians.

HOW SUPPLIED

TRADENAME Cream, 16.8%, is available as the following:
NDC xxxx-xxxx-xx, 2 gram aluminum tube, box of 1

Product Package

Keep out of reach of children

For topical use only by physicians in the physician's office.

Rx Only

Storage Conditions

Store refrigerated, 2-8°C (36-46°F).

Use contents within one week after opening.

Should not be used after 24 hours out of refrigerator.

TRADENAME cream is a registered TRADENAME of PhotoCure ASA.

PhotoCure ASA, Hoffsvæien 48, N-0377 Oslo, Norway

USA Contact: Clementi & Associates, 919 Conestoga Rd., Rosemont, PA 19010

Revision: January 9, 2004

PATIENT INFORMATION

TRADENAME Cream 16.8% (phonetic)
Generic name: methyl aminolevulinate hydrochloride

Read this Patient Information before you get treated with TRADENAME Cream and each time you get a treatment. There may be new information. This leaflet does not take the place of talking with your doctor about your condition or treatment. Ask your healthcare provider about anything you do not understand about TRADENAME Cream.

What is the most important thing I need to know about TRADENAME Cream?

- TRADENAME Cream with light treatment (Photodynamic therapy or PDT) is only done in medical offices by trained doctors.
- TRADENAME Cream is not applied by patients. TRADENAME Cream should not be applied by doctors who have not been trained in its use.

What is TRADENAME Cream?

TRADENAME Cream is a prescription cream used with PDT (light treatment) to treat skin growths on the face and scalp called actinic keratosis (AK). TRADENAME Cream is only used for AK skin growths that are thin and not dark colored. AK skin growths are not cancer. AK skin growths are caused partly by too much sun exposure. TRADENAME Cream and PDT work together to treat AK skin growths.

TRADENAME Cream has not been studied in children for any condition and should not be used in children.

Who should not use TRADENAME Cream?

Do not use TRADENAME Cream if:

- your skin over reacts to sun or light (photosensitivity)
- you are allergic to porphyrins or to any of the ingredients in TRADENAME Cream. The active ingredient is methyl aminolevulinate hydrochloride. TRADENAME Cream also contains peanut and almond oil. See the end of this leaflet for a complete list of ingredients in TRADENAME Cream.

Before treatment with TRADENAME Cream, tell your doctor:

- **about your medical conditions, including if you**

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- **are pregnant or planning to become pregnant.** It is not known if TRADENAME Cream can harm your unborn baby.
 - **are breastfeeding.** It is not known if TRADENAME Cream passes into your milk and if it can harm your baby. You should decide whether or not to stop breastfeeding while getting treatment with TRADENAME Cream. Talk to your doctor for help with this choice.
 - **are allergic to nuts or peanuts**
 - **have or had skin cancer or other skin growths on your body**
 - **have bleeding problems.**
- **about all the medicines you take, including prescription and non-prescription medicines, vitamins and herbal supplements.** It is not known if TRADENAME Cream and other medicines can affect each other.

How should I use TRADENAME Cream?

- TRADENAME Cream and PDT treatment is only done by trained doctors.
- You will receive 2 treatments with TRADENAME Cream and PDT 7 days (1 week) apart. Your doctor will check you three months after treatment to see if the treatment worked for you. (See the end of this leaflet for the section “Treatment with TRADENAME Cream and PDT.”)
- TRADENAME Cream is for skin use only. Do not get TRADENAME Cream in your eyes, mouth, or nose. Tell your doctor right away if this happens.

What should I avoid while using TRADENAME Cream?

During the 3 hours that TRADENAME Cream is on your skin:

- Avoid exposure to sunlight or bright indoor light during the 3 hours that TRADENAME Cream is on your skin. Wear a protective hat and clothing if you need to be outside in the sun.
- Avoid exposure to cold temperatures during the 3 hours that TRADENAME Cream is on your skin. Wear warm clothing and keep your treated skin site covered if you are in cold temperatures.

If for some unavoidable reason you are not treated with the lamp you should

- Carefully rinse off the Cream.
- Avoid exposure to sunlight, prolonged or intense light for two days after treatment.

What are the possible side effects of TRADENAME Cream with PDT treatment?

Common side effects of TRADENAME Cream with PDT treatment include the following skin reactions at the treated site:

- burning feeling

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- redness
 - pain
 - stinging
 - swelling
 - crusting, peeling, blisters, bleeding, itching, ulcers
 - infection

Tell your doctor if you get any of these side effects. Your healthcare provider should be able to treat these reactions according to standard treatments for such skin reactions. These reactions usually go away within 10 days of treatment. Redness may last for up to 1 month. If any of your skin reactions get worse and last longer than 3 weeks, call your doctor.

These are not all the side effects of TRADENAME Cream with PDT. Ask your doctor or pharmacist for more information.

General information about TRADENAME Cream

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets.

This leaflet summarizes the most important information about TRADENAME Cream. If you would like more information, talk with your doctor. You can ask your doctor for information about TRADENAME Cream that is written for health professionals.

[Sponsor: Please provide toll-free number and/or website, if available.]

What are the ingredients in TRADENAME Cream?

Active Ingredient: methyl aminolevulinate hydrochloride

Other Ingredients: Glyceryl monostearate, cetostearyl alcohol, poloxyl stearate, cholesterol, oleyl alcohol glycerin, white petrolatum, isopropyl myristate, refined peanut oil, refined almond oil, edetate disodium, methylparaben and propylparaben. The color of the product is cream to pale yellow.

Treatment with TRADENAME Cream and PDT

Your doctor will prepare your skin by gently scraping (debriding) your skin growths before treating with TRADENAME Cream and PDT. A small skin scraper is used to remove scales and crusts and to roughen the surface of any skin growths. This is to help TRADENAME Cream and PDT to reach all parts of the skin growths.



Figure 1: Lesion debridement

TRADENAME Cream is applied to the actinic keratosis skin growths and to a small area of the skin around the growths.



Figure 2: Cream application

The treated skin areas will be covered with a special clear bandage for about 3 hours.

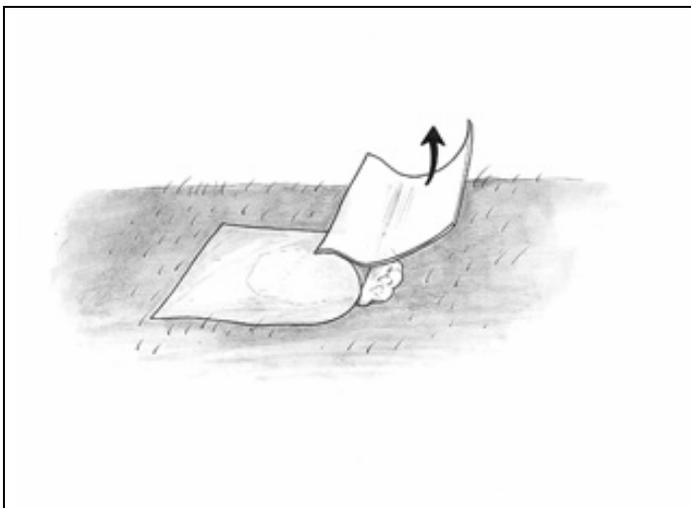


Figure 3: Clear bandage application

During these 3-hours you should avoid exposure of treated area to sunlight or bright indoor light. Exposure to light may make your treated skin area sting or burn. Your treated skin area may turn red or swell (photosensitive reactions). Wear a hat and protective clothes if you are exposed to sunlight during this time. Sunscreens will not help protect your treated skin during this time. In cold weather, your treated skin site should be protected from the cold with warm clothes or you should stay indoors for these 3 hours between the cream and light treatment.

The clear bandage will be removed and the area will be rinsed with a saline solution before the PDT (light) treatment.

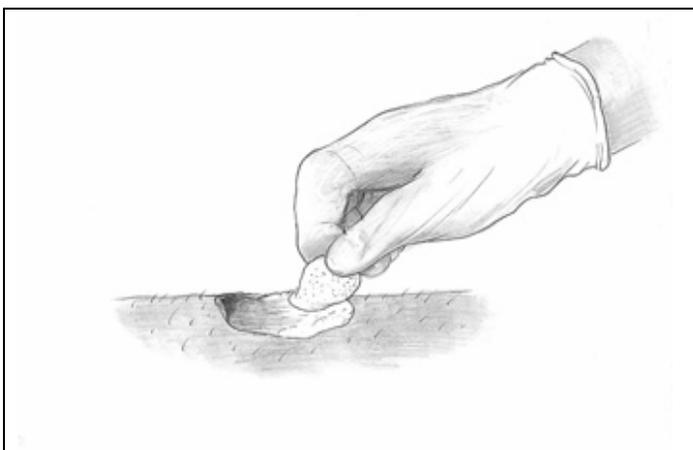


Figure 4: Cream removal

The skin growth will be treated with PDT. PDT lasts about 10 minutes for each area treated with the lamp. You will wear protective goggles to cover your eyes during this part of the treatment.

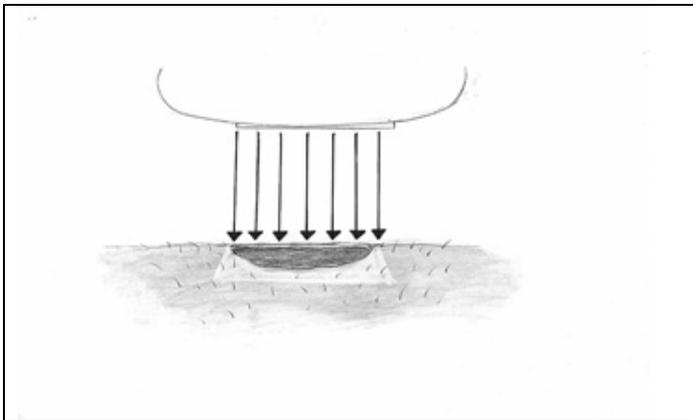


Figure 5: Illumination

More than 1 skin growth may be treated at a time. Your treated skin areas may burn, feel painful, sting, or tingle during light treatment. These symptoms may last for a few hours after the treatment. If you cannot have the light treatment 3 hours after TRADENAME Cream is applied, rinse the cream off your skin and you must protect your skin from sunlight and bright indoor light for 2 days.

This product should only be stored in refrigerators in pharmacies and medical offices.

Rx only

TRADENAME Cream is a registered TRADENAME of PhotoCure ASA.

Sponsor: PhotoCure ASA, Hoffsvveien 48, NO-0377 Oslo, Norway

U.S. Contact: Clementi & Associates, 919 Conestoga Rd., Rosemont, PA 19010

Manufacturer: Penn Pharmaceutical Services Ltd., Tafarnaubach Industrial Estate,
Tredegar, Gwent, NP2 3AA, UK.

<p style="writing-mode: vertical-rl; transform: rotate(180deg);"> TRADENAME Cream 16.8% 2 g NDC xxxx-xxxx-xx </p>	<p>2 g NDC xxxx-xxxx-xx</p> <p style="text-align: center;"> TRADENAME Cream 16.8% <i>(methyl aminolevulinate)</i> </p> <p style="text-align: center;">Must be dispensed and applied by a physician.</p> 			
<p>Each gram contains 210 mg of methyl aminolevulinate hydrochloride (equiv. to 168 mg methyl aminolevulinate), self-emulsifying glyceryl monostearate, cetostearyl alcohol, polyoxyl 40 stearate, methylparaben, propylparaben, edetate disodium, glycerin, white petrolatum, cholesterol, isopropyl myristate, peanut oil, refined almond oil, oleyl alcohol, and purified water.</p> <div style="border: 1px solid black; width: 100px; height: 20px; margin-left: auto; margin-right: auto;">Space for Barcode</div>				
<p><i>Directions for use:</i> See enclosed package insert. <i>Product Package:</i> Keep out of reach of children. For dermatologic use only. Rx only. <i>Storage Conditions:</i> Store refrigerated, 2 - 8 °C (36-46 °F). Use contents within one week after opening.</p> <table border="0" style="width: 100%;"> <tr> <td style="width: 33%; vertical-align: top;"> <p>Marketed by: PhotoCure ASA Hoffsveien 48 N-0377, Oslo, Norway</p> </td> <td style="width: 33%; vertical-align: top;"> <p>USA contact: Clementi - King 161 Washington St. Conshohocken, PA 19428</p> </td> <td style="width: 33%; vertical-align: top;"> <p>Manufactured for PhotoCure ASA by Penn Pharmaceutical Services Ltd.</p> </td> </tr> </table>		<p>Marketed by: PhotoCure ASA Hoffsveien 48 N-0377, Oslo, Norway</p>	<p>USA contact: Clementi - King 161 Washington St. Conshohocken, PA 19428</p>	<p>Manufactured for PhotoCure ASA by Penn Pharmaceutical Services Ltd.</p>
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<p style="writing-mode: vertical-rl; transform: rotate(180deg);"> Lot No.: xxxx Exp.date: xx/xxxx </p>				
	<p>2 g NDC xxxx-xxxx-xx</p> <p style="text-align: center;"> TRADENAME Cream 16.8% <i>(methyl aminolevulinate)</i> </p> <p style="text-align: center;">Must be dispensed and applied by a physician.</p> 			



2g **TRADE NAME**
Cream 16.8%
(methyl aminoclozinate)

Product Package keep out of reach of children. For use only as directed. Do not use if contents are expired.
Storage Conditions: Store refrigerated.

2 - 8 °C (36-46 °F). Use contents within one week after opening.

Must be diagnosed and applied by a physician.
Marketed by PharmCure ASA
Oslo, Norway

