® (aminolevulnic acid hydrochloride) gel, 10% with Nanoemulsion Technology

Ameluz® (aminolevulinic acid hydrochloride) gel, 10% for topical use, is a prescription drug for the lesion-directed and field-directed photodynamic therapy of actinic keratoses of mild- to-moderate severity on the face and scalp with red light, using the **BF-RhodoLED®** lamp.[1]

BF-RhodoLED® with Red Light

BF-RhodoLED® is an LED lamp emitting red light at a wavelength of 635 nm. It provides high energy efficiency plus controlled and constant light emission at the desired wavelength for the use in photodynamic therapy with the photosensitizer Ameluz®.

The combination of the unique nanoemulsion formulation of **Ameluz®** and the **BF-RhodoLED®** lamp provides clinically proven high clearance rates.

1 Ameluz® Prescribing Information . For Ameluz® full prescribing information and BF-RhodoLED® user manual please refer to: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=650daa9f-aeec-49ce-95b9-5fa20b988afd

Important Safety Information

AMELUZ® (aminolevulinic acid hydrochloride) gel, 10% with BF-RhodoLED® lamp

AMELUZ®, containing 10% aminolevulinic acid hydrochloride, is a non-sterile gel formulation for topical use only. Not for ophthalmic, oral, or intravaginal use.

AMELUZ®, in conjunction with lesion preparation, is only to be administered by a health care provider. Photodynamic therapy with AMELUZ® involves preparation of lesions, application of the product, occlusion and illumination with BF-RhodoLED®. The application area should not exceed 20 cm^2 and no more than 2 grams of AMELUZ® (one tube) should be used at one time. Lesions that have not completely resolved shall be retreated 3 months after the initial treatment. Refer to BF-RhodoLED® user manual for detailed lamp safety and operating instructions. Both patient and medical personnel conducting the PDT should adhere to all safety instructions.

Ameluz® shall not be used by persons who have known hypersensitivity to porphyrins or any of the components of AMELUZ®, which includes soybean phosphatidylcholine. Ameluz® should also not be used for patients who have porphyria or photodermatoses.

Transient Amnestic Episodes have been reported during postmarketing use of AMELUZ® in combination with photodynamic therapy (PDT). If patients experience amnesia or confusion, discontinue treatment. Advise them to contact the healthcare provider if the patient develops amnesia after treatment.

Eye exposure to the red light of the BF-RhodoLED® lamp during PDT must be prevented by protective eyewear. Direct staring into the light source must be avoided. AMELUZ® increases photosensitivity. Patients should avoid sunlight, prolonged or intense light (e.g., tanning beds, sun lamps) on lesions and surrounding skin treated with AMELUZ® for approximately 48 hours following treatment whether exposed to illumination or not.

AMELUZ® has not been tested on patients with inherited or acquired coagulation disorders. Special care should be taken to avoid bleeding during lesion preparation in such patients. Any bleeding must be stopped before application of the gel. AMELUZ® should not be used on mucous membranes or in the eyes.

Local skin reactions at the application site were observed in about 99.5% of subjects treated with AMELUZ® and narrow spectrum lamps. The very common adverse reactions (≥10%) during and after PDT were application site erythema, pain/burning, irritation, edema, pruritus, exfoliation, scab, induration, and vesicles. Most adverse reactions occurred during illumination or shortly afterwards, were generally of mild or moderate intensity, and lasted for 1 to 4 days in most cases; in some cases, however, they persisted for 1 to 2 weeks or even longer. Severe pain/burning occurred in up to 30% of treatments.

There have been no formal studies of the interaction of AMELUZ® with other drugs. Concomitant use of the following photosensitizing medications may increase the phototoxic reactions after PDT: St. John's wort, griseofulvin, thiazide diuretics, sulfonylureas, phenothiazines, sulphonamides, quinolones, and tetracyclines.

There are no available data on AMELUZ® use in pregnant women to inform a drug associated risk. No data are available regarding the presence of aminolevulinic acid in human milk, the effects of aminolevulinic acid on the breastfed infant or on milk production. Safety and effectiveness in pediatric patients below the age of 18 have not been established as AK is not a condition generally seen in the pediatric population. No overall differences in safety or effectiveness were observed between elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Please read the US Full Prescribing Information for Ameluz® and/or US User Manual of BF-RhodoLED® lamp available together at https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=650daa9f-aeec-49ce-95b9-5fa20b988afd.

You are encouraged to report side effects of Ameluz®. Please contact Biofrontera Inc. at 1-844-829-7434 or FDA at 1-800-332-1088 or www.fda.gov/medwatch.

Important Safety Information

Active Ingredient (in each tube): AMELUZ® (aminolevulinic acid hydrochloride)

Purpose: Photosensitizing agent

Uses: AMELUZ® gel, a porphyrin precursor, in combination with photodynamic therapy using BF-RhodoLED® lamp, is used for lesion-directed and field-directed treatment of actinic keratoses of mild-to-moderate severity on the face and scalp.

Warnings:

Do not use if you have a:

- Known hypersensitivity to photoactive substances known as porphyrins.
- Known hypersensitivity to soybeans
- Known hypersensitivity to any component of AMELUZ®.

Ask your health care provider before use if you have:

- Porphyria (hereditary disease that is characterized by abnormal production of a red blood pigment called heme).
- Photodermatoses (skin conditions caused by or made worse by exposure to light or ultraviolet radiation).

When using this product:

- **Transient Amnestic Episodes:** Photodynamic therapy may cause transient amnestic episodes (temporary loss of memory). If observed, the therapy must be stopped immediately. If observed after treatment, contact your health care provider.
- **Risk of Eye Injury:** Patients and health care providers must wear protective eyewear while operating BF-RhodoLED®
- **Photosensitivity:** Avoid sun exposure on the treated lesion sites and surrounding skin for approximately 48 hours following treatment
- **Risk of Bleeding:** Special care should be taken to avoid bleeding during lesion preparation in patients with inherited or acquired coagulation disorders. Bleeding must be stopped before application of the gel.

- **Ophthalmic Adverse Reactions:** Avoid applying AMELUZ® into the eyes. Wash eyes with water in case of accidental contact.
- **Mucous Membrane Irritation:** Avoid direct contact of AMELUZ® with the mucous membranes. Wash with water in case of accidental contact.
- **Concomitant use** of the following medications may increase the intensity of adverse reactions after light exposure related to photodynamic therapy: St. John's wort, griseofulvin, thiazide diuretics, sulfonylureas, phenothiazines, sulphonamides, quinolones, and tetracyclines.

Most common adverse reactions were:

- skin reddening
- scaling of the skin
- pain/burning
- scabbing
- irritation
- hardening
- swelling
- blistering
- itching

Most side effects occurred during illumination or shortly afterwards, were generally of mild or moderate intensity, and lasted for 1 to 4 days in most cases; in some cases they persisted for 1 to 2 weeks or even longer.

Pregnancy Warning: There is no available data on AMELUZ® use in pregnant women to inform a drug associated risk.

Lactation Warning: There is no available data regarding the presence of the active ingredient (aminolevulinic acid hydrochloride) in human milk, or the effects of aminolevulinic acid hydrochloride on the breastfed infant or on milk production.

Pediatric Warning: Safety and effectiveness in pediatric patients below the age of 18 has not been established.

Geriatric Warning: No overall differences in safety or effectiveness were observed between older (65 years and older) and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Directions:

- AMELUZ® is administered only by a health care provider.
- AMELUZ® is for topical use only.
- Photodynamic therapy with AMELUZ® involves preparation of lesions, application of the product, occlusion and illumination with BF-RhodoLED®
- Retreat lesions that have not completely resolved 3 months after the initial treatment.

Inactive Ingredients: xanthan gum, soybean phosphatidylcholine, polysorbate 80, medium-chain triglycerides, isopropyl alcohol, dibasic sodium phosphate, monobasic sodium phosphate, propylene glycol, sodium benzoate and purified water.

Other Information: Store in a refrigerator, 2°C – 8°C (36°F – 46°F). Excursions permitted to 15°C – 30°C (59°F– 86°F). The risk information provided here is not comprehensive.

To learn more, talk about AMELUZ® with your health care provider. The FDA approved product labeling can be found at https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=650daa9f-aeec-49ce-95b9-5fa20b988afd.

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