

LOVE HAVING FUN IN THE SUN?



**Actinic keratosis (AK)
skin lesions from
sun damage may lead
to skin cancer.^{1,2,†}**

INDICATION

AMELUZ[®] (aminolevulinic acid hydrochloride) topical gel, 10%, a porphyrin precursor, in combination with photodynamic therapy using BF-RhodoLED[®] or RhodoLED[®] XL lamp, is indicated for lesion-directed and field-directed treatment of actinic keratoses of mild-to-moderate severity on the face and scalp.

AMELUZ[®]
[aminolevulinic acid
HCl] topical gel, 10%
& **RhodoLED[®]**



[†]AK lesions are premalignant and may lead to squamous cell carcinoma (SCC)—the second most common skin cancer.¹⁻³

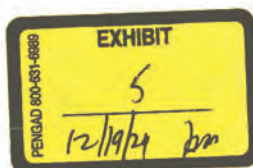
IMPORTANT SAFETY INFORMATION

AMELUZ[®] (aminolevulinic acid hydrochloride), topical gel, 10%

Purpose: Photosensitizing agent

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

Please see Important Safety Information throughout.



Sun-ITC-0168513

IPR2024-01312

Biofrontera Inc. et al v. Sun Pharmaceutical et al

Sun Pharmaceutical's Exhibit 2041

EX2041, Page 1

About actinic keratosis (AK)

What is AK?

- AKs are premalignant lesions of the skin that, when left untreated, can potentially develop into squamous cell carcinoma (SCC)—the second most common form of skin cancer^{2,4}
- AK is primarily caused by chronic sun damage and generally affects people aged 40 or older⁴

What are the signs of AK?

- AK lesions typically form on areas of the body most exposed to the sun—such as the face and scalp^{2,3}
- AK lesions can have a different clinical appearance^{2,3}
 - They are frequently scaly, range from normal skin color to reddish brown, and can be identified by sight and/or touch^{2,3}
- Because AKs originate in the skin layers below the visible surface, lesions can be present but still difficult to spot^{1,3,5}
- For every visible lesion within a sun-damaged area, there are likely other AKs that are easier felt than seen^{1,2,5}
 - Together, these lesions are considered a field^{1,3,5}

**For every AK lesion you can see,
there are likely more lesions that you can feel
but may be difficult to see.^{1,6}**



IMPORTANT SAFETY INFORMATION (selected)

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[®].

AMELUZ[®]
[aminolevulinic acid
HCl] topical gel, 10%
& RhodoLED[®]

2

IMPORTANT SAFETY INFORMATION (selected)

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).

Please see Important Safety Information throughout.

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Sun-ITC-0168514

AKs can indicate a potential unseen threat^{1-3,†}

Could you be at risk?

[†]More than a third of the general population over the age of 51 has at least 1 AK lesion that may be found on their head and scalp.⁷

- You may be at risk for AKs if you have:
 - Years of unprotected sun exposure⁸
 - Fair skin/light skin tones (especially natural blondes or redheads)³



AK lesions
on the face
and scalp

TALK TO YOUR HEALTHCARE PROVIDER
IF YOU THINK YOU HAVE AK

IMPORTANT SAFETY INFORMATION (selected)

When using this product:

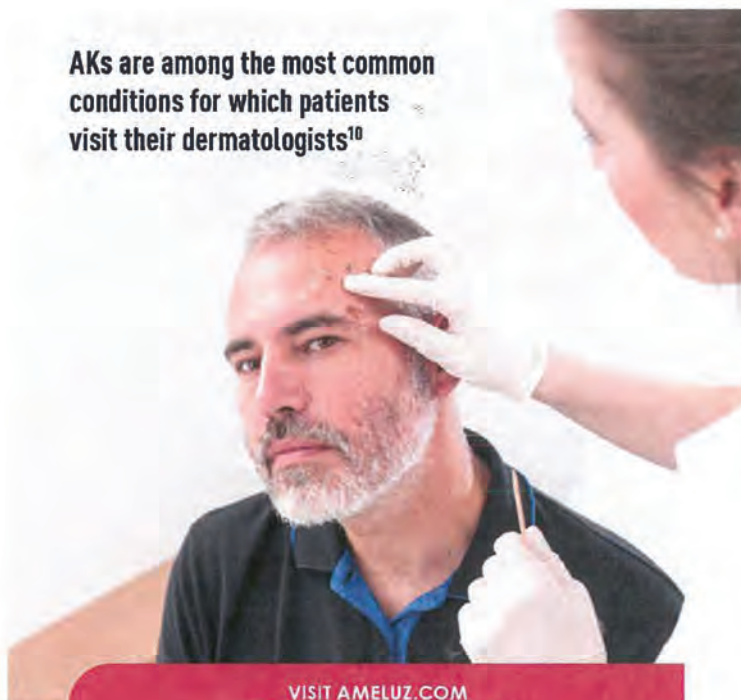
- **Ophthalmic Adverse Reactions:** Avoid applying AMELUZ[®] into the eyes. Wash eyes with water in case of accidental contact.
- **Mucous Membrane Irritation:** Avoid direct contact of AMELUZ[®] with the mucous membranes. Wash with water in case of accidental contact.

AMELUZ[®]
[aminolevulinic acid
HCl] topical gel, 10%
& RhodoLED[®]

Why should AK be treated?

- AKs increase your chance of developing a skin cancer called SCC^{2,7}
 - If left untreated, AKs of any severity can develop into a skin cancer called SCC. SCC is the second most common form of skin cancer^{2,9}

AKs are among the most common conditions for which patients visit their dermatologists¹⁰



VISIT AMELUZ.COM
TO LEARN MORE ABOUT AK

IMPORTANT SAFETY INFORMATION (selected)

When using this product:

- **Risk of Eye Injury:** Patients and health care providers must wear protective eyewear while operating BF-RhodoLED[®] or RhodoLED[®] XL.
- **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.

Please see Important Safety Information throughout.

Sun-ITC-0168515

Choose a therapy that treats the field^{11,†}

[†]AMELUZ[®] with BF-RhodoLED[®] or RhodoLED[®] XL is indicated for the lesion-directed and field-directed treatment of actinic keratoses of mild-to-moderate severity on the face and scalp.¹¹

AMELUZ[®] (aminolevulinic acid HCl) topical gel, 10% delivers results

In a clinical study of photodynamic therapy (PDT)
with AMELUZ[®] and BF-RhodoLED[®] (N=55)

91% of patients were 100%
cleared after 12 weeks[‡]

Placebo (12 weeks after the last treatment) (N=32)

22% of patients achieved 100%
clearance with placebo[‡]

[‡]Results from a phase 3 clinical trial with 87 patients presenting 4 to 8 mild-to-moderate AK lesions on the face/forehead and/or bald scalp treated with AMELUZ[®] or placebo and the BF-RhodoLED[®] lamp. Patients received a maximum of 2 PDTs and were examined 12 weeks and 12 months after the last treatment.^{11,12}

RhodoLED[®] XL and BF-RhodoLED[®] are approved as interchangeable light sources.

IMPORTANT SAFETY INFORMATION (selected)

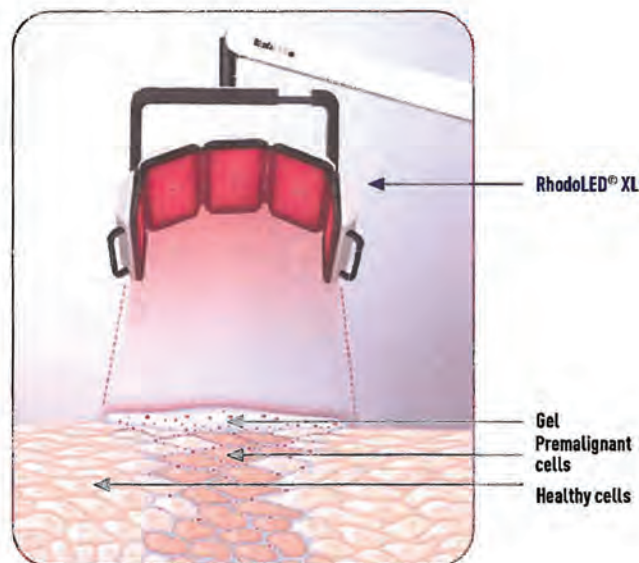
When using this product:

- **Allergic reactions:** AMELUZ[®] may cause allergic reactions before photodynamic therapy. AMELUZ[®] should be washed off and suitable treatment started. The allergic reactions can potentially include severe courses like sudden, severe allergic reaction with breathing difficulty, swelling, lightheadedness, fast heartbeat, sweating and loss of consciousness.
- **Transient Amnesic Episodes:** Photodynamic therapy may cause transient amnesic episodes (temporary loss of memory). If observed, the therapy must be stopped immediately. If observed after treatment, contact your health care provider.

AMELUZ[®]
[aminolevulinic acid
HCl] topical gel, 10%
& RhodoLED[®]

How AMELUZ[®] and RhodoLED[®] XL work together

AMELUZ[®] penetrates the epidermis (top layer) of your skin to reach the premalignant cells that cause AK. Its active ingredient is then converted into the light-activated agent called PpIX. The red light of BF-RhodoLED[®] or RhodoLED[®] XL illuminates these cells and activates the agent, setting off a reaction that destroys premalignant cells that cause AK—while leaving healthy skin cells mostly intact.^{7,11,13}



IMPORTANT SAFETY INFORMATION (selected)

When using this product:

- **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, sulfonyleureas, phenothiazines, sulphonamides, quinolones, and tetracyclines.

Please see Important Safety Information throughout.

The treatment process



Your healthcare provider will guide you through therapy with AMELUZ® (aminolevulinic acid HCl) topical gel, 10% and RhodoLED® XL

IMPORTANT SAFETY INFORMATION (selected)

When using this product:

- **Photosensitivity:** Avoid sun exposure on the treated lesion sites and surrounding skin for approximately 48 hours following treatment.
- **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.

AMELUZ®
[aminolevulinic acid
HCl] topical gel, 10%
& RhodoLED®

1

Your healthcare provider will prepare the skin and apply AMELUZ® (application area should not exceed 20 cm²).

2

After waiting the recommended time (3 hours) to allow AMELUZ® gel to penetrate the targeted cells, your healthcare provider will illuminate the area with RhodoLED® XL lamp for 13.5 minutes.

Your healthcare provider's staff will provide protective eyewear that must be worn during your RhodoLED® XL lamp treatment.



SAFETY

Adverse reactions and the safety of PDT with AMELUZ®

Most common side effects at the application site were:

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

Most side effects occurred during illumination or shortly afterwards, were generally of mild to 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.

The healing process: before and after patient images

**BEFORE
TREATMENT†**



**3 DAYS AFTER
TREATMENT†**



**14 DAYS AFTER
TREATMENT†**



†Individual results may vary. These patient photos are from a PDT treatment utilizing the BF-RhodoLED[®]. RhodoLED[®] XL and BF-RhodoLED[®] are approved as interchangeable light sources.

IMPORTANT SAFETY INFORMATION (selected)

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[®] or RhodoLED[®] XL.
- Retreat lesions that have not completely resolved 3 months after the initial treatment.

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**BEFORE
TREATMENT†**



**3 DAYS AFTER
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**11 DAYS AFTER
TREATMENT†**



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After red light† PDT treatment

For 48 hours after treatment, you should avoid exposing treated areas of the skin to sunlight and artificial sources of UV radiation (e.g., tanning beds or sunlamps).

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Notes

This image shows a single page of white paper with horizontal blue ruling lines. The lines are evenly spaced and run across the width of the page. There are no margins, text, or other markings on the paper.

AMELUZ[®]
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INDICATION AND IMPORTANT SAFETY INFORMATION

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Most common side effects at the application site were:

- | | | |
|-----------------------|--------------|--------------|
| • skin reddening | • scabbing | • swelling |
| • scaling of the skin | • irritation | • blistering |
| • pain/burning | • hardening | • 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.

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Inactive Ingredients:

xanthan gum, soybean phosphatidylcholine, polysorbate 80, medium-chain triglycerides, isopropyl alcohol, dibasic sodium phosphate, monobasic sodium phosphate, 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://www.ameluz.com/PI>.
- 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.

LOVE HAVING FUN IN THE SUN?

Don't delay treating
your AKs caused by
sun damage.^{2,3}



Visit [AMELUZ.com](https://www.ame-luz.com)
to learn more about
actinic keratosis.

ASK YOUR HEALTHCARE PROVIDER ABOUT
PDT WITH AMELUZ® (aminolevulinic acid
HCl) topical gel, 10% and RhodoLED® XL

AMELUZ®
[aminolevulinic acid
HCl] topical gel, 10%
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IMPORTANT SAFETY INFORMATION (selected)

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References: 1. Berman B, Amini S, Valins W, Block S. Pharmacotherapy of actinic keratosis. *Expert Opin Pharmacother*. 2009;10(18):3015-3031. 2. Reinhold U. A review of BF-200 ALA for the photodynamic treatment of mild-to-moderate actinic keratosis. *Future Oncol*. 2017;13(27):2413-2428. 3. Stockfleth E. The importance of treating the field in actinic keratosis. *J Eur Acad Dermatol Venerol*. 2017;31(Suppl 2):8-11. 4. Actinic keratosis risk factors. Skin Cancer Foundation. Updated January 2022. Accessed July 11, 2023. <https://www.skincancer.org/skin-cancer-information/actinic-keratosis/causes-and-risk-factors>. 5. Cockerell CJ. Histopathology of incipient intraepidermal squamous cell carcinoma ("actinic keratosis"). *J Am Acad Dermatol*. 2000;42(1 Pt 2):11-17. 6. Olsen EA, Abernethy L, Kulp-Shorten C, et al. A double-blind, vehicle-controlled study evaluating masoprocol cream in the treatment of actinic keratoses on the head and neck. *J Am Acad Dermatol*. 1991;24:738-43. 7. Flohil C, van der Leest R, Dowlatshahi E, Hofman A, de Vries E, Nijsten T. Prevalence of actinic keratosis and its risk factors in the general population: the Rotterdam Study. *J Invest Dermatol*. 2013;133(8):1971-1978. 8. Cancer.net Editorial Board. Skin cancer (non-melanoma): risk factors and prevention. Cancer.net. February 2022. Accessed October 13, 2023. <https://www.cancer.net/cancer-types/skin-cancer-non-melanoma/risk-factors-and-prevention>. 9. Fernández-Figueras MT, Carrato C, Sáenz X, et al. Actinic keratosis with atypical basal cells (AKI) is the most common lesion associated with invasive squamous cell carcinoma of the skin. *J Eur Acad Dermatol Venerol*. 2015;29:991-997. 10. Grada A, Muddasani S, Fleischer AB Jr, Feldman SR, Peck GM. Trends in office visits for the five most common skin diseases in the United States. *J Clin Aesthet Dermatol*. 2022;15(5):E82-E86. 11. AMELUZ® [prescribing information]. Woburn, MA: Biofrontera Inc; 2021. 12. Reinhold U, Dirschka T, Ostendorf R, et al. A randomized, double-blind, phase III, multicentre study to evaluate the safety and efficacy of BF-200 ALA (Ameluz) vs. placebo in the field-directed treatment of mild-to-moderate actinic keratosis with photodynamic therapy (PDT) when using the BF-RhodoLED lamp. *Br J Dermatol*. 2016;175(4):696-705. 13. Maisch T, Santarelli F, Schreml S, et al. Fluorescence induction of protoporphyrin IX by a new 5-aminolevulinic acid nanoemulsion used for photodynamic therapy in a full-thickness ex vivo skin model. *Exp Dermatol*. 2010;19(8):e302-e305.

Biofrontera

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