**Important Risk Information**

The Levulan® Kerastick® for Topical Solution plus blue light illumination using the BLU-U® blue light photodynamic therapy illuminator is indicated for the treatment of minimally to moderately thick actinic keratoses (grade 1 or 2) of the face or scalp. The most common adverse events include scaling/crusting, hypo/hyperpigmentation, itching, stinging and/or burning, erythema and edema. Severe stinging and/or burning was reported by at least 50% of the patients. Contraindicated in patients with cutaneous photosensitivity at wavelengths of 400-450 nm, porphyria, or known allergies to porphyrins, and in patients with known sensitivity to any of the components of the Levulan Kerastick for Topical Solution.

The BLU-U® is generally indicated to treat dermatological indications. The BLU-U® is specifically indicated to treat moderate inflammatory acne vulgaris.

References:

Please see full prescribing information attached.
BLU-U® blue light is optimized for PDT in unique and patented ways

BLU-U blue light penetrates up to 2 mm of skin:
- The epidermis is less than 2 mm thick.
- BLU-U light alone is effective and FDA cleared for moderate inflammatory acne vulgaris.
- When using BLU-U for acne, do not use this device with photosensitizing drugs.

BLU-U output is matched to the highest absorption peak of PpIX:
- BLU-U peak wavelength occurs at 417 ± 5 nm.
- The maximum absorption peak for porphyrins occurs at 410 nm.

BLU-U blue light has enough energy to produce a photodynamic response:
- Maximum clinical response with Levulan® Kerastick® (aminolevulinic acid HCl) Topical Solution, 20% is produced at 10 J/cm² at 1000 seconds.

BLU-U is designed to deliver a uniform light dose and stable wavelength to an entire treatment area:
- The large U-shaped design and tube spacing:
  - allows for the treatment of an entire face or scalp.
  - delivers consistent light dose all the way to the treatment “edges.”
- The BLU-U is designed with a stainless steel reflective wall behind the tubes to minimize loss of light within the U-shaped treatment area.
- Light tubes are spaced much closer together at the top and bottom than in the middle to compensate for light falloff in this area.

BLU-U is designed to deliver a consistent light dose:
- The phosphor in the fluorescent tubes produces a very stable and cost-effective wavelength.
- The BLU-U contains a microprocessor that continuously monitors and adjusts light output to maintain dose stability from the first to the last treatment.

Use with eyewear that blocks light of at least 500 nm and shorter with an optical density of two or greater.
**INDICATIONS AND USAGE**

The LEVULAN KERASTICK for Topical Solution, 20%, plus blue light illumination using the BLU-U Blue Light Photodynamic Therapy Illuminator is indicated for the treatment of minimally to moderately thick actinic keratoses (Grades 1 or 2, see table 2 for definition) of the face or scalp.

**CONTRAINDICATIONS**

The LEVULAN KERASTICK for Topical Solution, 20%, plus blue light illumination using the BLU-U Blue Light Photodynamic Therapy Illuminator is contraindicated in patients with cutaneous photosensitivity or cutaneous photosensitivity reactions to 5-aminolevulinic acid (5-ALA). Sensitivity to any of the components of the LEVULAN KERASTICK for Topical Solution, 20%.

**WARNINGS**

The LEVULAN KERASTICK for Topical Solution, 20%, contains alcohol and is intended for topical use only. Do not apply to the eyes or to mucous membranes. Excessive irritation may be experienced if this product is applied under occlusion.

**Precautions**

During the time period between the application of LEVULAN KERASTICK Topical Solution, 20%, and exposure to activating light from the BLU-U Blue Light Photodynamic Therapy Illuminator, the treatment site will become photosensitive. After LEVULAN KERASTICK Topical Solution, 20%, application, patients should avoid exposure to sunlight or to keratotic treatment sites to sunlight or bright indoor light (e.g., examination lamps, operating room lamps, tanning beds, or lights of close proximity) during the period prior to blue light treatment. Exposure may result in a stinging and/or burning sensation and may cause erythema, desquamation, or other 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 or by applying a broad-spectrum sunscreen with a sun protection factor (SPF) of 30 or higher.

**Pharmacology**

No assessment of effects of ALA HCl on fertility or reproductive function. Other studies have documented oxidative DNA damage in vivo and in vitro as a result of ALA exposure.

**Nursing Mothers**

The levels of ALA or its metabolites in the milk of mothers treated with LEVULAN KERASTICK Topical Solution, 20% have not been measured. Because many drugs are excreted in human milk, caution should be exercised when LEVULAN KERASTICK Topical Solution, 20% is administered to a nursing woman.

**Adverse Reactions**

In Phase 3 studies, no non-cutaneous adverse events were found to be consistently associated with LEVULAN KERASTICK Topical Solution, 20% application followed by blue light exposure.

Diffuse Photodynamic Therapy Response: The constellation of transient local symptoms of stinging and/or burning, itching, erythema and edema as a result of LEVULAN KERASTICK Topical Solution, 20% plus BLU-U treatment was observed in all clinical studies of LEVULAN KERASTICK Topical Solution, 20% Photodynamic Therapy for actinic keratosis treatment. Stinging and/or burning subsided between 1 minute and 24 hours after the BLU-U Blue Light Photodynamic Therapy Illuminator was turned off, and appeared qualitatively similar to the perceived pain with phototoxic photopropaphyla upon exposure to sunlight. There was no clear drug dose or light dose dependent change in the incidence or severity of stinging and/or burning.

In Phase 3 trials, the sensation of stinging and/or burning appeared to reach a plateau at 6 minutes into the treatment. Severe stinging and/or burning of one or more lesions being treated was reported by at least 50% of the patients at some time during treatment. The majority of patients reported that all lesions treated exhibited at least slight stings and/or burning. Less than 3% of patients discontinued light treatment due to stinging and/or burning.

The most common changes in lesion appearance after LEVULAN KERASTICK Topical Solution, 20% Photodynamic Therapy were erythema and edema. In 99% of active treatment patients, some or all lesions were erythematous shortly after treatment, while in 79% of vehicle treatment patients, some or all lesions were edematous. In 35% of active treatment patients, some or all lesions were edematous, while no vehicle-treated patients had edematous lesions. Both erythema and edema resolved to baseline or improved by 4 weeks after therapy. LEVULAN KERASTICK Topical Solution, 20% application to photosensitized perilesional skin resulted in photosensitization of photosensitized skin and in a photodynamic response. (See Precautions).

**TABLE 1 Post-PDT Cutaneous Adverse Experiences - ALA-018/019**

<table>
<thead>
<tr>
<th>Difficulty</th>
<th>Measure</th>
<th>LEVULAN (n=139) %</th>
<th>Vehicle (n=41) %</th>
<th>Mean %</th>
<th>SE %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
<tr>
<td>Pain</td>
<td>71%</td>
<td>1%</td>
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<td>0%</td>
<td>0%</td>
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<tr>
<td>Tenderness</td>
<td>4%</td>
<td>14%</td>
<td>7%</td>
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<tr>
<td>Erythema</td>
<td>6%</td>
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<td>Lichenoid</td>
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<tr>
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</tr>
</tbody>
</table>

**OVERDOSAGE**

LEVULAN KERASTICK Topical Solution Overdose: LEVULAN KERASTICK Topical Solution, 20% overdose has not been reported. In the unlikely event that the drug is ingested, monitoring and supportive care are recommended. The patient should be advised to avoid incidental exposure to intense light sources for at least 40 hours. The consequences of exceeding the recommended topical dosage are unknown.

**BLU-U Light Overdose:** There is no information on overdose of blue light from the BLU-U Blue Light Photodynamic Therapy Illuminator following LEVULAN KERASTICK Topical Solution, 20% application.

**The LEVULAN KERASTICK® phototherapeutic system is approved for use with the LEVULAN® 5-aminolevulinic acid (5-ALA) Topical Solution, 20% for photodynamic therapy.**