# Abbreviated Drug Review

**Trade Name (generic)**

Levulan Kerastick (aminolevulinic acid HCl) for Topical Solution, 20% | Indication not funded

**Indications**

- Aminolevulinic acid (AA) topical solution plus BLU-U Blue Light Photodynamic Therapy Illuminator is indicated for the treatment of minimally to moderately thick actinic keratosis (AK) of the face or scalp.

**Dosage**

- Apply 20% topical solution twice to AK lesions on face or scalp (not both simultaneously), and then, 14 to 18 hours later, illuminate lesions with the BLU-U illuminator; unresolved lesions may be retreated in 8 weeks. Must be applied by qualified clinician.

**Background**

- AA 20% topical solution plus BLU-U illumination has been prescribed in the U.S. since 1999 for minimally to moderately thick AK of the face or scalp.
- AA is a prodrug metabolized to protoporphyrin IX (PpIX), a photoactive compound that accumulates in the skin. Reactive oxygen species, which develop when oxygen is in the presence of photoactivated PpIX, destroy cells.
- Off-label uses of AA have included the treatment of basal cell carcinoma, Bowen's disease, and anogenital warts.

**Efficacy**

Two identically designed, randomized, multicenter, investigator-blinded, vehicle-controlled, phase 3 clinical trials (ALA-018, ALA-019) evaluated the efficacy of AA 20% gel plus BLU-U illumination vs vehicle plus BLU-U. The studies randomized (3:1) subjects (n=243 total) who had 4 to 15 Grade 1 (slightly palpable) or Grade 2 (moderately thick) AK lesions on the face or on the scalp. Subjects ranged from 34 to 89 years old (mean 66 years), and most subjects had fair skin with Fitzpatrick skin types I, II, or III (scale I to VI). About 85% of subjects were male, and all were Caucasian. The treatment regimen included two applications of AA then illumination with BLU-U (1000 seconds for a nominal exposure of 10 J/cm$^2$) 14 to 18 hours later. The primary endpoint was percent of patients with complete clearance of lesions 8 weeks after treatment. Results were analyzed with intent-to-treat analysis with missing data imputed using last observation carried forward.

| | ALA-018 | | | | ALA-019 | | | |
|---|---|---|---|---|---|---|---|---|
| Lesion location | AA (n=88) | Vehicle (n=29) | Risk difference (95% CI), p-value | NNT | AA (n=93) | Vehicle (n=33) | Risk difference (95% CI), p-value | NNT |
| Face | 68% (n=72) | 10% (n=21) | 58% (43 to 76%), p<0.001 | 2 | 70% (n=67) | 21% (n=20) | 49% (28 to 71%) p<0.01 | 2 |
| Scalp | 69% (n=16) | 25% (n=8) | 44% (6 to 81%), p=0.099 | NS | 46% (n=26) | 0% (n=13) | 46% (27 to 65%), p<0.01 | 3 |

**Safety**

**Common adverse reactions:** Erythema, edema, stinging/burning, scaling/crusting, hypo/hyperpigmentation, itching, erosion, wheal/flare, vesiculation, ulceration, bleeding/ hemorrhage, pain, pustules, tenderness, scabbing, dysesthesia, skin disorder not otherwise specified

**Contraindications:** Patients with cutaneous photosensitivity at wavelengths of 400 to 450 nm, porphyria or porphyrins allergies, sensitivity to Levulan components

**Warnings and precautions:** Protect treated lesions from bright indoor light and sunlight until BLU-U treatment or ≥40 hours after AA application; sunscreen does not protect against photosensitivity reactions; perform AA application by a qualified clinician; do not apply AA to eyes, mucous membranes, or perilesional skin; applying AA under occlusion may cause excessive irritation; AA has not been tested in patients who are <18 years old or who have coagulation defects; concomitant use of other known photosensitizing agents (e.g., thiazide diuretics, sulfonylureas) might increase the photosensitivity reaction of AA-treated AK; use AA cautiously in nursing mothers; use AA in pregnant women only if clearly needed

**Evidence Gaps/Limitations**

No studies found to support evidence for use in the treatment of Oregon Health Plan (OHP) funded conditions or co-morbidities.

**Recommendation**

Restrict use for OHP-funded conditions through Prior Authorization.

**References**

1. Levulan (aminolevulinic acid hydrochloride) [prescribing information]. Wilmington, MA: DUSA Pharmaceuticals; March 2010.
2. Center for Drug Evaluation and Research. Medical Review: Application number 20-965. http://www.accessdata.fda.gov/scripts/cder/drugsatfda/. Accessed March 2, 2017.

Author: Sherri Willard, PharmD

May 2017