Abbreviated Drug Review

Trade Name (generic)	
Ameluz (aminolevulinic acid hydrochloride) gel, 10%	Indication not funded

Indications

- Aminolevulinic acid (AA) gel plus BF-RhodoLED (BF-R) lamp is indicated for lesion- and field-directed treatment of mild-to-moderate actinic keratosis (AK) on the face and scalp.

Dosage

- 10% gel applied topically, 1 mm thick by a health care provider to a single or field of AK lesions (not to exceed an area of 20 cm^2 and 2 grams of gel [one tube] at any one time), followed by occlusion for 3 hours, and then by red light photodynamic therapy (PDT) with the BF-R lamp; retreated in 3 months if not resolved

Background

- AA has been prescribed as a 20% topical solution (Levulan Kerastick) plus BLU-U Blue Light PDT Illuminator 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. Upon photoactivation of PpIX, reactive oxygen species are formed which destroy cells within the AK lesion.
- AK lesions are caused by exposure to ultraviolet light and are more common in patients with fair skin (Fitzpatrick skin types I-III). In a small percentage of patients, lesions may progress to squamous cell carcinoma.

Efficacy

According to labeling, three randomized, multicenter, double-blind, vehicle-controlled clinical trials evaluated the efficacy of AA 10% gel plus PDT with a red light lamp. Patients (n=212 total) had 4 to 8 mild to moderate AK lesions on the face and/or bald scalp, ranged from 49 to 87 years old (mean 71 years), and most had Fitzpatrick skin types I, II, or III (scale I to VI). About 86% were male, and all were Caucasian. The treatment regimen included lesion preparation with alcohol, AA application, occlusion for 3 hours, removal of residual gel, then illumination with red light source (about 630 nm peak; 37 J/cm^2 dose) in Trials 1 and 2 or BF-R (635 nm; 37 J/cm^2) in Trial 3. Multiple light sources were used in Trial 1 and 2, and the published subgroup analyses by light source did not include comparative statistical analyses or sufficient data to confirm data presented in labeling. Patients without complete clearance of lesions after 12 weeks received a second course of identical therapy (42% of patients). Results for the primary endpoint (patients with complete clearance at 12 weeks after the last PDT) for AA versus vehicle, respectively, were:

Trial 1: 85% (n=106/125) vs. 13% (n=5/39); NNT=2 **Trial 2:** 84% (n=27/32) vs. 13% (n=2/16); NNT=2 **Trial 3:** 91% (n=50/55) vs. 22% (n=7/32); NNT=2

Safety

- **Contraindications:** Porphyria, photodermatoses, hypersensitivity to porphyrins or any AA gel component (including soybean phosphatidylcholine)
- **Warnings and precautions:** Risk of eye injury with BF-R lamp (wear eye protection); photosensitivity (protect treated areas from sunlight and prolonged, intense light for 48 hours); photoreaction with other photosensitizing agents; bleeding in patients with coagulation disorders; ophthalmic and mucous membrane reactions (avoid gel contact in these areas)
- **Common adverse reactions:** Application site reactions (e.g. erythema, pain/burning, irritation, edema, pruritus, exfoliation, scab, or induration), chills, headache, or skin exfoliation
- **Specific populations:** Safety in patients less than 18 years of age is not established
- **Toxicology:** May cause genotoxic effects

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 to OHP-funded conditions through Prior Authorization for physician administered and pharmacy claims.

References

1. Ameluz (aminolevulinic acid hydrochloride) [prescribing information]. Wakefield, MA: Biofrontera Inc; May 2016
2. Dirschka T, Radny P, Dominicus R, et al. Photodynamic therapy with BF-200 ALA for the treatment of actinic keratosis: results of a multicentre, randomized, observer-blind phase III study in comparison with a registered methyl-5-aminolaevulinate cream and placebo. *Br J of Dermatol*. 2012;166(1):137-146.
3. 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.
4. Szeimies RM, Radny P, Sebastian M et al. Photodynamic therapy with BF-200 ALA for the treatment of actinic keratosis: results of a prospective, randomized, double-blind, placebo-controlled phase III study. *Br J Dermatol.* 2010; 163:386-394.

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