

# Review of Efficacy, Cost, and Adherence of Field Therapies for Actinic Keratosis



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## SYNOPSIS

Field therapy for actinic keratosis (AK) offers the benefit of treating both visible clinical lesions and subclinical atypia. The primary goal is to reduce the risk of progression to keratinocyte carcinoma. When choosing a field therapy for AK, physicians should consider both the effective cost (EC)—defined as the approximated cost to achieve 100% AK clearance in a single patient—and patient adherence to treatment. A literature search revealed that the effective cost of 5-fluorouracil (5-FU) and in-office photodynamic therapy (PDT) are similar. However, the effect of patient adherence on real-world efficacy and long-term AK clearance favors in-office PDT and shorter-term topical regimens.

## OBJECTIVE

To compare efficacy, cost, and adherence of topical therapies and in-office PDT for AK.

## METHODS

The authors searched PubMed, Embase, Web of Science, and Google Scholar databases for articles on AK field therapy published between October 2020 and March 2021. The estimated cost of a given regimen was calculated as a projection of the per-unit cost multiplied by the number of units needed to complete the regimen. To calculate the total cost for PDT, the procedural cost was estimated from the average national Medicare reimbursement rate (as of May 23rd, 2021) and was added to the cost of the photosensitizer per treatment. Effective cost (EC) was calculated by dividing total cost (TC) by the clearance rate (CR),  $EC=TC/CR$ .

**Table 1. Costs of field-directed AK therapies**

Product	Regimen	Cost (\$)			
		Regimen	CPT	Total	Effective
5-FU (4% cream) <sup>1</sup>	Daily x 4 wk	262.50	169.93	432.93	541.16–801.72
ALA (10% gel) <sup>2</sup>	1-2 session, 3 months apart	299.00	240.76	539.76	593.14–870.58
5-FU (5% cream) <sup>3</sup>	Twice daily x 4 wk	384.94*	169.93	554.93	737.90 – 956.77
Imiquimod (5% cream) <sup>4</sup>	2x/wk x 16 wk	529.80	169.93	699.93	1093.64 – 2916.38
Tirbanibulin (1% ointment) <sup>5</sup>	Daily x 5 days	990.00	169.93	1502.93	2148.02 – 2636.20
5-FU (0.5% cream) <sup>6</sup>	Daily x 4 wk	1332.08	169.93	1502.91	2589.67 – 4693.78
Diclofenac sodium (3% gel) <sup>7</sup>	Twice daily x 12 wk	943.57	169.93	1113.50	2715.85 – 5860.52
Imiquimod (3.75% cream) <sup>8</sup>	Daily x two 2-wk cycles 2 wk off	1040.93	169.93	1210.86	3363.50

Cost/regimen estimated using wholesale acquisition cost (WAC) package prices and Medicare coverage rates for May 2021.

\*Average wholesale price.

5-FU = 5-fluorouracil; ALA = 5-aminolevulinic acid; CPT – Current Procedural Terminology; total cost = cost/regimen + CPT cost; effective cost = total cost/AK clearance rate.

1 Tolak, Hill Dermaceuticals, Stanford, FL

2 Ameluz, Biofrontera, Woburn, MA

3 Efudex, Bausch Health US, Bridgewater, NJ

4 Aldara, Valeant Pharmaceuticals

North America, Bridgewater, NJ

5 Klisyri, Almirall LLC, Malvern, PA

6 Carac, Bausch Health US, Bridgewater, NJ

7 Solaraze, PharmDerm, Melville, NY

8 Zyclara, Valeant Pharmaceuticals

North America, Bridgewater, NJ

## RESULTS

Commonly prescribed and studied FDA-approved topical field treatments are shown in Table 1. Only BF-200 ALA 10% gel has been approved by the FDA for field treatment and is thus included in this analysis. Effective cost of 5-FU 4% cream (\$541.16 – \$801.72) is similar to that of PDT with aminolevulinic acid (ALA) 10% gel (\$593.14 – \$870.58). However, total cost of 5-FU ranges from \$433 (4% cream) to \$1503 (0.5% cream), whereas total cost for a single round of PDT with 10% ALA gel is \$540. In addition, at-home topical therapies present significant barriers to compliance due to expected local skin reactions and long treatment regimens for many of these therapies, leading to potentially lower efficacy than is reported in clinical trials. This favors in-office PDT and shorter-term topical treatments.

## CONCLUSION

In-office 10% gel ALA-PDT is a cost-effective alternative to topical therapies and offers comparable efficacy in field-directed treatment of AK.

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