

Topical treatments for actinic keratoses: the bill, please!

Actinic Keratosis (AK) is a cutaneous pre-malignant lesion presenting with a scaly and reddish patch or plaque. It is caused by chronic ultraviolet light exposure, therefore, it affects most often sun-exposed areas of the body and is most common in elderly. Lesions are classified in three variants on the basis of their clinical thickness (Olsen score) that, however, does not match with the grade of histological dysplasia, as measured with the KIN score. All AKs should be treated because they are a precursor of invasive squamous cell carcinoma (iSCC).

In a few patients a single or few AKs develop on a normal skin and lesion-targeted therapies, e.g. lasers and cryotherapy, are the treatment of choice. However, in other patients a single anatomical area harbours multiple lesions (?5) and other clinical signs of photodamage indicating a field of cancerization with the consequent high risk of development of additional AKs and iSCC. Recent guidelines recommend using field directed treatments for these patients.

Treatment	Brand name	Average N. of lesions cleared	Average cost (€)	Total cost of treatment per patient per lesion cleared (€)	Total cost per patient per lesion cleared (€)	Total cost per lesion cleared (€) (average AK cleared/ average cost)	Average cost per 1 cm ² of cancerization area treated (€)
IMQ 5%	Aldara Cream 5%	8.79	628.33	78.32	115.41	71.44	1.95
DL MAL PDT	Metvix/Luxerm	15.67	255.49	24.99	28.95	16.31	0.87
InMeb	Picato	16.18	1039.12	83.34	103.50	64.23	3.21
c-PDT	Metvix	16.63	364.15	23.54	37.92	21.89	1.21
DHA	Solaraze 3%	6.55	848.74	207.87	264.70	129.50	3.22

The table reports the results of the costing analysis, including benefit of each treatment, expressed as an average number of lesions and corresponding average and total costs (Euro) per patient per lesion and per cleared patients per lesion.
c-PDT: conventional photodynamic therapy with methyl aminolevulinate; DL PDT: daylight photodynamic therapy with methyl aminolevulinate; DHA: diclofenac 3% + hyaluronic acid 2.5%; IMQ 5%: imiquimod 5%; InMeb: ingenol mebutate.

Tab. 1. Average cost per patient according to treatment and number of lesions cleared (Italy).

Cost and cost-effectiveness ratio of topical treatments have never been evaluated with respect to the size of the cancerization field.

With this study, our aim was to develop an economic model assessing the cost of topical treatments, per surface treated, per lesion and per lesion cleared for the management of AK in Italy, taking also into account the benefit-cost ratio. Afterwards, the analysis was replicated for Germany, Spain, France and the United Kingdom.

We used data from an observational study of 102 consecutive patients with multiple (?5) AKs on the face and/or scalp receiving treatment at the Department of Dermatology of the University of Brescia, Italy, from March to September 2016.

We compared daylight photodynamic therapy with methyl aminolevulinate (DL MAL PDT),

conventional photodynamic therapy with methyl aminolevulinate (c-PDT), diclofenac 3% + hyaluronic acid 2.5% (DHA), imiquimod 5% (IMQ) and ingenol mebutate (InMeb).

The cost of each treatment was calculated depending on the approval status of the drug, the literature data and the cancerization area requiring treatment.

Consultation costs, equivalent to €28.5 per visit in Italy, were applied to all treatments. For c-PDT the hourly rate of the nurse, equivalent to €30.00, was considered in addition to the rate of for the dermatologist and the direct costs related to medical supplies and disposable materials, estimated to be €5.00. The current analysis was performed from the payer's perspective and only direct costs were considered. Table I shows average cost per patient according to treatment and number of lesions cleared (Italy).

Assuming a similar population of patients across European countries and using the local prices of drugs, nurses and doctors' costs, we made a theoretical comparative calculation of the cost of the treatments throughout Europe.

In Italy, the average cost of treating a patient with c-PDT, DL PDT, DHA, InMeb and IMQ was €364.2, €255.5, €848.7, €1039.1, and €628.3, respectively (Table 1).

Taking into account the number of lesions cleared per patient, the cancerization area treated and the number of visits required with each treatment, the total cost per lesion treated per patient was estimated at €37.9, €29, €264.7, €103.5, and €115.4 respectively. The average cost per 1cm² area treated with c-PDT, DL PDT, DHA, InMeb and IMQ 5% was €1.2, €0.9, €3.2, €3.2 and €2, respectively.

These results were consistent when the analysis was replicated for other countries (Table 2).

Treatment	EU5	France	Germany	Spain	UK
IMQ 5%	€ 110.86	€ 109.54	€ 139.90	€ 80.63	€ 146.56
DL PDT	€ 22.29	€ 23.90	€ 20.86	€ 22.65	€ 27.70
ALA PDT	€ 27.24	N/A	€ 23.87	€ 27.17	€ 30.71
InMeb	€ 75.81	€ 73.78	€ 83.43	€ 86.23	€ 94.83
c-PDT	€ 27.64	€ 29.02	€ 25.17	€ 25.88	€ 35.80
5-FU	€ 15.95	€ 15.36	N/A	N/A	€ 27.74
DHA	€ 210.39	N/A	€ 305.15	€ 203.00	€ 196.51

ALA PDT: photodynamic therapy with aminolevulinic acid; c-PDT: conventional photodynamic therapy with methyl aminolevulinate; DL PDT: daylight photodynamic therapy with methyl aminolevulinate; DHA: diclofenac 3% + hyaluronic acid 2.5%; IMQ 5%: imiquimod 5%; InMeb: ingenol mebutate; 5-FU: 5-fluorouracil.

Tab. 2. Country specific results on the average cost per lesion treated.

Overall, our analysis suggests that MAL c-PDT and DL PDT are associated with the lowest cost as well as the lowest cost per lesion cleared, so they can be considered an effective treatment option

for AK management with a favourable value for money profile.

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Publication

[Evaluation of the costs of topical treatments for actinic keratosis based on lesion response and the affected area.](#)

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