

Cost-effectiveness of ingenol mebutate versus diclofenac 3% for Actinic Keratosis treatment in Spain

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Introduction

- Actinic keratosis (AK) is caused by proliferation of atypical epidermal keratinocytes due to prolonged exposure to exogenous factors such as ultraviolet radiation^{1,2}.
- Ingenol mebutate³ and diclofenac 3%⁴ are among available treatments in Spain, indicated for AK treatment.

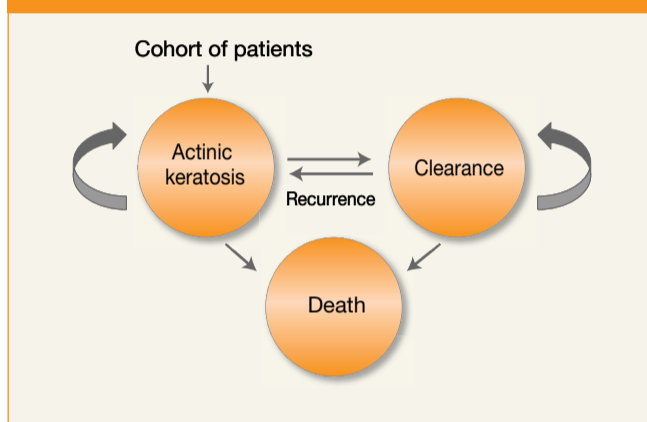
Objective

To assess the efficiency of ingenol mebutate vs diclofenac 3% for AK treatment from the Spanish National Health System (NHS) perspective.

Methods

- A markov model with three distinct health states: AK, clearance and death (Figure 1), was used to simulate the 5-year evolution of a AK patient. Annual AK recurrence rate (20%)⁵ was applied.

Figure 1. Markov model structure



- In the absence of head to head studies, effectiveness in terms of clearance rates were obtained by indirect comparison between clinical trials (42.24% and 34.07% for ingenol mebutate and 24.64% and 25.07%

Table 1. Health resource consumption and unitary costs (€, 2015)

PHARMACEUTICAL COST			
Active ingredient	Presentations	Retail Price VAT ⁸	Treatment duration
Ingenol mebutate	Picato® 150 µg/g gel, 3 tubes of 0.47 g	€105.22	face and scalp: 3 days trunk and extremities: 2 days
	Picato® 500 µg/g gel, 2 tubes of 0.47 g	€109.45	
Diclofenac 3%	Solaraze® 30 mg/g gel, 1 tube of 25 g	€30.57	90 days
	Solaraze® 30 mg/g gel, 1 tube of 60 g	€73.37	
HEALTH RESOURCES			
Dermatology	Visits	Number	Unit cost ¹⁰
	(First consultation)	1	€57.37
	(Successive consultation)	2	€31.43
Annual total visits		3 (regardless of treatment)	

for diclofenac on face-scalp and trunk-extremities, respectively).

- Utilities values for AK (0.98) and clearance (1.00)⁶ were used to estimate quality-adjusted life years (QALY).
- Total cost estimation (€, 2015) included: drug cost, and dermatology visits cost (for adverse events and disease management).

- A 3% annual discount rate was applied⁷.
- Drug cost estimation (Table 1) considered retail price plus VAT⁸ with 7.5% of mandatory deduction⁹, according to recommended doses^{3,4}.
- Unitary costs (€, 2015) were obtained from a national database¹⁰ (Table 1).
- Deterministic and probabilistic sensitivity analyses (SA) were performed.

Results

- Ingenol mebutate showed higher effectiveness than diclofenac 3% (0.193 incremental clearances and 0.011 incremental QALY (on face and scalp), and 0,129 incremental clearances and 0.007 incremental QALY (on trunk and extremities). (Table 2)
- Ingenol mebutate, with fewer costs and higher health benefits, was a dominant strategy in terms of incremental cost-effectiveness ratio and cost-utility ratio.
- Deterministic SA confirmed the results robustness because ingenol mebutate resulted a dominant treatment in all the analyses. (Table 3)

Figure 2. Probabilistic sensitivity analyses results

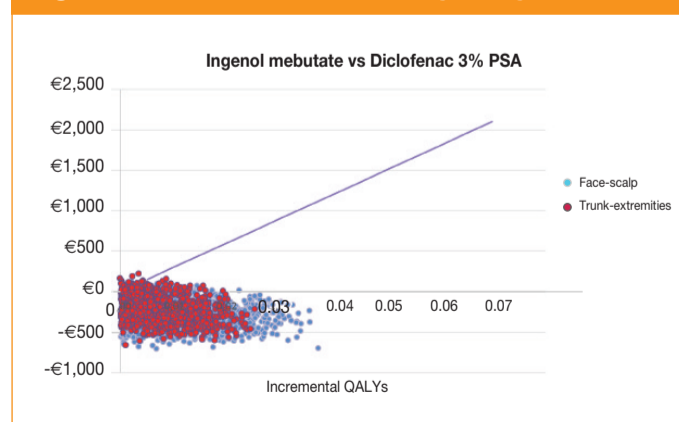


Table 2. Base case results

INGENOL MEBUTATE VS DICLOFENAC 3%	Face and scalp			Trunk and extremities		
	Total Costs	Total Clearances	Total QALYs	Total Costs	Total Clearances	Total QALYs
Ingenol mebutate	€551.50	0.536	4.451	€622.27	0.477	4.447
Diclofenac 3%	€849.11	0.343	4.440	€844.93	0.348	4.440

Table 3. Deterministic sensitivity analyses results

INGENOL MEBUTATE VS DICLOFENAC 3%	Face and scalp			Trunk and extremities		
	Incremental costs (€)	Incremental clearances	Incremental QALYs	Incremental costs (€)	Incremental clearances	Incremental QALYs
Emergency visits due to management of AEs in 5% of patients	-289.70	0.193	0.011	-212.90	0.129	0.007
Intake of additional antibiotic (30% of patients with ingenol mebutate and 5% with diclofenac 3%)	-297.31	0.193	0.011	-222.33	0.129	0.007
Decrement of efficacy (33%) in non-adherent	-283.03	0.177	0.011	-207.60	0.114	0.007
Discount rate (0%)	-316.14	0.193	0.012	-236.40	0.129	0.008
Discount rate (5%)	-286.38	0.193	0.011	-214.34	0.129	0.007
Time horizon (30 years)	-716.24	0.193	0.029	-539.95	0.129	0.019

QALY: Quality adjusted life years.

- Ingenol mebutate remained a dominant option vs diclofenac in 96% for face-scalp and 91% for trunk-extremities of the 1,000 MonteCarlo simulations of probabilistic SA (Figure 2).

Conclusions

Ingenol mebutate was a dominant strategy for Spanish NHS, compared to diclofenac 3%, for treatment of patients with AK both, face-scalp and trunk-extremities.

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