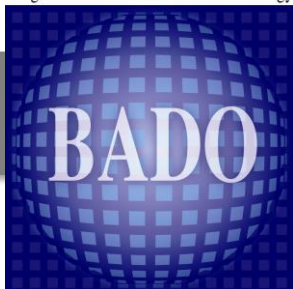


Topical immunotherapy and skin cancer: indications

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Dermatology

University Hospital Leuven



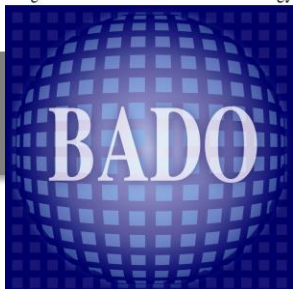
Topical pharmacotherapy and skin cancer

Table I. Topical drugs used for the treatment of skin cancer

| Drug | Available strengths | Official oncologic indications | Off-label/investigational oncologic indications | Pregnancy category | Mechanism of action |
|--------------------|---|---|---|--|--|
| 5-fluorouracil | 0.5%, 1%, 2%, and 5% | AKs and superficial BCCs (approved by the FDA) | BD, SC, EQ, EPD, and melanoma metastases | X | Interference with DNA synthesis |
| Imiquimod | 2.5%, 3.75%, and 5% | AKs and superficial BCCs (approved by the FDA) | Nodular BCCs, BD, LM, EQ, EPD, melanoma metastases | C | Modification of immune response |
| Didofenac | 3% gel in 2.5% hyaluronic acid | AKs (approved by the FDA) | BD | B | Increased apoptosis through cyclooxygenase inhibition |
| Ingenol mebutate | 0.015% and 0.05% gel | AKs (approved by the FDA) | BCCs | C | Induction of direct cellular death and inflammatory response |
| Retinoids | Tretinoin 0.05% and 0.1% cream; isotretinoin 0.1% cream; adapalene 0.1% and 0.3% gel; and tazarotene 0.1% gel | — | AKs, LM, and BCCs | C (tretinoin, adapalene) X (tazarotene) | Control of cell proliferation and differentiation |
| Resiquimod* | 0.01%, 0.03%, 0.06%, and 0.1% gel | — | AKs | — | Modification of immune response |
| Piroxicam | 1% gel | — | AKs | C | Increased apoptosis through cyclooxygenase inhibition |
| Dobesilate* | Calcium dobesilate 2.5% and potassium dobesilate 5% | — | AKs and BCCs | — | Inhibition of fibroblast growth factors |
| Betulinic acid* | Galenic preparations (ointment and oleogel) | — | AKs | — | Cytotoxic, antiproliferative, and apoptotic effects |

AK, Actinic keratosis; BCC, basal cell carcinoma; BD, Bowen disease; EPD, extramammary Paget disease; EQ, erythroplasia of Queyrat; FDA, US Food and Drug Administration; LM, lentigo maligna; SC, solar cheilosis.

*Not commercially available.



Imiquimod 5% (Aldara)

IMIQUIMOD

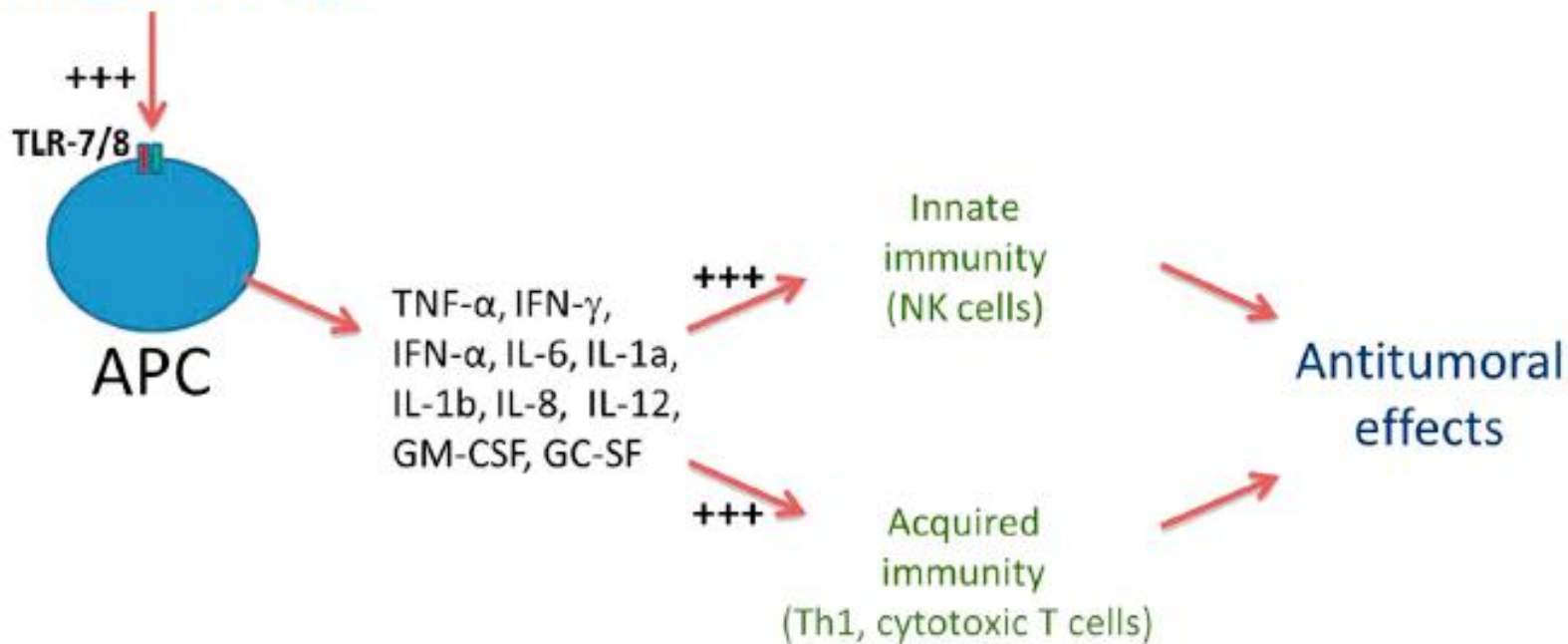


Fig 2. Primary mechanisms of action of imiquimod. *APC*, Antigen-presenting cell; *GC-SF*, granulocyte colony-stimulating factor; *GM-CSF*, granulocyte-macrophage colony-stimulating factor; *IFN*, interferon; *IL*, interleukin; *TLR*, Toll-like receptor; *TNF*, tumor necrosis factor.

Imiquimod (Aldara®) and superficial BCC

Belgian Association of Dermato-Oncology



BADO

II – Elementen van de voorwaarden vermeld onder punt a) van § 4110000 van hoofdstuk IV van het K.B. van 21.12.2001:

Ik ondergetekende, dokter in de geneeskunde, gespecialiseerd in dermato-venerologie: verklaar dat de hierboven vermelde patiënt één of meerdere kleine superficiële basaalcelcarcinomen vertoont op de romp, de ledematen of de nek en dat andere beschikbare behandelingen niet geschikt zijn omwille van de mogelijke aan de behandeling gerelateerde morbiditeit en/of slechte cosmetische resultaten.

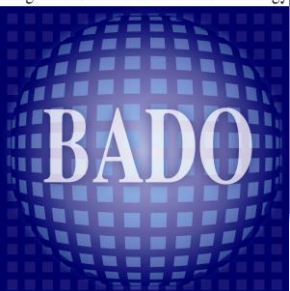
Deze patiënt heeft bijgevolg de terugbetaling nodig voor een 30 dagen behandeling met de specialiteit ALDARA™ aan een posologie van 5 zakjes per week (maximaal 3 verpakkingen).

Ik vraag bijgevolg de terugbetaling aan voor 3 verpakkingen ALDARA™ voor deze patiënt voor een maximale periode van 3 maanden.
Ik hou de nodige elementen ter beschikking van de adviserend-geneesheer om te bewijzen dat mijn patiënt zich op dit ogenblik in de betrokken situatie bevindt.



Imiquimod (Aldara®) and superficial BCC



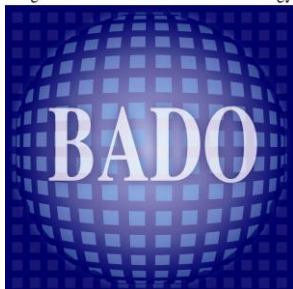


Photodynamic therapy versus topical imiquimod versus topical fluorouracil for treatment of superficial basal-cell carcinoma: a single blind, non-inferiority, randomised controlled trial

Aimée H M M Arits, Klara Mosterd, Brigitte A B Essers, Eefje Spoorenberg, Anja Sommer, Michette J M De Rooij, Han P A van Pelt, Patricia J F Quaedvlieg, Gertruud A M Krekels, Pierre A F A van Neer, Joris J Rijzewijk, Adrienne J van Geest, Peter M Steijnen, Patty J Nelemans, Nicole W J Kelleners-Smeets

Lancet oncology, 2013

- Primary outcome:
proportion of patients tumor-free at both 3 and 12 months
 - MAL-PDT: 72,8 %
 - Imiquimod : 83,4 %
 - 5-FU: 80,1 %
- conclusion: Topical 5-FU was non-inferior and imiquimod was superior to MAL-PDT for R/ of sBCC



Imiquimod (Aldara®) and actinic keratosis

II – Elementen van de voorwaarden vermeld onder punt a) van § 4880000 van hoofdstuk IV van het K.B. van 21.12.2001:

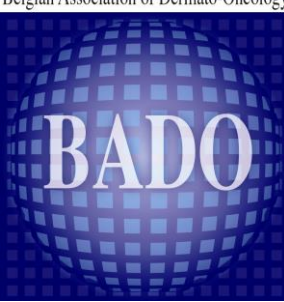
Conform punt a) van § 4880000 van hoofdstuk IV van het K.B. van 21.12.2001 :

Ik ondergetekende, arts-specialist in de dermato-venereologie, verklaar dat de hierboven **vermelde immuno-competente volwassen patiënt klinisch typische niet-hyperkeratotische, niet-hypertrofe actinische keratose op gelaat en hoofdhuid** vertoont en dat de grootte van de laesies en hun aantal de werkzaamheid en/of de aanvaardbaarheid van cryotherapie beperken alsook dat andere topicale behandelingsmogelijkheden gecontraïndiceerd of minder geschikt zijn.

Ik heb mijn patiënt over het praktisch aanbrengen van deze crème en over de reiniging van de behandelde zone ingelicht.

Deze patiënt komt bijgevolg in aanmerking voor de terugbetaling van een behandeling van maximum twee keer 4 weken met de specialiteit ALDARA™, aan 3 zakjes per week (één verpakking per 4 weken).

Ik houd de bewijsstukken die de diagnose bevestigen bij deze patiënt ter beschikking van de adviserend geneesheer.



Current therapies for actinic keratosis

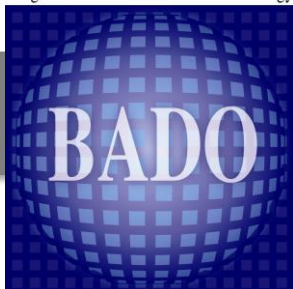
Field carcinogenesis

→ field directed therapy

- Mainly based on inducing cell death
 - 5-FU
 - PDT
 - Diclofenac
 - Ingenol Mebutate
- Or immunomodulation
 - Imiquimod

Single AK: destruction of 1 lesion

- Cryotherapy
- Electrocoagulation
- lasertherapy



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*Not commercially available.



- primary R/ of lentigo maligna (LM)
- adjuvant therapy after prior wide excision
 - persistent involvement of LM at the excision margin without clinical residual tumor
 - narrowly excised LM



A quantitative systematic review of the efficacy of imiquimod monotherapy for lentigo maligna and an analysis of factors that affect tumor clearance

Ariana N. Mora, BA,^a Pritesh S. Karia, MPH,^a and Bichchau Michelle Nguyen, MD, MPH^b
Boston, Massachusetts

- based on 347 tumors from 45 studies
- Imiquimod offers a 76% histologic and 78 % clinical clearance rate
- Cumulative dose and treatment intensity affect tumor clearance