Pre- and post-treatment care for actinic keratoses: An Australian and New Zealand perspective

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Background
Actinic keratoses (AKs), also known as solar keratoses, are precancerous skin lesions that typically occur following long-term exposure to ultraviolet radiation. AKs can evolve into cutaneous squamous cell carcinoma (SCC) if left untreated. Treatments for AKs typically cause temporary, irritable erythematous skin barrier disruption.

Objective
The objective of this article is to provide recommendations for the pre-treatment and post-treatment care for AKs in order to improve patient outcomes, particularly in the Australian and New Zealand setting.

Discussion
Many of the treatments for AKs have associated side effects that might affect skin barrier function. Post-treatment care is required to aid skin repair and to protect the skin. Patients should be instructed on how to care for the skin during the healing process using a gentle skin cleanser and a moisturiser. Routine sun protection measures all year round reduce recurrence and progression of AKs.

ACTINIC KERATOSES (AKs) are precancerous skin lesions that typically occur on the skin of adults that have had long-term exposure to ultraviolet (UV) radiation.[1] The prevalence of AKs in the Australian White population aged over 40 years is between 40 and 60%.[2]

People who are at risk of AKs include those who have fair skin, have genetic factors associated with increased susceptibility to UV radiation and have accumulated a greater lifetime exposure to UV radiation due to geographical location, outdoor occupations and outdoor activities.[1] AKs typically present in areas of greatest sun exposure; more than 80% of all AKs are found on the upper limbs and head and neck region.[3,4]

AKs can evolve into cutaneous squamous cell carcinoma (SCC) if left untreated; however, the rate of conversion varies widely between studies and ranges between 0.1 and 10%.[5] Although the transformation rate is relatively low, patients with AKs need to understand that they are at five-fold higher risk for skin cancers, including melanoma, compared to the general population and should have their skin checked regularly.[3,6] It is reasonable to treat all AKs in order to minimise the risk of developing SCCs.[7]

The selection of treatment is usually individually tailored and is based on the site of the AKs, and treatment-related factors such as efficacy, tolerability, time frame, cost and total surface area to be treated need to be considered. Patient characteristics and preferences should be considered such as associated symptoms, the risk of progression to SCC and the cosmetic appearance of the AKs before, during and after treatment.[4]

Treatments for AKs can be field- or lesion-directed. Field-directed treatments can be used to manage multiple AKs and keratinocyte changes of an entire field, such as the forehead or the full face. Field-directed treatment might provide benefits in reducing the risk of developing new AKs, limiting AK recurrence, as well as treating subclinical damage.[4] Field-directed treatments commonly offered in Australia and New Zealand include imiquimod, photodynamic therapy (PDT), diclofenac in hyaluronic acid, 5-fluorouracil (5-FU), either as monotherapy or in combination with calcipotriol or salicylic acid, and tirbanibulin (approved in Australia[8] but not commercially available at the time of writing).

Lesion-directed treatments are used to manage a few or isolated AKs. These treatments offer the benefit of treatment completion within one visit, with the patient only having to manage post-treatment care. However, there are practical limitations to the absolute number of individual AK lesions that can be treated in this manner.[4] Lesion-directed treatments currently offered in Australia and New Zealand include cryosurgery, curettage and laser.

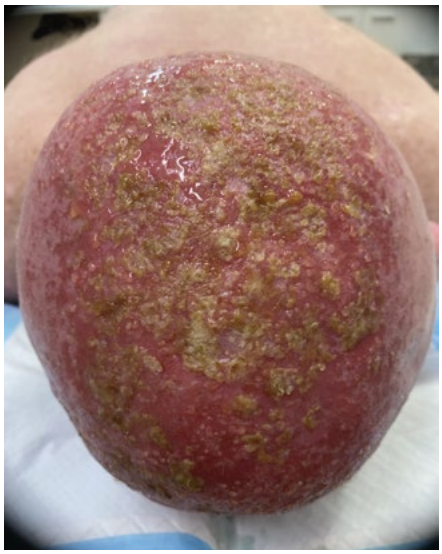

Figure 1. Scalp of a man aged in his 50s with a severe adverse reaction to 5-fluorouracil 5% cream, showing confluent erythema, oedema, crusting and lymphorrhoea. He had Olsen grade 2 solar keratoses on his scalp and had been applying the cream twice daily for the preceding eight days. He had previously used the cream without this reaction in the past. He was systemically well, with no fevers and minimal discomfort. Treatment was ceased and his scalp was managed with hygiene measures and twice daily methylprednisolone aceponate 0.1% fatty ointment. The patient was instructed to not use 5-fluorouracil 5% cream again, and went on to have daylight photodynamic therapy to treat his face, ears and neck, with a tolerable and moderate response.

AKs recurrence is common, particularly in those patients with multiple lesions. Long-term rates of recurrence range between 39 and 85%, indicating that the majority of patients will experience recurrent lesions in the long term.[9] Most patients treated for AKs will require regular surveillance and retreatment.

Temporary side effects such as erythema, itching, burning and stinging from treatments for AKs might cause discomfort. Post-treatment care is important to aid skin repair and to protect the skin; however, there are no guidelines outlining pre- and post-treatment care in Australia or New Zealand. This paper outlines recommendations based on expert opinions from a group of dermatologists, general practitioners and a pharmacist for the pre- and post-treatment care for AKs in Australia and New Zealand.

Pre- and post-treatment care guidelines for AKs

Guidance on pre- and post- treatment care is provided in Table 1 and are described below. The guidance provided reflect the clinical practice of the authors and are not mandatory guidelines, as it is expected that there will be a wide variation in pre- and post-treatment care across Australia and New Zealand.

Field-directed treatments

When selecting a field treatment, refer to local prescribing advice or product information for guidance on application, precautions and immediate post-treatment care. Topical agents such as 5-FU, 5-FU combinations and imiquimod are commonly used, have good efficacy and can be applied focally or in broad areas. At one-year post-treatment, in a large randomised controlled trial, 74.7% of patients using 5-FU 5% cream had a partial response of at least 75% clearance.[10] These agents all have the potential for generating local skin reactions such as erythema, itching, burning and crusting. Although the side effects are temporary, they can result in non-compliance and clinicians should work with the patient to customise the treatment to achieve the desired outcomes.[3,4] PDT requires the application of a photosensitiser to the area of skin to be treated, before exposure to a light source. This mode of treatment also has reported good efficacy and has the added benefit of administration in the office setting, which might offer improved compliance compared to topical agents administered by patients at home. Reactions include erythema, stinging, itching, oedema and exudation, which can take around 10 days to heal.[3,4]

Patients should receive a thorough explanation of what to expect during a field treatment, including a timeline of photos with mild versus strong responses, and reference materials to review before commencing their treatment. They should also be informed about potential cosmetic changes (pigmentation, colourations) post-treatment. Progress review appointments should be offered and reasons to discontinue treatment and seek immediate review should be carefully outlined. Table 2 outlines recommendations for undesirable reactions post-treatment and Figure 1 shows an image of an undesirable reaction to 5-FU and describes the measures that were undertaken to manage the reaction.

Pre-treatment care

Patients should be advised to remove make-up, wash the area and dry thoroughly before applying treatment for AKs. Barrier breakdown can potentiate the effects of treatment. Consider curettage, cryotherapy or the application of a keratolytic agent such as lactic acid, salicylic acid or urea for 2–4 weeks or until palpable scale is reduced (Table 3) for hyperkeratotic AKs prior to field AK treatment.

Post-treatment care

Some guidance on post-treatment care for field treatments is shown in Table 4. If the patient has experienced unexpected or untoward reactions to the field-directed treatment, or if the skin texture/tone has not returned to normal after one week, photographs of the treated skin are encouraged to show the healthcare practitioner. Patient follow-up is encouraged for non-responsive lesions for review and consideration for biopsy. AKs that are tender on palpation or do not resolve with treatment should be re-examined with a heightened concern for malignancy. Lesions that are indurated or tender to palpation are best addressed surgically, with histology to exclude malignancy.

Patients should be instructed on how to care for the skin during the healing process, once skin texture and tone has returned to normal after treatment. Instruct the patient to use a gentle cleanser that is acceptable for all skin types. Consider using a barrier repair cream and an emollient that hydrates the damaged skin and do not sting such as Cicaplast (La Roche-Posay, St Quen, France), Cicalfate (Eau Thermale Avène, Lavaur, France) and Bepanthen (Bayer Consumer Health NSW, Australia). Petroleum jelly can also be used.

Sun protection

Provide advice on reducing or preventing further sun damage by ensuring appropriate

Table 1. Recommendations for pre- and post-treatment care and the prevention of relapse for the treatment of actinic keratoses

Pre-treatment care	Post-treatment care	Prevention of relapse
Field-directed treatments		
• Remove make-up • Wash the area with a gentle soap-free, fragrance-free cleanser • Dry thoroughly • Consider curettage or the application of a keratolytic agent for hyperkeratotic AKs	• Use a gentle cleanser with a pH ≈ 5 that is acceptable for all skin types • Consider a barrier repair cream such as a soothing balm with panthenol • Consider an emollient that is fragrance free with a hydrating formulation Sun protection • Use sun protection every day and minimise exposure at peak UV rating. Sun protection should be used when outdoors or near a window • Use clothing with a high UPF that covers the body from wrist to ankle. Wear sunglasses and a wide-brimmed hat • Apply sunscreen with SPF 50+ UVA/UVB protection on all exposed areas. Apply daily on all exposed sites and use an appropriate amount of sunscreen • Use clothing on any sites that are inflamed or broken. Do not use sunscreen on these sites • Reapply SPF 50+ broad-spectrum sunscreen twice daily. Apply every 2 hours when skin is exposed to water, if in the sun for prolonged periods of time or if sweating excessively	• Consider the use of oral nicotinamide in the morning and evening if the patient has a high burden of keratinocyte cancer • Consider the use of topical retinoids for chronic actinic damage Sun protection • Use sun protection every day and minimise exposure at peak UV rating. Sun protection should be used when outdoors or near a window • Use clothing with a high UPF that covers the body from wrist to ankle. Wear sunglasses and a wide-brimmed hat • Apply sunscreen with SPF 50+ UVA/UVB protection on all exposed areas. Apply daily on all exposed sites and use an appropriate amount of sunscreen • Reapply SPF 50+ broad-spectrum sunscreen twice daily. Apply every 2 hours when skin is exposed to water, if in the sun for prolonged periods of time or if sweating excessively
Lesion-directed treatments		
Consider curettage for hyperkeratotic AKs	• Follow the same guidelines as for field-directed treatments including sun protection • Cryotherapy can result in skin blistering and so sunscreen and other topical products should be avoided in those areas until the skin is repaired	• Follow the same guidance as for field-directed treatments including sun protection • Field treatment should be considered if relapse occurs

AKs, actinic keratoses; UPF, ultraviolet protection factor; UV, ultraviolet.

outdoor clothing, practising sun-avoidant behaviour (shade seeking and avoiding peak UV times) and the use of sunscreens. Advise patients that regular use of SPF 50+ broad-spectrum sunscreen not only prevents the development of AKs, but also helps with the remission of existing AKs.[11]

Advise the patient to use sun protection *every day* regardless of the weather and to minimise exposure to the sun at the peak UV rating. Sun protection should be used whenever the patient is outdoors or near a window.

Sun protection is best provided using clothing with a high ultraviolet protection factor (UPF) that covers the body from wrist to ankle. Advise the patient to also wear sunglasses and a wide-brimmed hat.

A sunscreen with SPF 50+ UVA/UVB protection suitable for the patient's skin type should be applied daily on all exposed sites apart from sites that are still inflamed or broken due to treatment. Advise the patient to use appropriate clothing on inflamed skin until the skin barrier is restored to protect the area from the sun. Ensure that an adequate amount of SPF 50+ broad-spectrum sunscreen is applied. The recommended application is 5 mL (a teaspoon) for each arm, leg, body front, body back and face (including neck and ears). This equates to a total of 30 mL for a full body application.[12]

SPF 50+ broad-spectrum sunscreen should be *reapplied*. Twice daily application (eg morning and early afternoon) is particularly important in the summer months (potentially all-year round in the northern parts of Australia). Sunscreen should be *reapplied* every two hours when skin is exposed to water, the person has been sweating excessively, skin has been rubbed or they are in the sun for prolonged periods of time.

Prevention of relapse

Advise the patient to apply sun protection as described above. Consider the use of oral nicotinamide (500 mg twice daily)

Table 2. Recommendations for undesirable reactions/outcomes post field treatment

Undesirable reaction	Recommendation
Allergic reaction: major swelling and redness in the first 2–3 days after treatment	• Cessation of the treatment • Trial treatment for a short period of time or treat smaller areas • Consider a different field therapy or a different formulation • Apply topical corticosteroid for a brief period to moderate the response. For example, apply hydrocortisone 1% ointment twice a day or methylprednisolone aceponate (Advantan; Leo Pharma, Qld, Australia) fatty ointment at night for a couple of days. An ointment base will be more soothing and cause less irritation
Infection: vesicles or pustules and major pain	• Swab the area to confirm if the infection is herpes simplex virus (HSV), in particular near the mouth or eye for patients with a past history of HSV. If ophthalmologic HSV infection is suspected, then ophthalmologic emergency management needs to be organised • In the case of a small number of pustules, prescribe local antibiotherapy (covering staphylococcus and streptococcus). If pustules cover an extensive area, oral antibiotics might be warranted. If the patient has a fever, an emergency infusion of antibiotics might need to be organised
Major ulcerations	• Cessation of the treatment is the best way to avoid ulcerations. Patients should be instructed to stop treatment if they develop any pain to prevent major ulcerations. The treatment can be uncomfortable, but the patient should be able to perform their normal activities • Apply a topical potent steroid in an ointment base until relief is achieved (do not prescribe steroid in a cream base as it can sting the damaged skin) • Apply a barrier cream such as Cicaplast, Cicalfate or Bepanthen • After the skin is healed, lingering skin redness or pigmentation changes can persist for weeks

Table 3. Recommendations for pre-treatment care with keratolytic agents

Product	Concentrations	Frequency	Potential side effects
Salicylic acid	5–10% as a lotion, cream or ointment	• Low concentration of keratolytic agents (eg 5–10%) need to be applied once or twice a day for around a month with no occlusion • High concentrations of keratolytic agents (eg 20%) only need to be applied for a few days with occlusion	• Redness • Burning • Skin irritation • These side effects can be avoided if the patient is instructed to stop the application of keratolytic agents if they experience pain
Urea	10–30% cream		
Lactic acid	10–20% cream		

in the morning and evening for patients who have a high burden of keratinocyte cancer.[13] Patients with a history of multiple SCC every year might also be considered for chemoprophylaxis with acitretin, an oral retinoid.[14] Topical retinoids can also be considered in the management of patients with less severe chronic actinic damage.[15]

Lesion-directed therapies

Pre-treatment care

For cryotherapy and curettage, no pre-treatment care is usually required as the AK is removed within one visit. Curettage or topical keratolytics (such as salicylic acid) can be considered to remove the overlying hyperkeratosis prior to cryotherapy. Particular care needs to be taken to ensure informed consent of patients is received for cryotherapy, including cosmetic outcomes.

Post-treatment care

Cryotherapy can result in skin blistering and so sunscreen and other topical products should be avoided in those areas until the skin is repaired. The same post-treatment care guidance described for field-directed treatments should be followed.

Prevention of relapse

Field treatment should be considered if relapse occurs.

Conclusions

AKs, which are skin cancer precursors and an indicator of increased skin cancer risk, are important to treat to facilitate skin cancer diagnosis and to reduce long-term sequelae. Many treatment options are available such as directed mechanical and field treatments. These treatments might be complicated by irritable erythematous skin barrier disruption, which can be mitigated by using a gentle skin cleanser and moisturiser use. Routine sun protection measures including high-coverage sun protective clothing, a wide-brimmed hat, sunglasses and broad-spectrum SPF 50+ sunscreen application, all year round, reduce recurrence and progression of AKs.

Table 4. Post-treatment care for common field treatment modalities

Field treatment modality	Post-treatment care
• 5-FU • 5-FU+calcipotriol • Imiquimod	• Redness of the affected areas occur generally within 3–5 days[16] • Within 11–14 days, residual erythema of the affected skin is likely and can take weeks to fade. Patients should limit their exposure to sun during and immediately following treatment[16] • A topical cream or emollient such as Cicalfate, Cicaplast, Bepanthen or petroleum jelly can be applied for several days. These products can be put in the refrigerator for a cooling effect • Post treatment review for efficacy should be undertaken between 4 and 8 weeks. If residual lesions are still present, then further treatment and/or biopsy might be warranted
Daylight PDT	• The patient should avoid sun exposure for 2 days after treatment • Skin reactions will peak in intensity at 2–3 days and rapidly resolve[17] • Most skin reactions on the face and scalp resolve within 7 days of treatment and any residual erythema usually resolves within 3 months[17]

5-FU, 5-fluorouracil; PDT, photodynamic therapy.

Key points

- There are no guidelines for pre- and post-treatment care for AKs in Australia or New Zealand.
- Many AK treatments have side effects that might affect skin barrier function.
- Post-treatment care is important to aid skin repair and to protect the skin.
- Consult the product information for AK prescription treatment as they might have specific post-care advice.
- Routine sun protection measures reduce recurrence and progression of AKs.

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