The publication of guidance on the risks and benefits of sun exposure\textsuperscript{1} is evidence of growing awareness and concern about the potential adverse effects of sunlight on skin and the development of skin cancer in particular. The incidence of skin cancers has been increasing in the UK and Europe for some time. In 1993, the incidence of melanoma in the UK was 11.1 per 100,000 but by 2012 it was 23.0 per 100,000, making it the fifth most common cancer.\textsuperscript{2} But this is dwarfed by the increased incidence of nonmelanoma skin cancer (NMSC), which has been rising by about 5 per cent annually since the early 1990s.\textsuperscript{3} In 2013, the estimated age-standardised rate was 125.2 per 100,000;\textsuperscript{2} however, it is known that these cancers are under-reported.

Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) have different developmental pathways, but photodamage of the skin by UV light is a risk factor common to both.\textsuperscript{4} Photodamage can give rise to actinic keratoses (AKs) – keratinocytes with enlarged, irregular and hyperchromatic nuclei that may progress to SCC.\textsuperscript{5} However, the risk of progression is small and uncertain and it is not possible to predict which lesions will undergo malignant change: estimates range up to 0.075 per cent per year overall and 0.53 per cent in people with a history of NMSC, but this is balanced by rates of regression of 15–63 per cent of lesions after one year and recurrence rates of 15–53 per cent of lesions.\textsuperscript{6}

It is self-evident that photodamage is not confined to the isolated points on the skin where AKs develop. Affected skin contains both clinically apparent AKs and subclinical changes that progress to AKs.\textsuperscript{7} There is potential for premalignant and malignant cells to develop throughout the area of UV-damaged skin and, as with isolated lesions, these areas may regress and recur.\textsuperscript{6} These findings introduced the concept of field carcinisation to dermatology\textsuperscript{8} and the development of field-directed treatment that aims to reduce the risk of SCC by eradicating both clinically apparent and subclinical lesions.\textsuperscript{9} Optimal man-

**Topical agents for preventing and treating actinic keratosis**

STEVE CHAPLIN

Actinic keratoses are skin lesions that can occur as a result of long-term UV damage and can sometimes progress to squamous cell carcinoma. This article discusses the treatment options for both lesion-directed and field-directed topical therapy, to reduce the future risk of squamous cell carcinoma.
management of AK therefore involves both lesion-directed and field-directed therapies.\(^9,10\) Field-directed options include photodynamic therapy and topical agents.

**Topical treatments**

The agents currently licensed for topical treatment of AK are listed in Table 1: fluorouracil is additionally licensed for the treatment of malignant lesions and superficial BCC. They form a diverse group, chemically, pharmaceutically and pharmaco-logically, with a differing balance of therapeutic and adverse effects, but they share a pattern of application site reactions of varying severities. All are suitable for both lesion-directed and field-directed therapy, though some are preferred for smaller fields (up to the size of the palm of the hand – about 10 x 10cm in a man – or most of the forehead) due to the severity of local adverse effects.\(^10\)

In general, exposure to sunlight or tanning beds should be avoided during treatment. There is a small risk that excipients may cause contact dermatitis and contact with the eyes and mucus membranes should be avoided. Use during pregnancy is not recommended, either due to lack of information or evidence of harm in animal models.

**Field-directed therapy**

The purpose of field treatment is to remove clinically apparent and subclinical lesions and to reduce the risk of developing SCC in the future. While the removal of obvious AKs is readily assessed, follow-up studies have not been of sufficient duration to show that treatment reduces the longer-term risks.

**Topical treatments for larger field areas**

*Diclofenac 3% gel (Solaraze)*

Diclofenac is a relatively COX-2-selective NSAID that is believed to act by stimulating apoptosis, and inhibiting cell proliferation and angiogenesis.\(^11\) Given twice daily for 12 weeks, diclofenac 3% gel is considered to be a milder option for field therapy that is appropriate for thin keratoses.\(^10\) At the recommended dose of 0.5g of gel per 25cm\(^2\), a course of treatment for such an

<table>
<thead>
<tr>
<th>Agent</th>
<th>Indication</th>
<th>Dose</th>
<th>Common adverse effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diclofenac 3% gel (Solaraze)</td>
<td>Treatment of actinic keratosis</td>
<td>Apply twice daily 0.5g (pea-size) for a 5 x 5cm lesion site. Usual duration of therapy 60–90 days. Maximum 8g daily</td>
<td>Contact dermatitis, erythema, rash, inflammation, irritation, pain, blistering, temporary hair discolouration, hyperaesthesia, paraesthesia</td>
<td>Longer duration treatment more effective; full effect may not be apparent for 30 days after end of treatment</td>
</tr>
<tr>
<td>Fluorouracil 5% cream (Efudix)</td>
<td>Superficial premalignant and malignant skin lesions; keratoses including senile, actinic and arsenical forms; keratoacanthoma; Bowen's disease; superficial basal cell carcinoma</td>
<td>Premalignancy: apply once or twice daily Malignancy: once or twice daily under occlusive dressing Continue until there is a marked inflammatory response. Usual duration 3–4 weeks. Maximum treated area 500cm(^2) (approx. 23 x 23cm)</td>
<td>Normal response includes early and severe inflammation (erythema, which may become intense and blotchy), followed by a necrotic phase with skin erosion before healing</td>
<td>Topical steroids relieve discomfort. Facial lesions respond more quickly than those on the trunk or lower limbs; hands and forearms respond most slowly. Healing may not be complete until 1–2 months after end of therapy</td>
</tr>
<tr>
<td>Ingenol mebutate gel (Picato)</td>
<td>150µg/g: nonhyperkeratotic, nonhypertrophic actinic keratosis on the face and scalp</td>
<td>One tube (70µg) once daily to area up to 25cm(^2) (ie 5 x 5cm) for 3 days</td>
<td>Erythema, flaking/scaling, crusting, swelling, vesiculation/pustulation and erosion/ulceration. Typically begin within 1 day and peak up to 1 week after treatment. Face and scalp lesions usually resolve within 2 weeks, trunk and extremities within 4 weeks</td>
<td>Optimal effect after 8 weeks. Repeat if response incomplete after 8 weeks or if lesions recur</td>
</tr>
<tr>
<td></td>
<td>500µg/g: nonhyperkeratotic, nonhypertrophic actinic keratosis on trunk and extremities</td>
<td>One tube (235µg) to area up to 25cm(^2) (ie 5 x 5cm) once daily for 2 days</td>
<td></td>
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</table>

Sources: BNF Online, February 2016; Summaries of Product Characteristics (www.medicines.org.uk)

Table 1. Topical treatments for actinic keratosis: indications and adverse effects (cont. on p. 34)
area of would require the prescription of approximately two 50g tubes at a basic NHS cost of £76.60. Note that the concentration of diclofenac in Solaraze is three times greater than in the topical anti-inflammatory formulation Voltarol 1.16% Emulgel.

Systemic absorption of diclofenac from this formulation is variable (1–12 per cent) and the gel is contraindicated in people with hypersensitivity to NSAIDs, eg with a history of asthma or urticaria on exposure. Caution is therefore advised when treating individuals with a history of adverse reactions to systemic NSAIDs. Diclofenac can be applied under a loose bandage, but not under an occlusive dressing.

Complete resolution rates with diclofenac 3% gel range from approximately 30 to 50 per cent. Meta-analysis of seven trials, including one involving immunosuppressed patients, showed that the number needed to treat (NNT) to achieve the outcome “completely improved” for diclofenac 3% gel com-

<table>
<thead>
<tr>
<th>Agent</th>
<th>Indication</th>
<th>Dose</th>
<th>Common adverse effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imiquimod 3.75% cream (Zyclara) (£113/28 sachets)</td>
<td>Clinically typical, nonhyperkeratotic, nonhypertrophic, visible or palpable actinic keratosis of the full face or balding scalp in immunocompetent adults when other topical options are contraindicated or less appropriate</td>
<td>Up to 2 sachets applied once daily before bedtime to the treatment field for 2 treatment cycles of 2 weeks separated by treatment-free 2-week period. Reassess if no response after 8 weeks</td>
<td>Erythema, scab and exfoliation/application site dryness. Systemic adverse effects include headache, fatigue, myalgia, arthralgia</td>
<td>Treatment should be suspended if local effects severe but treatment cycle should not be extended</td>
</tr>
<tr>
<td>Imiquimod 5% cream (Aldara) (£48.60/12 sachets)</td>
<td>Clinically typical, nonhyperkeratotic, nonhypertrophic actinic keratoses on the face or scalp in immunocompetent adults when the size or number of lesions limit the efficacy and/or acceptability of cryotherapy and other topical options are contraindicated or less appropriate</td>
<td>Superficial basal cell carcinoma in adults: 5 times per week for 6 weeks before sleep and leave on skin for approx 8 hours Actinic keratosis: 3 times per week for 4 weeks before sleep and leave on skin for approx 8 hours. Cover the treatment field; maximum dose one sachet. Maximum treatment duration 8 weeks. If lesions persist, repeat for another 4 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluorouracil 0.5%/salicylic acid 10% (Actikerall 5mg/g plus 100mg/g Cutaneous Solution) (£38.30/25ml)</td>
<td>For treating specific lesions. Slightly palpable and/or moderately thick hyperkeratotic actinic lesions in immunocompetent adults</td>
<td>Once daily until the lesions clear completely or up to a maximum of 12 weeks. Reduce frequency to 3 times weekly if severe side-effects. Apply less frequently to areas with thin epidermis and monitor more often. Multiple actinic keratoses can be treated simultaneously; total area treated should not exceed 5 x 5cm</td>
<td>Erythema, inflammation, irritation, pain, pruritus, bleeding, erosion, scab, exfoliation, headache</td>
<td>Not intended for field therapy. Response may be apparent at 6 weeks but complete healing delayed for up to 8 weeks after end of treatment</td>
</tr>
</tbody>
</table>

Sources: BNF Online, February 2016; Summaries of Product Characteristics (www.medicines.org.uk)
pared with the vehicle (hyaluronic acid gel) alone was three to five, with no significant difference between 60-day and 90-day treatment periods.³³ Trials evaluating efficacy on the scalp, arm/forearms and back of the hands reported more variable results than those assessing lesions on the face or forehead. In the meta-analysis, treatment was associated with minor adverse events such as dry skin (number needed to harm 4.4 vs vehicle).

**Imiquimod 3.75% cream (Zyclara)**

Imiquimod modifies the immune response by acting as an agonist at toll-like receptors 7 and 8; this induces an increase in the expression of cytokines with antitumour activity, notably TNF-alpha and interferon-gamma.¹¹ It may also have antiangiogenic activity and facilitate apoptosis.

Imiquimod 3.75% is licensed only for use on the full face or balding scalp and when other topical treatments are contraindicated or less appropriate (this would include, for example, a large field for which the adverse effects of other topical agents are not cosmetically acceptable). A treatment cycle comprises once-daily application for two weeks, followed by a two-week treatment-free interval before repeating two weeks of treatment. The cream is applied at night and left on the skin for eight hours. The basic NHS cost of a treatment cycle, at the maximum dosage of two 250mg sachets daily, is £226.

Treatment with imiquimod is associated with an increase in the number of visible lesions because it stimulates the local immune response and reveals subclinical lesions. The intensity of this reaction is positively related to the clearance rate. Patients should be warned of this and encouraged to persist with treatment but a rest period is recommended if the lesions are severe and cause discomfort. Treatment can be resumed when this is resolved, but the length of the cycle should not be increased to compensate for the missed doses. The outcome can be assessed after full regrowth of skin at eight weeks.

In a pooled analysis of two phase 3 trials involving 319 patients with 5–20 visible or palpable lesions on the face or scalp, the rate of complete clearance eight weeks after completing treatment was significantly greater with imiquimod 3.75% than vehicle (36 vs 6 per cent).¹⁴ Partial clearance rates (≥75 per cent reduction in AK lesions) were 59 and 23 per cent respectively, with a reduction in lesion count of 82 and 25 per cent. Follow-up of a small group of patients with complete clearance (n=42) showed that this was sustained for 12 months in 41 per cent.¹⁵

Common adverse effects include predictable application site reactions (including erythema, dryness, scabbing, exfoliation, pain and swelling), nausea and flu-like symptoms such as fatigue, myalgia and arthralgia. Skin hypopigmentation and skin infection may also occur.

**Treatments for smaller field areas**

**Fluorouracil 5% cream (Efudix)**

Fluorouracil is an antimetabolite that inhibits DNA synthesis and cell proliferation and promotes cell death.¹¹ As field therapy, it is applied in a thin film once daily in the evening¹¹ (though the licensed indication allows for twice daily use) for four weeks. The total area treated should not exceed 500cm² (approximately 23 × 23cm); larger areas should be treated a section at a time. The hands should be washed after application and the area treated should be washed the next morning. Treatment continues until there is a marked inflammatory response with some erosion – usually about four weeks. Healing may take up to two months and follow-up at three months is recommended.¹⁰

The response to treatment with fluorouracil 5% follows a course of erythema, vesiculation, erosion, ulceration, necrosis and epitelisation. A mild topical steroid may be needed to relieve discomfort. In severe cases, this response may be associated with pain and ulceration, and inflammation is exacerbated by an occlusive dressing.

A systematic review that included nine randomised trials of fluorouracil 5% (none vs vehicle) found that it reduced lesion count by approximately 80 per cent, though this was assessed earlier than eight weeks in seven studies.¹⁶ Rates of complete clearance averaged 49 per cent and one study involving 24 patients found this was sustained at 12 months in one-third. However, the review authors concluded that the quality of studies was poor.

A recent trial randomised 932 people with two or more NMSCs in the preceding five years to treatment with twice daily fluorouracil 5% cream to the face and ears for four weeks or vehicle.¹⁷ After a mean follow-up of 2.6 years, those treated with fluorouracil had significantly fewer AK lesions at six months (mean 3.0 vs 8.1) and throughout the trial, and more had complete clearance at six months (38 vs 17 per cent).

Assuming a 40g tube is sufficient for one course, treatment with fluorouracil 5% cream costs £32.90.

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**Figure 1.** Time course of mean composite local-skin-response scores (sum of six individual scores ranging 0–4; max. score 24) in patients with actinic keratosis on the face/scalp or trunk/extremities after treatment with ingenol mebutate gel or placebo (vehicle gel)¹⁸

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**Ingenol mebutate gel 0.015% (face or scalp)**

**Ingenol mebutate gel 0.05% (trunk or extremities)**

**Placebo (face or scalp)**

**Placebo (trunk or extremities)**

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**Imiquimod 3.75% vs adverse events such as dry skin (number needed to harm 4.4 vs vehicle).**
Ingenol mebutate gel (Picato)
Ingenol mebutate induces local cell death, resulting in the production of proinflammatory cytokines and infiltration of immunocompetent cells and an inflammatory response in the epidermis and upper dermis, and epidermal necrosis. It is available in two strengths. The weaker formulation (150µg/g) is licensed for the treatment of the face and scalp: one 0.47g tube is applied once daily for three consecutive days. The higher strength (500µg/g) is licensed for treating the trunk and extremities: one 0.47g tube is applied once daily for two consecutive days. The cost of a course of treatment is £195 and £130, respectively.

A single tube covers an area up to 5 x 5cm. The gel is allowed to dry for 15 minutes and left unwashed for six hours. It should not be applied within two hours of having a shower or covered by an occlusive dressing. The hands should be washed after application.

The key evidence for the efficacy of ingenol mebutate is provided by four vehicle-controlled trials, two studying the treatment of AK on the face and scalp (n=547) and two on the trunk and extremities (n=458), reported in pooled analyses.18 These studies were double-blinded, but it is possible that blinding was compromised by the marked skin reaction associated with treatment. At eight weeks after ending treatment, the complete clearance rate for AK on the face and scalp was significantly greater for ingenol mebutate (42 vs 3.7 per cent with vehicle), with partial clearance in 64 and 7.4 per cent of patients respectively. The NNT for complete clearance in one patient treated with ingenol mebutate was 2.6, and 1.8 for partial clearance. Ingenol mebutate was also effective in patients with AK on the trunk or extremities, with complete clearance rates significantly greater than vehicle (34 vs 4.7 per cent) and partial clearance rates of 49 vs 6.9 per cent. NNTs were 3.4 and 2.4 respectively.

Observational follow-up of patients with a complete response at eight weeks showed that over 80 per cent of original lesions remained cleared at 12 months, though one or more new lesions or recurrences developed in about half of patients overall.18 In a separate study in 203 patients with AK on the face or scalp with lesions persisting eight weeks after treatment with ingenol mebutate, or in whom lesions emerged after 26 or 44 weeks, the complete clearance rate after a second treatment cycle was significantly greater than with vehicle (47 vs 18 per cent), with an overall clearance rate at 12 months of 50 per cent.19

Ingenol mebutate causes erythema, flaking, scaling and crusting within one day; this reaches maximum intensity during the first week after treatment, but usually resolves within two weeks for the face and scalp and four weeks for the trunk and extremities (see Figure 1).18 Treatment is assessed after eight weeks.

Imiquimod 5% cream (Aldara)
The licensed indication of imiquimod 5% cream is similar to that of the weaker (3.75%) formulation, but the intensity of the

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Brand name</th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
<th>Field Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topical</td>
<td>Diclofenac 3% gel</td>
<td>Solaraze</td>
<td>✓ ✓ ✓ ✓</td>
<td>✓ ✓ ✓ ✓</td>
<td>✓ ✓ ✓ ✓</td>
</tr>
<tr>
<td>Fluorouracil 5% cream</td>
<td>Efudix</td>
<td>✓ ✓ ✓ ✓</td>
<td>✓ ✓ ✓ ✓</td>
<td>✓ ✓ ✓ ✓</td>
<td>✓ ✓ ✓ ✓</td>
</tr>
<tr>
<td>Imiquimod 5% cream</td>
<td>Aldara</td>
<td>✓ ✓ ✓ ✓</td>
<td>✓ ✓ ✓ ✓</td>
<td>✓ ✓ ✓ ✓</td>
<td>✓ ✓ ✓ ✓</td>
</tr>
<tr>
<td>Fluorouracil 0.5% + salicylic acid 10% soln.</td>
<td>Actikerall</td>
<td>✓ ✓ ✓ ✓</td>
<td>✓ ✓ ✓ ✓</td>
<td>✓ ✓ ✓ ✓</td>
<td>✓ ✓ ✓ ✓</td>
</tr>
<tr>
<td>Imiquimod 3.75% cream</td>
<td>Zyclara</td>
<td>✓ ✓ ✓ ✓</td>
<td>✓ ✓ ✓ ✓</td>
<td>✓ ✓ ✓ ✓</td>
<td>✓ ✓ ✓ ✓</td>
</tr>
<tr>
<td>Ingenol mebutate 0.015% gel***</td>
<td>Picato</td>
<td>✓ ✓ ✓ ✓</td>
<td>✓ ✓ ✓ ✓</td>
<td>✓ ✓ ✓ ✓</td>
<td>✓ ✓ ✓ ✓</td>
</tr>
</tbody>
</table>

✓ relative recommendation ✓ ✓ Strong recommendation X Not recommended in primary care
*It may be preferable to divide larger areas into smaller ones and treat them sequentially; **Face and scalp; ***Trunk and limbs

Figure 2. Topical therapies recommended for actinic keratosis by severity (source: Primary Care Dermatology Society)28
treatment regimen is lower. A maximum of one 250mg sachet of cream is applied three times per week for four weeks before bedtime and left on the skin for eight hours. The hands should be washed after application.

Outcome can be assessed four weeks later and the treatment repeated if lesions persist. If the second course fails at assessment after four to eight weeks, an alternative treatment should be tried. Treatment should be suspended if the local reaction is intense or inflammation occurs, but the duration should not subsequently be increased. The basic NHS cost of imiquimod 5% is £48.60 per four-week treatment period. The available evidence suggests that imiquimod is not effective for lesions on the forearms and hands.

Meta-analyses of randomised trials of imiquimod include studies with a treatment duration of 16 weeks. Two trials evaluated the 12-week regimen licensed in the UK for the treatment of AK. After one or two four-week treatments on the face or balding scalp, complete clearance rates were 55 per cent with imiquimod 5% and 2.3 per cent with vehicle. For lesions on the head, complete clearance rates were 54 per cent after eight weeks vs 15 per cent with vehicle. At one year, recurrence rates were 39 per cent after treatment with imiquimod and 57 per cent after vehicle.

Imiquimod 5% is less well tolerated than the weaker formulation. The Primary Care Dermatology Society recommends warning patients to expect marked erythema and crusting (about a quarter of patients experience severe erythema and one-fifth have severe scabbing and crusting); treatment may need to be scheduled to avoid holidays and important social occasions. Common systemic adverse effects include headache, anorexia, fatigue, myalgia and arthralgia.

Lesion-directed topical treatments

The Primary Care Dermatology Society recommends two options for pharmacological treatment of AK lesions: fluorouracil 5% cream (applied nightly for four weeks) or fluorouracil 0.5% plus salicylic acid 10% (a keratolytic) cutaneous solution (Actikerall). Cryotherapy is an additional option for areas other than the lower legs.

Fluorouracil 0.5% plus salicylic acid 10% cutaneous solution (Actikerall)

Actikerall is painted onto the lesions with a brush and left to dry without covering. The solution forms a film over the lesion that should be removed before the next application. Contact with adjacent skin should be avoided. The solution contains dimethyl sulfoxide, which may be irritant, and it can stain textiles and acrylic baths.

Clinical experience with Actikerall is limited to the face, forehead and bald scalp, treating up to 10 lesions at a time with an application area not exceeding 5 x 5cm. In one trial, patients with four to 10 mild-to-moderate AK lesions were treated with Actikerall for up to 12 weeks. Eight weeks after the end of treatment, biopsy found no AKs in 72 per cent of patients treated with Actikerall and in 45 per cent of those using the vehicle; the complete clearance rate was significantly greater with Actikerall (55 vs 15 per cent). After 12 months, 86 per cent of lesions did not recur after treatment with Actikerall compared with 80 per cent after using the vehicle and more patients rated their clinical improvement as “very good” or “good” (93 vs 67 per cent).

Comparative efficacy

Many trials of topical treatments have been published, but comprehensive analyses have not provided conclusive evidence of...
• Increase physician awareness of the potential risks of squamous cell carcinoma and the progression of actinic keratosis to squamous cell carcinoma
• Develop topical treatments with shorter treatment durations but equal clinical efficacy
• Address physician concerns around the impact of topical treatment on quality of life through treatments employing a shorter duration
• Address physician concerns around completion of full courses of treatment through treatments with shorter durations
• Treatment regimens should be simple as this may increase levels of adherence and persistence (and subsequent clinical outcomes)
• Modes of communication to physicians around actinic keratosis as a disease and its treatment should be varied and include talks, presentations and conferences
• Treatment expectations should be clearly communicated to patients through the availability and use of photographs
• Patients should be provided with clear information on actinic keratosis and its treatments to help manage expectations of treatment

Adherence
Considering the marked cosmetic impact of field-directed topical treatments for AK, there have been surprisingly few publications documenting adherence rates. In one small study, interviews with patients showed that the treatment-related factor they were most concerned about was effectiveness, but pain, ulceration, cosmetic appearance, and social and leisure factors influenced satisfaction with treatment.29 A UK study included 305 patients who had treated AK (50 per cent only on the face or scalp, 35 per cent also on the body, and 15 per cent on the body only) with diclofenac gel, fluorouracil 5% cream, imiquimod 5% cream or fluorouracil/salicylic acid solution currently or within the previous 12 months.30 The rate of nonadherence (defined as using more or less than the recommended dose, or more or less frequently than recommended) and nonpersistence (ending treatment prematurely) was 88 per cent. Duration of treatment adversely affected adherence and patient-perceived efficacy (see Figure 3). The authors concluded that less intrusive treatments of shorter duration are needed.

A consensus panel of dermatologists agreed that “real-world efficacy” does not match the results reported in clinical trials and they made eight recommendations to improve adherence (see Table 2).31 These can be summarised as: minimise the duration of treatment; and promote awareness and education among clinicians and patients.

Future therapies
Candidates for new topical treatments for AK come from existing and new pharmacological classes and include the immunomodulatory resiquimod; the topical NSAID piroxicam; dobesilate, an inhibitor of fibroblast growth factors; and the antineoplastic agent betulinic acid.31,32 Recent evidence suggests that oral nicotinamide32 and oral NSAIDs33 may also have potential, not least because they offer the prospect of a different adverse effect profile.

References
10. Primary Care Dermatology Society. Actinic keratosis. February
Actinic keratosis

15. Hanke CW, et al. Complete clearance is sustained for at least 12 months after treatment of actinic keratoses of the face or balding scalp via daily dosing with imiquimod 3.75% or 2.5% cream. J Drugs Dermatol 2011;10:165–70.

Declaration of interests
None to declare.

Steve Chaplin is a pharmacist who specialises in writing on therapeutics