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Management of atopic eczema in primary care

A national clinical guideline

March 2011

KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

LEVELS OF EVIDENCE

1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, eg case reports, case series
4	Expert opinion

GRADES OF RECOMMENDATION

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A	At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; *or* Extrapolated evidence from studies rated as 1++ or 1+
C	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; *or* Extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+

GOOD PRACTICE POINTS

☑	Recommended best practice based on the clinical experience of the guideline development group

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ISBN 978 1 905813 72 8

Published March 2011

Citation text
Scottish Intercollegiate Guidelines Network (SIGN). Management of atopic eczema in primary care. Edinburgh: SIGN; 2011. (SIGN publication no. 125). [March 2011]. Available from URL: http://www.sign.ac.uk

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1 Introduction

1.1 THE NEED FOR A GUIDELINE

Atopic eczema (AE) is a common chronic inflammatory skin disorder. The cause of atopic eczema is complex and not fully understood. Both genetic and environmental factors are likely to contribute, with defects in epithelial barrier function arising from abnormalities in structural proteins such as filaggrin making the skin both excessively permeable and more prone to damage from environmental irritants and allergens.[1]

The disorder affects both sexes equally and usually starts in the first months of life. In the UK, 15-20% of school-aged children and 2-10% of adults will be affected by the condition at some stage.[2] A study of atopic eczema in the Scottish population found an overall one-year period prevalence of 2.3%.[3] Prevalence was highest in children less than two years of age (9.8%), and diminished with increasing age. Thirty eight per cent of all patients with atopic eczema were adults. The most common progression of atopic eczema is for it to resolve during childhood, but it may persist into adult life or recur in the teenage or early adult years. Occasionally, it may develop for the first time in mature adulthood.

Depending on disease severity, atopic eczema may have a considerable adverse effect on the quality of life of affected individuals (eg through sleep disturbance) and their families. Atopic eczema may adversely influence a child's emotional and social development and may predispose to psychological difficulties.[4,5]

The annual cost to the NHS of treating atopic eczema in the mid-nineties was £125 million, and the annual personal cost to the UK population £297 million.[6] The annual societal cost of lost working days was estimated at £43 million, making the total annual UK expenditure on atopic eczema in the mid-nineties £465 million. In 2002 the cost of community dispensed prescriptions for topical corticosteroids for atopic eczema was estimated as £11.6 million.[2]

The majority of the treatment for atopic eczema is delivered by the primary healthcare team, with only a minority of patients referred to secondary care.[7] Atopic eczema is a multifaceted condition that can be a therapeutic challenge, especially in primary care. There appears to be real potential for improving the outcome of its treatment in the community[8] and perhaps the cost effectiveness of treatment.

1.2 REMIT OF THE GUIDELINE

1.2.1 OVERALL OBJECTIVES

This guideline focuses on providing recommendations for the management of atopic eczema in children and adults in primary care, based on current evidence for best practice. It includes advice on the various topical treatments for atopic eczema (including emollients (moisturisers), topical corticosteroids, topical calcineurin inhibitors and dressings), anti-infective treatments (such as antibiotics and antiseptics), antihistamines, complementary therapies and the roles of diet and environmental factors. It excludes treatments that are usually carried out in secondary care, such as phototherapy and systemic immunosuppressant drugs. The key questions on which the guideline is based are outlined in Annex 1.

1.2.2 TARGET USERS OF THE GUIDELINE

This guideline will be of interest to all community based healthcare professionals who manage patients with atopic eczema particularly general practitioners, health visitors, practice and community based nurses, dietitians and pharmacists, as well as patients with atopic eczema and their carers.

1.3 DEFINITIONS

The words eczema and dermatitis are interchangeable: atopic eczema is the same as atopic dermatitis. The studies cited use both terms, but for consistency, the condition is referred to as atopic eczema throughout the guideline. The term eczema describes a skin disorder that is usually itchy and which is characterised by observable changes that include redness, blistering, oozing, crusting, scaling, thickening and sometimes colour change although not all of these changes will necessarily occur together.

The term atopic is used to describe conditions such as eczema, asthma, seasonal rhinitis and hay fever, which often have a genetic basis and may be associated with sensitisation to common environmental allergens.

1.4 STATEMENT OF INTENT

This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

1.4.1 PRESCRIBING OF MEDICINES OUTWITH THEIR MARKETING AUTHORISATION

Recommendations within this guideline are based on the best clinical evidence. Some recommendations may be for medicines prescribed outwith the marketing authorisation (product licence). This is known as 'off label' use. It is not unusual for medicines to be prescribed outwith their product licence and this can be necessary for a variety of reasons.

Generally the unlicensed use of medicines becomes necessary if the clinical need cannot be met by licensed medicines; such use should be supported by appropriate evidence and experience.[9]

Medicines may be prescribed outwith their product licence in the following circumstances:

- for an indication not specified within the marketing authorisation
- for administration via a different route
- for administration of a different dose.

"Prescribing medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescribers' professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines."

Any practitioner following a SIGN recommendation and prescribing a licensed medicine outwith the product licence needs to be aware that they are responsible for this decision, and in the event of adverse outcomes, may be required to justify the actions that they have taken.

Prior to prescribing, the licensing status of a medication should be checked in the current version of the British National Formulary (BNF).[9]

1.4.2 ADDITIONAL ADVICE TO NHSSCOTLAND FROM NHS QUALITY IMPROVEMENT SCOTLAND AND THE SCOTTISH MEDICINES CONSORTIUM

NHS QIS processes multiple technology appraisals (MTAs) for NHSScotland that have been produced by the National Institute for Health and Clinical Excellence (NICE) in England and Wales.

The Scottish Medicines Consortium (SMC) provides advice to NHS Boards and their Area Drug and Therapeutics Committees about the status of all newly licensed medicines and any major new indications for established products.

SMC advice and NHS QIS validated NICE MTAs relevant to this guideline are summarised in section 14.3.

2 Key recommendations

The following recommendations were highlighted by the guideline development group as the key clinical recommendations that should be prioritised for implementation. The grade of recommendation relates to the strength of the supporting evidence on which the evidence is based. It does not reflect the clinical importance of the recommendation.

2.1 REFERRAL

D **An emergency referral to a dermatologist or paediatrician should be arranged by telephone where there is clinical suspicion of eczema herpeticum** *(widespread herpes simplex).*

D **Patients should be referred to a dermatologist where there is:**

- **uncertainty concerning the diagnosis**
- **poor control of the condition or failure to respond to appropriate topical treatments**
- **psychological upset or sleep problems**
- **recurrent secondary infection.**

2.2 EMOLLIENT THERAPY

C **Patients with atopic eczema should have ongoing treatment with emollients.**

2.3 TOPICAL CORTICOSTEROID THERAPY

A **Patients should be advised to continue with emollient therapy during treatment with topical corticosteroids.**

B **Patients with atopic eczema should be advised to apply topical corticosteroids once daily.**

A **Twice weekly maintenance therapy with a topical corticosteroid should be considered in patients with moderate to severe atopic eczema experiencing frequent relapses.**

2.4 TOPICAL CALCINEURIN INHIBITORS

C **Topical tacrolimus should be considered, in patients aged two years and older, for short term, intermittent treatment of moderate to severe atopic eczema that has not been controlled by topical corticosteroids or where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly skin atrophy.**

2.5 ORAL ANTIBIOTICS

B **Oral antibiotics are not recommended in the routine treatment of non-infected atopic eczema.**

3 Diagnosis, referral and patient education

3.1 DIAGNOSIS

There are no laboratory or diagnostic tests for atopic eczema. The diagnosis of atopic eczema is based on visual assessment and patient history.

Diagnostic criteria have been developed but are mainly used in research settings. In a systematic review of cross-sectional and case control studies, the UK diagnostic criteria were the most extensively validated for atopic eczema in comparison to the Hanifin and Rajka diagnostic criteria, Schulz-Larsen criteria, Diepgen criteria, and Kang and Tian diagnostic criteria. The sensitivity and specificity for the UK diagnostic criteria ranged from 10-95% and 90.4-98.3% respectively. The authors recommended the use of criteria in interventional studies as opposed to daily clinical management.[10] The UK diagnostic criteria are described in Table 1.[11] 2++

Table 1: UK Working Party Diagnostic Criteria[11]

The patient must report an itchy skin condition (or parental report of scratching or rubbing in a child) in the last 12 months, plus three or more of the following:

- history of involvement of the skin creases (front of elbows, behind knees, fronts of ankles, around neck or around eyes)
- personal history of asthma or hayfever (or history of atopic disease in first degree relative if child aged under four years)
- a history of generally dry skin in the last year
- onset under the age of two years (not used if child aged under four years)
- visible flexural dermatitis (including dermatitis affecting cheeks or forehead and outer aspects of limbs in children under four years).

A systematic review suggests that there is no evidence that atopic testing such as skin prick testing or measurement of specific immunoglobulin E (IgE) levels enhances the initial diagnosis of atopic eczema.[12] 2+

3.2 SEVERITY ASSESSMENT AND QUALITY OF LIFE

A guide to visual assessment of eczema severity, as proposed by NICE, is described in Table 2. 4

Table 2: A guide to severity of eczema[1]

Skin/physical severity	
Clear	Normal skin, no evidence of active atopic eczema
Mild	Areas of dry skin, infrequent itching (with or without small areas of redness)
Moderate	Areas of dry skin, frequent itching, redness (with or without excoriation and localised skin thickening)
Severe	Widespread areas of dry skin, incessant itching, redness (with or without excoriation, extensive skin thickening, bleeding, oozing, cracking and alteration of skin pigmentation)

There are numerous scoring systems for assessing the severity of atopic eczema. In a systematic review, only three were considered sufficiently tested and validated; SCORing Atopic Dermatitis (SCORAD), Eczema Area and Severity Index (EASI) and Patient Orientated Eczema Measure (POEM).[13] 2+

There is a correlation between severity of eczema symptoms and some aspects of quality of life (QoL) for patients and their families, with factors such as itching and lack of sleep having a high impact.[14,15] 3

☑ When assessing the severity of atopic eczema, healthcare professionals should take into consideration the adverse effects on quality of life of patients and their families.

3.3 DERMATOLOGICAL COMORBIDITIES AND ASSOCIATED DISORDERS

Atopic eczema may predispose to and coexist with other dermatological disorders that may complicate diagnosis, such as hyper-IgE syndrome, scabies, herpes simplex infection, staphylococcal and streptococcal infection, superficial fungal infection and contact dermatitis (irritant and allergic).

Widespread herpes simplex (eczema herpeticum) should be considered in any patient with rapidly deteriorating atopic eczema.

Some rare genetic disorders are associated with a pattern of cutaneous inflammation that resembles atopic eczema. These include Wiskott-Aldrich syndrome, anhidrotic ectodermal dysplasia, phenylketonuria, Netherton's syndrome, ataxia-telangiectasia and agammaglobulinaemia.

3.4 REFERRAL

The Centre for Change and Innovation for NHSScotland formed criteria for referral to a dermatology consultant and criteria for emergency referral.[16] The recommendations below are adapted from these criteria. Referral for consideration of food allergy investigation is discussed in section 11.1. 4

D **An emergency referral to a dermatologist or paediatrician should be arranged by telephone where there is clinical suspicion of eczema herpeticum** *(widespread herpes simplex).*

D **Patients should be referred to a dermatologist where there is:**

- **uncertainty concerning the diagnosis**
- **poor control of the condition or failure to respond to appropriate topical treatments**
- **psychological upset or sleep problems**
- **recurrent secondary infection.**

3.5 EDUCATIONAL INTERVENTIONS

A Cochrane review identified four studies on the effect of parent education interventions on eczema severity in children. In two of the studies the interventions were effective in terms of reduced clinical severity scores. There was heterogeneity in the format (group and one to one), content and setting (nurse-led, multidisciplinary) of the interventions meaning that results could not be combined. The review also described the findings of studies examining various group and individual educational interventions for adult patients and how these may improve knowledge and understanding of treatments.[17] 1^{++}

The lack of consistency in the trials means that no evidence based recommendation can be made.

4 Emollient therapy

4.1 EFFECTIVENESS

Emollients (moisturisers) soften the skin, aid in restoring the impaired barrier function of the epidermis, reduce the itch of dry skin,[18] increase the efficacy of topical corticosteroids[19,20] and have a steroid sparing action.[21] Emollients replace the natural surface oils which tend to be deficient in AE and which are essential both in preventing irritant materials, infection and allergy-inducing substances from entering the skin and water from leaving the skin. | 1^- 1^+

Although long term emollient therapy is considered the mainstay of treating atopic eczema, a systematic review conducted in 2000 did not identify any high quality clinically relevant evidence in support of emollient monotherapy.[22] | 1^{++}

Expert opinion (from a clinical guideline for children but applicable to adults) supports the use of emollients in the treatment of atopic eczema to restore the defective skin barrier. It recommends that healthcare professionals offer a range of emollients allowing selection of the most appropriate to the patient, and that prescriptions should be reviewed frequently.[1] | 4

C **Patients with atopic eczema should have ongoing treatment with emollients.**

☑ To optimise adherence to emollient therapy, creams, lotions, ointments, or a combination can be used, depending on patient choice. Prescriptions should be reviewed regularly.

☑ Patients and parents/carers of children should be educated about regularly applying emollients onto dry skin and eczematous areas even when eczema is under control.

Table 3 describes the types of emollient products available.[1] Several of the products are designed to substitute for conventional bath and shower products, which may act as drying agents or deposit irritant residues onto the skin and should be avoided by people with AE. | 4

Table 3: Types of emollient products[1]

Type	Description
Emollient creams and ointments	These products are designed to be left on the skin. Creams soak into the skin faster than ointments.
Emollient soap substitutes	These products contain emollient ingredients with very mild emulsifiers. They are used instead of soap and other detergents.
Emollient semidispersing bath oils	These contain oils and emulsifiers that disperse the oil in the water. This combination has a cleansing effect if gently rubbed over the skin.
Non-dispersing emollient bath oils	These products contain oils with no emulsifying agent. The oil forms a layer on the surface of the water which is deposited on the skin on getting out of the bath.
Adjuvant emollient products	Some emollient products contain additional ingredients such as antipruritics and antiseptics.

4.2 APPLICATION TECHNIQUE

No evidence was identified on the frequency with which to apply emollients or the most appropriate application techniques. When an eczema treatment regimen involves both an emollient and topical corticosteroid (TCS), there is no evidence on which to base their order of application. Suggested prescribing quantities for a week of emollient therapy are shown in Annex 2.

The following good practice points are based on the clinical experience of the guideline development group.

☑
- Patients should be advised to apply emollients liberally and frequently (at least 2-4 times a day). It is particularly important to use emollients during or after bathing.
- Sufficient quantity of emollient should be prescribed.
- The emollient should be applied smoothly in the general direction of growth of body hair in order to prevent accumulation at hair bases which might predispose to folliculitis.
- Emollients can become contaminated with bacteria. The use of pump dispensers minimises the risk of microbial contamination. If the emollient is in a pot the required amount should be removed with a clean spoon or spatula. Fingers should not be inserted into pots. Emollients should not be shared with others.

5 Topical corticosteroid therapy

5.1 POTENCY

Topical corticosteroids (TCS) are categorised into four groups according to potency (ie the effectiveness in reducing inflammation): mild, moderately potent, potent and very potent.[9] TCS potency is dependent on a number of factors including the unique properties of corticosteroid moiety, formulation and penetration into the skin. Potency of a TCS is not simply a function of concentration. The British National Formulary outlines the range of compounds and formulations available.[9]

No good quality evidence was identified to assist in the choice of TCS potency in the treatment of atopic eczema.

The NICE guideline on management of atopic eczema in children suggested a stepped/matched approach, matching potency of TCS with severity of the eczema: mild potency TCS for mild disease, moderate potency for moderate disease and potent TCS reserved for short term use in severe eczema.[1] | 4

☑ The choice of TCS potency should be tailored to the age of the patient, the body region being treated, and the degree to which the skin is inflamed. For delicate areas of skin, such as the face and flexures, only mild or moderately potent preparations should be used. On the face, especially in children, it is reasonable to start with a mildly potent TCS.

5.2 EFFECTIVENESS

A systematic review of randomised controlled trials (RCT) identified 83 on the use of TCS in AE. Studies were generally of less than one month duration and of poor methodological quality. A wide range of treatment outcome measures were used. Although results of studies could not be combined, where outcomes were reported there were large positive treatment effects when compared to placebo.[22] | 1^{++}

No comprehensive evidence was identified comparing TCS with each other in terms of effectiveness.

Continuation with emollient therapy during treatment with TCS has been shown to improve treatment outcomes (see *section 4.1*).[19,20] | 1^{+}

A **Patients should be advised to continue with emollient therapy during treatment with topical corticosteroids.**

5.2.1 ONCE VERSUS TWICE DAILY APPLICATION

A systematic review of 10 RCTs reviewed moderate to potent TCS in patients with moderate to severe eczema to assess the optimum frequency of application. Both once daily and twice daily application of TCS was effective, without clear evidence that the twice daily application confers any significant clinical advantage over once daily. The methodological quality for the majority of studies was deemed to be poor (poor concealment, inadequate randomisation) and participant numbers were small.[2] | 1^{++}

B **Patients with atopic eczema should be advised to apply topical corticosteroids once daily.**

☑ If there is an inadequate response to once daily application, the frequency should be increased to twice daily.

5.2.2 MAINTENANCE THERAPY

Although constant use of TCS is undesirable due to risk of local and systemic adverse effects, no evidence was identified to support any particular TCS treatment strategy in terms of maximum duration of continuous use or the frequency with which this can be repeated.

Three RCTs suggest that adding twice weekly TCS application to emollient based maintenance therapy following stabilisation of eczema reduces relapse rate.

Adults and children with AE receiving long term (up to 48 weeks) fluticasone propionate cream (0.05%) twice weekly in addition to regular daily emollients were 7.7 times less likely (95% CI (confidence interval) 4.6 to 12.8, $p < 0.001$) to have an AE relapse than patients receiving intermittent vehicle cream and daily emollients.[23] 1+

In a large multicentre trial (n = 295) in adults with moderate to severe atopic eczema, topical fluticasone propionate applied as maintenance therapy (in addition to emollient) on two consecutive evenings each week reduced relapse rate following stabilisation of the condition. Patients applying fluticasone propionate cream (0.05%) were 5.8 times less likely (95% CI 3.1 to 10.8, $p < 0.001$) to experience relapse during the 16 week follow up than those using emollient and placebo. Those using the ointment formulation (0.005%) were 1.9 times less likely (95% CI 1.2 to 3.2, $p = 0.010$) to experience relapse when compared to patients allocated to emollient plus placebo.[24] 1+

A large RCT (n = 249) in adolescent and adult patients with moderate to severe atopic eczema demonstrated that patients receiving maintenance therapy with methyl-prednisolone aceponate cream (0.1%), applied twice weekly, with daily emollient therapy, for 16 weeks had a 3.5-fold lower risk of suffering a relapse of their eczema than those treated with emollient alone.[25] This preparation is not licensed in the UK. 1++

A **Twice weekly maintenance therapy with a topical corticosteroid should be considered in patients with moderate to severe atopic eczema experiencing frequent relapses.**

5.3 ADVERSE EFFECTS

The local adverse effects of TCS usage include skin thinning, bruising, perioral dermatitis, folliculitis, pruritus, allergic contact dermatitis and the spread of fungal infection. In a systematic review the short term use of TCS was not associated with observable skin thinning. Some RCTs have reported that early skin atrophy can be reversed on stopping TCS.[22] 1++

☑ Patients being treated with intermittent courses of topical corticosteroids should be reviewed every three to six months (depending on TSC potency and site of application) to ascertain response to therapy and assess skin for potentially reversible atrophic changes.

A systematic review of RCTs assessing the safety of topical corticosteroids for atopic eczema found that evidence does not support an association between TCS usage and skin malignancies, systemic malignancy or systemic infection. TCS usage around the eyes has been associated with glaucoma and cataracts, although the degree of risk has not been established. Although the local adverse effects of TCS are well described, the review concluded there are insufficient vehicle control studies of adequate duration to quantify the incidence or degree of risk.[26] 1+

In a small, short term pilot study (n = 20), the twice daily application of clobetasone butyrate ointment (0.05%) for three weeks to treat eyelid eczema in patients with atopic keratoconjunctivitis did not affect intraocular pressure and did not cause any adverse effects.[27] 1+

B **Topical corticosteroids should be used with caution in the periocular region.**

A systematic review of the effect of topical steroids on the hypothalamic-pituitary-adrenal (HPA) axis in children identified 10 observational studies. Findings were inconsistent. Although some studies reported an association between TCS use and HPA axis suppression as measured by plasma cortisol level, others reported no effect. There was a wide range of interventions and study durations.[26] 1+

Three small short term studies conducted since the systematic review were identified.

A randomised study of the effect of a two week course of a potent TCS (mometasone furoate) on bone growth in children with mild to moderate atopic eczema showed no statistically significant effect.[28] 1-

In an open label study, the daily application of a very potent TCS (fluocinonide cream, 0.1%) to at least 20% of the body surface area of children as young as three months for two weeks did not suppress the HPA axis in any child. The twice daily application of fluocinonide cream (0.1%) did cause HPA axis suppression in 10% of patients, although the risk was no greater for infants and young children than for adolescents.[29] 2+

A potent TCS (hydrocortisone butyrate, 0.1%) applied three times daily to at least 25% of the body surface of children with atopic eczema aged 5-12 years, for up to four weeks, was not associated with adrenal suppression in any of the 20 children in the study.[30]

There is insufficient consistent evidence on which to base a recommendation for growth monitoring.

5.4 APPLICATION TECHNIQUE

The 'fingertip unit' (FTU) has been used as a method of determining the amount of TCS to apply (*see Annex 3*). The FTU is defined as the volume of a ribbon of cream or ointment the length of the distal phalanx of an adult's index finger expressed from a tube with a 5 mm diameter nozzle.[31]

☑ The fingertip unit should be used to guide patients on topical corticosteroid quantities required.

☑ Patients should be advised to apply topical corticosteroids in an amount sufficient to adequately cover the areas of inflamed skin even if the skin is excoriated.

6 Topical calcineurin inhibitors

6.1 STATUS AND INDICATIONS FOR USE

Topical calcineurin inhibitors (TCIs) are non-steroidal immunomodulating agents licensed for the treatment of atopic eczema. Two TCIs are available: tacrolimus as 0.03% and 0.1% ointments (both licensed for moderate to severe eczema, the 0.03% ointment licensed for use in children aged two years and over), and 1% pimecrolimus cream (licensed for mild to moderate eczema in patients aged two years and over).

In 2010 the Scottish Medicines Consortium issued advice restricting the use of tacrolimus 0.03% and 0.1% ointments for treatment and maintenance therapy to initiation by doctors with a specialist interest and experience in treating atopic dermatitis using immunomodulatory therapy. This can include general practitioners (*see section 14.3*).

In 2004 the Scottish Medicines Consortium rejected pimecrolimus for use within NHSScotland.

Since the long term safety of both TCIs is still being evaluated it is currently recommended that TCIs should not be used as first line treatment unless there is a specific reason to avoid or reduce the use of topical corticosteroids.[1,9]

6.2 COMPARATIVE EFFECTIVENESS WITH TOPICAL CORTICOSTEROIDS

6.2.1 ADULTS

A systematic review identified two comparisons of tacrolimus ointment with potent TCS in adults with moderate to severe AE. Tacrolimus (0.1%) was as effective as potent TCS in achieving marked improvement in the condition at three weeks. Tacrolimus (0.03%) was less effective than hydrocortisone butyrate (0.1%).[32] In adults with moderate to severe atopic eczema, tacrolimus ointment (0.1%) was more effective than a combined TCS regimen (hydrocortisone acetate (1%) on face and hydrocortisone butyrate (0.1%) on trunk and limbs) in achieving improvement at 12 weeks.[32] 1++

A systematic review identified two RCTs comparing pimecrolimus cream (1%) with moderate potency and potent corticosteroids in adults with moderate to severe atopic eczema. In both trials pimecrolimus was significantly less effective at three weeks in achieving clear or almost clear eczema than the TCS.[33] 1++

6.2.2 CHILDREN

A systematic review reported on two trials comparing tacrolimus with hydrocortisone acetate (1%) (mild potency TCS) in children. Both 0.03% and 0.1% tacrolimus were significantly more effective than the TCS in improving the condition at three weeks. The review did not identify any trials comparing pimecrolimus with mild corticosteroid in children.[32] 1+

6.3 REDUCTION IN USE OF TOPICAL CORTICOSTEROIDS

In a vehicle controlled study in patients aged 12 years or older with head and neck eczema who were intolerant of, or dependent on TCS, use of pimecrolimus for 12 weeks was associated with reversal of skin atrophy.[34] 1+

In the long term management of patients with atopic eczema, pimecrolimus used by adults for 26 weeks provided significantly more TCS-free days than the placebo and reduced the number of flares requiring TCS application.[35] Another RCT, in adults with moderate to severe atopic eczema, using pimecrolimus for up to a year, found that a significant number of patients (276 out of 658; 42%) could be maintained without TCS for up to a year in the pimecrolimus group.[36] 1++ 1+

6.4 ADVERSE EFFECTS

In a systematic review of RCTs the most common adverse effects of tacrolimus and pimecrolimus were skin irritation and burning. The rate of skin burning was greater than with TCS.[32] A non-statistically significant trend towards increased incidence of infections when using TCIs, particularly virally mediated, was noted in a systematic review of medication safety.[26] 1+

In a systematic review no evidence was identified to show that use of pimecrolimus was associated with skin thinning.[33] Furthermore, an RCT demonstrated that pimecrolimus cream (0.1%) may reverse TCS induced skin atrophy.[34] Similarly, long term treatment (one year) with tacrolimus ointment in atopic eczema appears non-atrophogenic and may also reverse TCS induced skin atrophy, although this observation was based on a small number of patients.[37] 1+ 1- 2+

There are significant concerns around increased risk of malignancy (including skin cancers and lymphomas) following TCI use, based on post-marketing surveillance reports.[26,38] Since these treatments are relatively new there is insufficient evidence to make a definitive statement on whether patients with atopic eczema treated with a TCI are at an increased risk of developing malignancy. This uncertainty around long term safety profile limits the use of TCIs to moderate and severe AE and to a second line therapy. 1+ 2+

6.5 MAINTENANCE THERAPY

In adults, 12 month maintenance therapy, applying 0.1% tacrolimus ointment twice weekly was effective in preventing, delaying and reducing the occurrence of atopic eczema exacerbations.[39] 1+

6.6 RECOMMENDATIONS

C **Topical tacrolimus should be considered, in patients aged two years and older, for short term, intermittent treatment of moderate to severe atopic eczema that has not been controlled by topical corticosteroids or where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly skin atrophy.**

☑ As a precaution against the possibility that the normal immunological response to infection may be suppressed, topical calcineurin inhibitors should not be applied to skin which appears actively infected.

7 Dressings and wet wrap treatment

7.1 DRESSINGS

NICE outlined a range of dressing types used in the management of atopic eczema *(see Table 4)*. No RCTs were identified relating to the efficacy of dry wrap, occlusive or medicated bandages.[1]

Table 4: Dressings used in the management of atopic eczema[1]

Type of dressing	Method used
Dry wrap dressings	Open-weave tubular bandage or crepe bandage used as a protective dressing, eg to keep greasy moisturisers in place.
Occlusive/semi-occlusive dressings	These include vapour-permeable films and membranes and hydrocolloid dressings. They can be used over topical preparations. Nappies, sleep suits and pyjamas may also have an occlusive effect and enhance skin penetration of topical preparations.
Medicated bandages	Cotton bandages impregnated with a variety of therapeutic substances such as tar or ichthammol. The bandages are usually applied over topical preparations in a spiralling and pleated fashion in the direction of venous return. A layer of self gripping, elasticised, non-adhesive bandage is usually needed over the bandage (topical preparation) to keep it in place. The bandages can only be used on the limbs. They cannot be applied to the trunk and face as they may tighten as they dry.

☑ Patients with non-infected moderate to severe eczema should be advised to cover affected areas with dry wrap dressings to provide a physical barrier to scratching and improve retention of emollient.

7.2 WET WRAP TREATMENT

Wet wrapping generally consists of two layers of open-weave tubular bandage applied over topical preparations. The bottom layer is soaked in warm water, squeezed out and then put onto the skin over the topical preparation. The top layer is dry. Wet wraps can be worn under nightwear or ordinary clothes and used during the day or night. They are available in bandage form or as garments.[1]

A NICE systematic review identified four small RCTs of wet wrap dressing treatment over TCS in children. Results could not be combined due to the range of techniques and timings used, the range of TCS dilutions, the definitions of eczema severity and lack of methodological information provided. The review concluded that there is no evidence that wet wrap therapy is more effective than conventional TCS treatment in patients with mild to moderate eczema. Higher study withdrawal rates, difficulties with application and increased use of antibiotics were reported with wet wrap therapy. Observational studies suggested that growth and bone turnover were not affected by two week periods of use of TCS under wet wrap dressings.[1] 1++

A review examining two small clinical studies and published expert opinion supports the use of wet wrap treatment with diluted TCS in children with severe atopic eczema where there has been a lack of response to conventional treatment. It is suggested that use should be limited to a short term basis of up to seven days (with once daily application) to minimise potential adverse effects of steroid absorption.[40] 1+

No RCT evidence was identified on the efficacy of wet wrap dressings used with emollient.

There is insufficient consistent evidence on which to base a recommendation for wet wrap use in the primary care setting.

8 Antimicrobial measures

8.1 INTRODUCTION

Although the skin lesions of around 90% of patients with atopic eczema are colonised with *Staphylococcus aureus* compared to (< 5%) of individuals with healthy skin, the nature of the association between *S. aureus* and the aetiology or promotion of the disorder is unclear. The degree of colonisation is associated with disease severity. Staphylococcal antigens have been shown to act as super-antigens in patients with atopic eczema and may induce toxin-specific IgE, titres of which correlate with the severity of atopic eczema.[41]

Although staphylococci are the main organisms isolated, other organisms, particularly streptococci, may cause infection.

☑ Routine swabbing of skin is not indicated in the management of patients with atopic eczema.

☑ Swabs of potential *S. aureus* carriage sites (of both the patient and family members) should be considered in patients with recurrent infection.

☑ In patients with atypical features, or where there is concern about possible streptococcal infection, skin swabs of affected areas should be considered.

8.2 EFFECTIVENESS OF ANTIMICROBIAL MEASURES

8.2.1 ORAL ANTIBIOTICS

In a Cochrane review oral antibiotics were not associated with benefit in patients with non-infected eczema (2 trials, 66 participants) or infected eczema (1 trial, 33 participants).[41] 1++

B **Oral antibiotics are not recommended in the routine treatment of non-infected atopic eczema.**

☑ In the absence of a clear evidence base, the current standard practice of short term oral antibiotic treatment for patients with clinically infected eczema should continue. Treatment of bacterial infections should be based on local and regional antibiotic sensitivities.

8.2.2 TOPICAL ANTIBIOTICS COMBINED WITH CORTICOSTEROIDS

Although, in some studies, they are associated with reduction in *S. aureus* colonisation, a systematic review found no clear evidence that topical antibiotics combined with TCS provided clinical benefit in AE treatment compared to TCS alone. Overall methodological quality of trials was poor and it is not possible to provide an evidence based recommendation for practice.[41] 1++

8.2.3 ANTISEPTICS

A Cochrane review identified a small number of diverse studies and found no benefit for antibacterial soaps, bath additives or topical antibiotics/antiseptics in the treatment of atopic eczema.[41] 1++

9 Antihistamines

The role of histamine in the mechanism of itch and inflammation in atopic eczema has not yet been clearly defined. Whilst some studies have suggested that histamine is important in this respect, others have cast doubt on its significance.[42,43]

Acute episodes of urticaria may be a coexisting problem in patients with eczema and the NICE guideline on atopic eczema in children recommends the use of antihistamines where this is a problem.[1] | 4

The NICE systematic review identified several small short term trials on oral antihistamines from which no conclusions could be drawn, and one large placebo-controlled RCT in children with AE aged under two years (n = 795) which examined the use of cetirizine (0.25 mg/kg twice daily) for 18 months as a preventative intervention against development of asthma. As a secondary outcome the effects of treatment on the severity of AE were measured. There was no statistically significant difference between the treatment and placebo groups at any time point, although in infants with the most severe AE (SCORAD ≥ 25 at baseline), there was a corticosteroid sparing effect. The safety of cetirizine over the 18 months time period was confirmed.[44,45] | 1 + +

A well designed placebo-controlled trial of fexofenadine (60 mg twice daily) in adults (n = 400), given as an adjunct to topical hydrocortisone butyrate (0.1%) found a rapid, small, but statistically significant improvement in both daytime and nocturnal pruritus in the treatment group when compared with the placebo plus TCS group.[43] The safety profile of fexofenadine was deemed equivalent to that of the placebo, although the study duration was only one week. | 1 + +

There is insufficient evidence on which to base a recommendation for antihistamines in atopic eczema.

☑ Short term bedtime use of sedating antihistamines should be considered in patients with atopic eczema where there is debilitating sleep disturbance.

10 Environmental factors

A number of environmental factors and irritants have been suggested as potential triggers for the development, severity and exacerbation of atopic eczema.[1] There is little good quality evidence on the effects of manipulating environmental factors in the management of atopic eczema.

10.1 HOUSE DUST MITE

A systematic review of five RCTs found a small reduction in house dust mite levels through vacuuming, use of acaricide spray and specialist bedding. The clinical benefits in the management of atopic eczema from this reduction is unclear.[22] | 1^{++}

10.2 EXPOSURE TO PETS

A systematic review concluded that there is no evidence to ascertain whether exposure to a cat or dog in the home contributes to disease flares in atopic eczema.[46] | 1^{++}

10.3 CLOTHING

A systematic review identified two RCTs on clothing materials and their effects on the symptoms of atopic eczema. It was concluded that cotton clothing did not confer any benefits when compared to other fabrics constructed with smooth fibres.[22] | 1^{++}

Limited RCT evidence based on small studies suggests that silver coated textiles can reduce AE symptoms, possibly via an antibacterial effect.[47-49] | 1^{-}

10.4 TEMPERATURE AND HUMIDITY

No good quality evidence was identified on the effectiveness of the avoidance of extremes of temperature or humidity in the management of patients with established atopic eczema.

10.5 IRRITANTS

No good quality trials were identified to address the effectiveness of avoidance of irritants such as washing powders, fabric softeners and fragranced products in the management of atopic eczema.

☑ Where an irritant effect is suspected, patients should be advised to avoid biological washing powders, fabric conditioners and fragranced products such as soaps and shower gels.

11 Dietary interventions

11.1 FOOD ALLERGY AND DIETARY EXCLUSION

The role of food allergy in atopic eczema remains controversial. Around 35-40% of children seeing a specialist for atopic eczema have some form of food allergy.[50] Although, there is an association between IgE mediated food allergy and atopic eczema severity in infants, it is unclear whether hypersensitivity to food is a major factor in causing and maintaining atopic eczema.

A Cochrane review of nine RCTs involving 421 patients, concluded that there is no benefit in the use of a milk- or egg-free diet, elemental or few-foods diet in unselected patients with atopic eczema.[51] Studies were generally of poor quality with inadequate concealment and high dropout rates. Findings from one study in the review indicated that an egg-free diet may be beneficial for selected infants who are IgE positive to eggs. 1++

Detailed discussion of the management of food allergy is beyond the scope of this clinical guideline. Referral for allergy investigation may be appropriate where food allergy is suspected.[16]

C **Dietary exclusion is not recommended for management of atopic eczema in patients without confirmed food allergy.**

☑ Where there is suspicion of food allergy in infants or children with atopic eczema, general practitioners should refer to an allergist or paediatrician with a special interest in allergy.

11.2 INFANT FEEDING

11.2.1 MATERNAL FOOD ANTIGEN AVOIDANCE

A Cochrane review of four studies concluded that maternal food antigen avoidance (through diets excluding milk, eggs, wheat and a range of other foods) during pregnancy and breast feeding does not have a protective effect on the development of atopic eczema during the first 18 months of life.[52] 1+

A **The exclusion of foods during pregnancy and breast feeding to prevent the development of atopic eczema in infants is not recommended.**

11.2.2 BREAST FEEDING

A meta-analysis of prospective studies found that exclusive breast feeding for three months or more was protective against the development of infant atopic eczema where there was a positive family history of atopy (OR 0.58, 95%CI 0.41 to 0.92), but in a small number of studies in individuals without a family history of atopy there was no protective effect (OR 1.43; 95% CI 0.72 to 2.86).[53] 2++

B **Parents should be advised that exclusive breast feeding for three months or more may help prevent the development of infant eczema where there is a family history of atopy.**

11.2.3 FORMULA FEEDING

A Cochrane review concluded that there is no evidence of reduction in the incidence of infant eczema or prevalence of childhood eczema from feeding with hydrolysed formulas rather than exclusive breast feeding. Limited evidence from a single trial suggests that use of an extensively hydrolysed casein-containing formula as a supplement to breast feeding when compared to supplementary use of cow's milk formula may protect against infant and childhood eczema.[54] 1++

B **Hydrolysed formulas should not be offered to infants in preference to breast milk for the prevention of atopic eczema.**

11.2.4 WEANING

A systematic review of nine cohort studies concluded that introducing solids prior to four months of age may contribute to the development of eczema. Results should be viewed with caution, as there were a number of methodological biases.[55] 2+

Current UK guidelines based on recommendations from the WHO recommend that weaning should start at six months.[56]

11.3 FOOD SUPPLEMENTS

11.3.1 PREBIOTICS

A systematic review identified two studies on the effects of supplementing infant formula with prebiotic on preventing of atopic eczema. There was heterogeneity between the studies and results were conflicting. It is not possible to make a recommendation.[57] 1++

11.3.2 PROBIOTICS

A Cochrane review conducted a meta-analysis of five studies in infants at high risk of allergic disease and reported a reduction in infant eczema with probiotic use (relative risk (RR) 0.82, 95% CI 0.70, 0.95).[58] There was significant heterogeneity across the studies in terms of patient groups, outcomes and probiotic strain. No recommendations can be drawn. 1++

Another Cochrane review found no benefit to probiotic used as a treatment in children with eczema.[59] Again, heterogeneity across studies was great and no recommendation for practice can be made. 1++

11.3.3 MINERALS AND VITAMINS

NICE identified one small poor quality study on zinc supplementation in children with eczema and one poor quality RCT on vitamin E supplementation in adults and children with eczema.[1] No good quality evidence was identified on which to base any recommendation.

12 Complementary and alternative therapies

12.1 PSYCHOLOGICAL AND RELAXATION THERAPIES

A Cochrane systematic review identified one small study comparing the effectiveness of hypnotherapy and biofeedback in children with AE. The outcome measure of severity was unvalidated and there was a high drop-out rate. The review described the findings of studies of psychological interventions in adults and noted some potential benefit for habit reversal techniques, although stressing that these are specialist interventions.[17] 1++

12.2 HERBAL REMEDIES

A Cochrane review of Chinese herbs in the treatment of patients with atopic eczema identified four small poor quality RCTs of the standardised mixture of herbs called Zemophyte. No conclusions could be drawn from the results of the studies.[60] 1++

The following good practice point is adapted from the NICE guideline on management of eczema in children.[1]

Patients with atopic eczema and their parents or carers should be informed that:

☑
- they should be cautious with the use of herbal medicines and be wary of any herbal product that is not labelled in English or does not come with information about safe usage
- topical corticosteroids are deliberately added to some herbal products intended for use by patients with atopic eczema
- liver toxicity has been associated with the use of some Chinese herbal medicines intended to treat atopic eczema.

12.3 DEAD SEA TREATMENT

A small RCT (n = 30) in adults with atopic eczema 'but without active disease' trialled bathing one arm in a Dead Sea salt solution and one in tap water for 15 minutes per day for six weeks.[61] There was a decrease in transepidermal water loss, a 40% decrease in skin roughness, 14% increase in stratum corneum hydration and an improvement in redness in the arm regularly bathed in a solution of Dead Sea salts. In the subgroup which was found at baseline to have elevated transepidermal water loss there was a large improvement (approximately 30%) in transepidermal water loss. The clinical applicability of the study is uncertain. 1-

12.4 OTHER THERAPIES

No methodologically robust evidence was identified on the use of acupuncture, homeopathy or reflexology in the treatment of patients with atopic eczema.

13 Provision of information

This section reflects the issues likely to be of most concern to patients and their carers. These points are provided for use by health professionals when discussing atopic eczema with patients, parents and carers and in guiding the production of locally produced information materials.

13.1 CHECKLIST FOR PROVISION OF INFORMATION

This section explains what information patients/carers can reasonably expect to be provided with at the key stages of the patient journey. The following checklist was designed by members of the guideline development group based on their clinical experience and their understanding of the evidence base.

Diagnosis

- Provide patients and parents or carers of children with eczema with an explanation of what eczema is, including possible causes and, if applicable, why other siblings do not have the condition.
- Emphasise that eczema is not infectious.
- Provide reassurance that the condition can be improved through a variety of treatment options.
- Provide written information on the condition.
- Provide contacts details of organisations that provide support and assistance for carers of people with eczema (*see section 13.2*).

Treatment

Patients or parents/carers should receive a full explanation of how to use treatments and a demonstration of how to apply dressings (if applicable). It is essential that they understand the instructions for each type of treatment prescribed to them and have the opportunity to discuss concerns regarding potential side effects.

- Explain the importance of using emollients even when the condition is well controlled.
- Provide advice on the safe use of emollients, in particular how they can cause bathing surfaces to become slippery and how paraffin based emollients can be flammable.
- Outline how and when topical treatments should be applied, for how long they can be used, and how to manage changes in severity of the condition ('flare up').
- Discuss the safety of steroid treatments.
- Explain how to identify infection and what to do about it.

Many patients will consider using complementary and alternative therapies. Healthcare professionals should discuss the lack of evidence of effectiveness of alternative and complementary therapies with patients, encouraging them to tell their doctor, nurse or pharmacist what they have been using, so that their conventional treatment can be adjusted accordingly and appropriate advice given.

13.2 SOURCES OF FURTHER INFORMATION

British Association of Dermatologists
Willan House, 4 Fitzroy Square
London W1T 5H
Tel: 0207 383 0266 • Fax: 0207 388 5263
www.bad.org.uk

The British Association of Dermatologists is the professional organisation for dermatologists in the UK. The website provides patient information leaflets.

British Skin Foundation
4 Fitzroy Square
London W1T 5HQ
Tel: 0207 391 6341
www.britishskinfoundation.org.uk

The British Skin Foundation is a registered charity which raises funds for skin disease research. The website provides patient information leaflets.

Eczema Scotland
Email: contact@eczemascotland.org
www.eczemascotland.org

Eczema Scotland promotes the work of the National Eczema Society in Scotland.

National Eczema Society
Hill House, Highgate Hill
London N19 5NA
Tel: 020 7281 3553 • Helpline: 0800 089 1122 (8am to 8pm Monday to Friday)
Email: info@eczema.org
www.eczema.org

The National Eczema Society is a patient support organisation, offering help and information to anyone affected by eczema.

NHS Choices
www.nhs.uk

NHS Choices is a comprehensive healthcare information service.

14 Implementing the guideline

This section provides advice on the resource implications associated with implementing the key clinical recommendations, and advice on audit as a tool to aid implementation.

Implementation of national clinical guidelines is the responsibility of each NHS Board and is an essential part of clinical governance. Mechanisms should be in place to review care provided against the guideline recommendations. The reasons for any differences should be assessed and addressed where appropriate. Local arrangements should then be made to implement the national guideline in individual hospitals, units and practices.

14.1 RECOMMENDATIONS WITH POTENTIAL RESOURCE IMPLICATIONS

Recommendation		Section	Likely resource implication
B	**Patients with atopic eczema should be advised to apply topical corticosteroids once daily.**	5.2.1	Reduced prescribing costs
C	**Topical tacrolimus should be considered, in patients aged two years and older, for short term, intermittent treatment of moderate to severe atopic eczema that has not been controlled by topical corticosteroids or where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly skin atrophy.**	6.6	Increased prescribing costs

14.2 AUDITING CURRENT PRACTICE

A first step in implementing a clinical practice guideline is to gain an understanding of current clinical practice. Audit tools designed around guideline recommendations can assist in this process. Audit tools should be comprehensive but not time consuming to use. Successful implementation and audit of guideline recommendations requires good communication between staff and multidisciplinary team working.

The guideline development group has identified the following as key points to audit to assist with the implementation of this guideline:

- Proportion of patients diagnosed with AE who:
  - are directed to or provided with written information on the condition
  - have appropriate quantities of emollient on repeat prescription
  - have had instruction on correct application of topical preparations.
- Record of advice to patients on:
  - recognising signs of infection
  - how to deal with flares and when to re-attend the GP.
- Regular review of TCS prescriptions in place.

14.3 ADDITIONAL ADVICE TO NHSSCOTLAND FROM THE SCOTTISH MEDICINES CONSORTIUM

In April 2010, tacrolimus 0.1% ointment was accepted for restricted use within NHSScotland.

Licensed indication under review: the maintenance treatment of moderate to severe atopic dermatitis for the prevention of flares and the prolongation of flare-free intervals in adult patients (16 years) experiencing a high frequency of disease exacerbations (ie occurring four or more times per year) who have had an initial response to a maximum of six weeks treatment of twice daily tacrolimus ointment (lesions cleared, almost cleared or mildly affected).

SMC restriction: Use is restricted to initiation by doctors with a specialist interest and experience in treating atopic dermatitis using immunomodulatory therapy (this can include general practitioners).

In March 2010, tacrolimus 0.03% ointment was accepted for restricted use within NHSScotland.

Licensed indication under review: for maintenance treatment of moderate to severe atopic dermatitis in children (aged 2-15 years) for the prevention of flares and the prolongation of flare-free intervals in patients experiencing a high frequency of disease exacerbations (ie occurring four or more times per year) who have had an initial response to a maximum of six weeks treatment of twice daily tacrolimus ointment (lesions cleared, almost cleared or mildly affected).

SMC restriction: Use is restricted to initiation by doctors with a specialist interest and experience in treating atopic dermatitis using immunomodulatory therapy (this can include general practitioners).

In August 2004 pimecrolimus was rejected for use within NHSScotland.

15 The evidence base

15.1 SYSTEMATIC LITERATURE REVIEW

The evidence base for this guideline was synthesised in accordance with SIGN methodology. A systematic review of the literature was carried out using an explicit search strategy devised by a SIGN Information Officer. Databases searched included Medline, Embase, Cinahl, PsychInfo and the Cochrane Library. The year range was 2004-2009. The main searches were supplemented by material identified by individual members of the development group, including key reviews from outside the search period. Each of the selected papers was evaluated by members of the group using standard SIGN methodological checklists before conclusions were considered as evidence.

15.1.1 PATIENT ISSUES

At the start of the guideline development process, a SIGN Information Officer conducted a standard SIGN literature search for qualitative and quantitative studies that addressed patient issues of relevance regarding atopic eczema, with a date range 2002-2008. A further search was conducted on patient and social aspects. The results of the two searches were summarised and presented to the guideline development group to inform them of key patient issues for consideration when devising the key questions. Databases searched include Medline, Embase, Cinahl and PsychInfo.

15.2 RECOMMENDATIONS FOR RESEARCH

The guideline development group was not able to identify sufficient evidence to answer all aspects of the key questions asked in this guideline. The following areas for further research have been identified:

- Studies on the efficacy of different formats and delivery of patient information in improving management, self care and adherence with treatment in patients with atopic eczema.
- Interventions to promote adherence with emollient and topical corticosteroid therapies.

15.3 REVIEW AND UPDATING

This guideline was issued in 2011 and will be considered for review in three years. Any updates to the guideline in the interim period will be noted on the SIGN website: **www.sign.ac.uk**.

16 Development of the guideline

16.1 INTRODUCTION

SIGN is a collaborative network of clinicians, other healthcare professionals and patient organisations and is part of NHS Quality Improvement Scotland. SIGN guidelines are developed by multidisciplinary groups of practising clinicians using a standard methodology based on a systematic review of the evidence. The views and interests of NHS Quality Improvement Scotland as the funding body have not influenced any aspect of guideline development, including the final recommendations. Further details about SIGN and the guideline development methodology are contained in 'SIGN 50: A Guideline Developer's Handbook', available at **www.sign.ac.uk**

16.2 THE GUIDELINE DEVELOPMENT GROUP

Dr Michael Tidman *(Chair)*	*Consultant Dermatologist, Royal Infirmary of Edinburgh*
Ms Karen Braithwaite	*Pharmacist, Aberlour Pharmacy, Moray*
Ms Juliet Brown	*Information Officer, SIGN*
Mrs Jane Calder	*Senior Dietitian, St John's Hospital, Livingston*
Miss Jennifer Layden	*Programme Manager, SIGN*
Sister Janice Lowe	*Clinical Nurse Specialist in Dermatology, Royal Infirmary of Edinburgh*
Dr Pamela McHenry	*Consultant Dermatologist, Royal Hospital for Sick Children, Glasgow*
Dr Mary Mealyea	*Associate Specialist in Dermatology, Royal Hospital for Sick Children, Glasgow*
Dr Olivia Schofield	*Consultant Dermatologist, Royal Infirmary of Edinburgh*
Dr Tracey Secrett	*General Practitioner, Bearsden*
Dr Doug Smith	*General Practitioner, Banchory*
Sister Anne Smith	*Director, Eczema Scotland, and Clinical Nurse Specialist in Dermatology, Royal Infirmary of Edinburgh*
Ms Ailsa Stein	*Programme Manager, SIGN*
Dr Lorna Thompson	*Programme Manager, SIGN*
Mrs Eileen Wallace	P*atient Representative, Stirling*
Dr Stephen Wedderburn	*General Practitioner, Aberdeen*

The membership of the guideline development group was confirmed following consultation with the member organisations of SIGN. All members of the guideline development group made declarations of interest and further details of these are available on request from the SIGN Executive.

Guideline development and literature review expertise, support and facilitation were provided by the SIGN Executive. All members of the SIGN Executive make yearly declarations of interest and further details of these are available on request.

In particular, the following staff are thanked for their involvement.

Mr Euan Bremner	*Guideline Coordinator*
Mrs Lesley Forsyth	*Events Coordinator and Executive Secretary to SIGN Council*
Mrs Karen Graham	*Patient Involvement Officer*
Miss Katie Kerr	*Administrative Assistant*
Mr Stuart Neville	*Publications Designer*

16.3 ACKNOWLEDGEMENTS

SIGN is grateful to the following former member of the guideline development group who has contributed to the development of the guideline.

Dr David Haldane	*Consultant in Occupational Health, NHS Greater Glasgow and Clyde*

16.4 CONSULTATION AND PEER REVIEW

16.4.1 NATIONAL OPEN MEETING

A national open meeting is the main consultative phase of SIGN guideline development, at which the guideline development group presents its draft recommendations for the first time. The national open meeting for this guideline was held on 1 October 2009 and was attended by 157 representatives of all the key specialties relevant to the guideline. The draft guideline was also available on the SIGN website for a limited period at this stage to allow those unable to attend the meeting to contribute to the development of the guideline.

16.4.2 SPECIALIST REVIEW

This guideline was also reviewed in draft form by the following independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. The guideline group addresses every comment made by an external reviewer, and must justify any disagreement with the reviewers' comments. All expert referees made declarations of interest and further details of these are available on request from the SIGN Executive.

SIGN is very grateful to all of these experts for their contribution to the guideline.

Dr Peter Arkwright	*Senior Lecturer in Paediatric Immunology, Royal Manchester Children's Hospital*
Dr Gerard Baptist	*General Practitioner, Aultbea and Gairloch Medical Practice, Ross-shire*
Dr Paula Beattie	*Consultant Dermatologist, Royal Hospital for Sick Children, Glasgow*
Mr Scott Bryson	*Lead Specialist in Pharmaceutical Public Health, NHS Greater Glasgow and Clyde*
Professor Christine Clark	*Chairman, Skin Care Campaign, Rossendale*
Dr Iain Campbell	*General Practitioner, Glasgow*
Dr Pam Ewan	*Consultant Allergist, member of Anaphylaxis Working Group*
Dr Niall Hyndman	*Principal General Practitioner, Carmondean Medical Group, Livingston*
Mrs Serena Liddell	*Dermatology Liaison Nurse, Royal Infirmary of Edinburgh*
Dr Andrew Marshall	*General Practitioner Principal, The Broomhill Practice, Glasgow*
Dr David McKay	*Consultant Dermatologist, Royal Infirmary of Edinburgh*
Dr Mini Mishra	*Senior Medical Officer, Primary and Community Care Directorate, Edinburgh*
Dr Val Doherty	*Specialty Medical Adviser in Dermatology, Royal Infirmary of Edinburgh*
Dr Patrick Cadigan	*Registrar, The Royal College of Physicians, London*
Dr Barbara Jane Roemmele	*General Practitioner, The Clinic, Glasgow*
Ms Kathleen Ross	*Head of Paediatric Dietetics, Royal Aberdeen Children's Hospital*

Dr Carina Venter	*Senior Allergy Dietitian, The David Hide Asthma and Allergy Research Centre, St Mary's Hospital, Newport, Isle of Wight*
Professor Hywel Williams	*Professor of Dermato-Epidemiology, Nottingham University Hospitals NHS Trust*
Dr Joanne Walsh	*General Practitioner, member of Food Allergy Working Group*

The following expert referees commented collectively on behalf of the Royal College of Paediatrics and Child Health.

Dr Carol Ewing	*Consultant Paediatrician, Royal Manchester Children's Hospital*
Dr Venkata Paturi	*Consultant Paediatrician, North Tees and Hartlepool NHS Foundation Trust*
Professor John Warner	*Professor of Paediatrics, St Mary's Hospital, Imperial College Healthcare NHS Trust*

16.4.3 SIGN EDITORIAL GROUP

As a final quality control check, the guideline is reviewed by an editorial group including the relevant specialty representatives on SIGN Council to ensure that the specialist reviewers' comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. All members of the Editorial group make declarations of interest and further details of these are available on request from the SIGN Executive. The editorial group for this guideline was as follows.

Dr Gerard Baptist	*General Practitioner, Aultbea and Gairloch Medical Practice, Ross-shire*
Dr Keith Brown	*Chair of SIGN; Co-Editor*
Dr Roberta James	*SIGN Programme Director; Co-Editor*
Dr Vijay Sonthalia	*British Medical Association Scottish General Practice Committee*
Dr Sara Twaddle	*Director of SIGN; Co-Editor*
Professor Hywel Williams	*Professor of Dermato-Epidemiology, Nottingham University Hospitals NHS Trust*

The following editorial reviewers commented collectively on behalf of the Royal College of Paediatrics and Child Health.

Dr Carol Ewing	*Consultant Paediatrician, Royal Manchester Children's Hospital*
Professor John Warner	*Professor of Paediatrics, St Mary's Hospital, Imperial College Healthcare NHS Trust*

Abbreviations

AE	atopic eczema
BNF	British National Formulary
CI	confidence interval
EASI	Eczema Area and Severity Index
FTU	fingertip unit
HPA	hypothalamic-pituitary-adrenal
IgE	immunoglobulin E
MTA	multiple technology appraisal
NHS QIS	NHS Quality Improvement Scotland
NICE	National Institute for Health and Clinical Excellence
POEM	Patient Orientated Eczema Measure
QoL	quality of life
RCT	randomised controlled trial
RR	relative risk
SCORAD	SCORing Atopic Dermatitis
SIGN	Scottish Intercollegiate Guidelines Network
SMC	Scottish Medicines Consortium
TCI	topical calcineurin inhibitor
TCS	topical corticosteroid
WHO	World Health Organisation

Annex 1

Summary of key questions used to develop the guideline

This guideline is based on a series of structured key questions that, where possible, define the population concerned, the intervention (or diagnostic test) under investigation, the type of comparison used, and the outcomes used to measure the effectiveness of the interventions. These questions form the basis of the systematic literature search.

THE KEY QUESTIONS USED TO DEVELOP THE GUIDELINE

Key question	See guideline section
1. Which diagnostic criteria and scoring tools are most useful in the diagnosis and assessment of severity of atopic eczema in primary care?	3
2. What factors influence the effectiveness of emollient therapy in reducing the symptoms of atopic eczema?	4
3. What factors should be considered in order to maximise benefit from the use of topical corticosteroids in patients with atopic eczema?	5
4. What is the most appropriate usage of topical calcineurin inhibitors (tacrolimus/pimecrolimus) in the management of patients with atopic eczema?	6
5. What is the evidence that occlusive dressings are beneficial in the treatment of patients with atopic eczema?	7
6. What is the evidence that antimicrobial measures are beneficial in the treatment of patients with atopic eczema?	8
7. What is the evidence that systemic antihistamines are beneficial in the treatment of patients with atopic eczema?	9
8. What is the evidence for the management of environmental factors in the control of atopic eczema symptoms?	10
9. What is the evidence for the influence of dietary factors in the management of patients with atopic eczema?	11
10. What is the evidence for the safety and efficacy of complementary and/or alternative or adjuvant therapies in the management of patients with atopic eczema?	12

Annex 2

Emollient quantities

Emollients – suitable quantities for prescribing for one week[9]

Body site	Creams and ointments (g)	Lotions (ml)
Face	15-30	100
Both hands	25-30	200
Scalp	50-100	200
Both arms or both legs	100-200	200
Trunk	400	500
Groins and genitalia	15-25	100

These recommended amounts are for one week, twice daily application for an adult. To keep the skin well hydrated, leave-on emollients should be applied in adequate amounts to sufficiently cover dry and inflamed areas. Quantities required will vary with the size of the patient, the severity and extent of skin dryness.

Annex 3

Fingertip unit (FTU)

A fingertip unit is described as "the amount of ointment expressed from a tube with a 5 mm diameter nozzle, applied from the distal skin crease to the tip of the palmar aspect of the index finger".[31,62] The following tables provide a guide to the use of FTU.

Adult fingertip unit measures for use in adults

Skin area	FTU per dose
Face and neck	2.5
Torso and abdomen	7
Back and buttocks	7
Entire arm and hand	4
A hand and fingers (front and back)	1
Entire leg and foot	8

Adult fingertip unit measures for use in children

	3-6 MONTHS	1-2 YEAR OLD	3-5 YEARS	6-10 YEARS
Face and neck	1	1.5	1.5	2
Torso and abdomen	1	2	3	3.5
Back and buttocks	1.5	3	3.5	5
Entire arm and hand	1	1.5	2	2.5
Entire leg and foot	1.5	2	3	4.5

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ISBN 978 1 905813 72 8

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