NICE National Institute for Health and Care Excellence

NICE guidance

Frequency of application of topical corticosteroids for atopic eczema

Technology appraisal guidance
Published: 25 August 2004

www.nice.org.uk/guidance/ta81

Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

This appraisal relates to the frequency of application of topical corticosteroids in the treatment of atopic eczema. It does not include the use of topical agents that combine corticosteroids with other active agents (for example, antimicrobials or salicylic acid).

1.1 It is recommended that topical corticosteroids for atopic eczema should be prescribed for application only once or twice daily.

1.2 It is recommended that where more than one alternative topical corticosteroid is considered clinically appropriate within a potency class, the drug with the lowest acquisition cost should be prescribed, taking into account pack size and frequency of application.

2 Clinical need and practice

2.1 Atopic eczema (synonymous with atopic dermatitis) is a chronic relapsing skin condition characterised by intense itching, dry skin, redness, inflammation and exudation. It affects mainly the flexor surfaces of the elbows and knees, as well as the face and neck.

2.2 The term 'atopic' refers to the association with atopy (a state of hypersensitivity to common environmental allergens that may be inherited), and differentiates atopic eczema from other forms of eczema such as irritant, allergic contact, discoid, venous, seborrhoeic and photosensitive eczema, which have different disease patterns and aetiologies.

2.3 Estimates of prevalence vary but suggest that the condition may affect as many as 15% to 20% of school-age children and 2% to 10% of adults. Most people with atopic eczema (more than 80%) experience mild disease; only around 2% to 4% of people with eczema have a severe form of the disease. Despite the lower prevalence, the presentation of disease in adults is often more severe and chronic in nature.

2.4 In most people with atopic eczema, the condition begins in early childhood, often in the first year of life, when it can be particularly severe. Findings from the National Child Development Study (NCDS), developed from the birth cohort of 1958, suggested an incidence of around 50 cases per 1,000 in the first year of life, falling to 5 new cases per 1,000 per year for the rest of childhood. In around 60% of children, the condition clears by the time they reach their teens. However, the tendency towards dry and irritable skin generally persists and later recurrences are common.

2.5 The aetiology of atopic eczema is complex and not fully understood. Genetic factors are important but environmental factors, such as house dust mites, pollen, tobacco, air pollution and low humidity, may cause its onset and/or exacerbate existing symptoms. More persistent disease has been consistently linked with early disease onset, severe widespread disease in early life, concomitant asthma or hay fever, and a family history of atopic eczema. The condition is exacerbated by soap and detergents, clothes containing wool or certain synthetic fibres, and

extremes of temperature.

2.6 The severity of atopic eczema varies enormously, from an occasional dry, scaly patch to a debilitating disease, where much of the body is covered by excoriated, bleeding and infected lesions. Its course may be continuous for prolonged periods or of a relapsing-remitting nature, characterised by acute flare-ups.

2.7 Itching skin (pruritus) is a major symptom of atopic eczema. A vicious circle can occur, where itching and scratching damage the skin and increase inflammation, which in turn increases the itch. Damage to the skin from scratching can cause bleeding, secondary infection and thickening of the skin (lichenification).

2.8 The impact of atopic eczema on quality of life can be considerable, and varies according to disease severity. In addition to the burden imposed by daily treatment, studies have shown not only that the condition affects everyday activities such as work or school and social relationships, but also that people with atopic eczema may also experience anxiety, depression and other psychological problems. Sleep disturbance is common, especially during flare-ups, which in turn can lead to problems with irritability and lack of concentration. Severe atopic eczema in children can also have a significant impact on family life, with parents and carers having to cope with the demands associated with caring for a child with a chronic illness.

2.9 Historically, there have been variations over the clinical definition and diagnosis of atopic eczema. A UK Working Party has developed criteria for use in epidemiological studies, and these are now commonly used, although further validation is required. To qualify as a case of atopic eczema using these criteria, the person must have had an itchy skin condition in the past 12 months, plus three or more of the following:

- a history of flexural involvement (that is, affecting the bends of the elbows or behind the knees)
- a history of a generally dry skin
- a personal history of other atopic disease (in children younger than 4 years, a history of atopic disease in a first-degree relative may be included)
- visible flexural dermatitis as defined by a photographic protocol

- onset before the age of 2 years (not used in children younger than 4 years).

2.10 There is uncertainty and a lack of standardisation around clinical assessment of disease severity, both in practice and in trial settings. Although a number of scoring systems have been used to categorise the disease as mild, moderate or severe, usually by aggregating scores from a range of symptoms and disease characteristics, none of these scoring systems has been accepted as a 'gold standard' and there remains general debate over their use.

2.11 Atopic eczema in childhood shows a reverse social class gradient, with higher rates in socioeconomically advantaged groups and smaller families. There is also evidence of variation in prevalence by region, with the highest rates recorded in the South East and industrialised Midlands, and the lowest rates in Wales and Scotland.

2.12 Management of atopic eczema takes place predominantly in primary care, and aims to relieve symptoms and prevent complications such as infections until remission occurs. This management involves skin care, anti-inflammatory treatment, and the identification and avoidance of exacerbating factors. Providing people with good-quality information about these issues is essential to successfully managing and treating atopic eczema. Referral to secondary care is advised only if the condition is severe and has not responded to appropriate therapy.

2.13 Emollients are a first-line therapy for atopic eczema and aim to retain the skin's barrier function (keeping water in and irritants or pathogens out) and to prevent painful cracking. Frequent and continuous use is recommended even in the absence of symptoms. Preparations available include bath oils, soap substitutes and moisturisers; generally the greasier the preparation, the better the effect, although people using very greasy products may consider them unacceptable.

2.14 Topical corticosteroids are the first-line treatment for flare-ups of atopic eczema. In order to reduce exposure to topical corticosteroids, they are used only intermittently to control exacerbations. Treatment regimens for topical steroids vary with disease severity, with clinicians usually recommending use of the mildest potency products possible to treat the condition, in order to minimise the potential adverse effects. Emollients are used together with the topical

corticosteroids.

2.15 Where there are associated bacterial or fungal infections, corticosteroids are combined with other substances (such as antimicrobials or salicylic acid) in topical preparations.

2.16 Other treatments for atopic eczema include antihistamines, topical immunomodulators, and wet wraps (when a layer of emollients with or without corticosteroids is applied to the skin and wrapped in wet bandages, followed by dry bandages, and left overnight), which may be used in an attempt to maximise the effect of treatment.

2.17 Treatments of last resort in resistant severe cases include systemic corticosteroids, phototherapy and systemic use of immunosuppressants.

3 The technology

3.1 Topical corticosteroids have anti-inflammatory and immunosuppressive effects. The mechanism of the anti-inflammatory activity of topical steroids in general is unclear, although various symptomatic components of the inflammatory pathway are known to be suppressed.

3.2 Thirty preparations of topical corticosteroids are included in this appraisal (see appendix B). Topical corticosteroids are classified according to their potency. This is determined by the amount of vasoconstriction a topical corticosteroid produces and the degree to which it inhibits inflammation (a more potent product increases suppression to the inflammatory pathway). In the UK, 4 potencies are recognised: mild, moderately potent, potent and very potent. Across the different potencies, products have different formulations and different strengths (for example, 0.025%, 0.1%, 0.5%) and are available in various preparations (for example, ointment, cream, lotion, foam).

3.3 The most widespread side effect of topical corticosteroid treatment is skin atrophy, where the skin becomes thin and may become easily bruised. This is more likely to occur on areas where the skin is already thin, such as the face or flexures. Absorption is greatest in these areas and therefore the use of potent steroids on these sites should generally be avoided. The skin may recover gradually after stopping treatment, but the original structure may never return. Prolonged or excessive use of potent steroids causes the dermis to lose its elasticity and stretch marks (striae) to appear, which are permanent. Children, especially babies, are particularly susceptible to side effects. The more potent corticosteroids are contraindicated for infants less than 1 year old. For full details of side effects and contraindications, see the summaries of product characteristics (SPCs) for the topical corticosteroids.

3.4 Guidelines from the British Association of Dermatologists suggest that the best way of using topical corticosteroids is probably twice daily for 10 to 14 days when the eczema is active, followed by a 'holiday period' of emollients only. The National Prescribing Centre recommends that, in general practice, topical corticosteroids be used in short bursts (for 3 to 7 days) to treat exacerbations of disease.

3.5 There are varying recommendations about the frequency of application. The BNF states that "corticosteroid preparations should normally be applied once or twice daily. It is not necessary to apply them more frequently". Although there are few empirical data to assess the patterns of prescribing with respect to frequency of application, it appears that a twice-daily regimen is the most widespread approach to the use of topical corticosteroids in atopic eczema. However, the SPCs for some of the topical corticosteroids indicate that some are licensed for more frequent use (up to 4 times a day), and two products are licensed for use only once a day in atopic eczema. For individual posologies, see appendix B.

4 Evidence and interpretation

The appraisal committee considered evidence from a number of sources. The remit given to NICE by the Department of Health and Welsh Assembly Government was to advise on the clinical and cost effectiveness of once-daily use compared with more frequent use of same-potency topical corticosteroids in the treatment of people with atopic eczema. The evidence appraised was restricted to comparisons of topical corticosteroids for atopic eczema within the same potency class.

4.1 Clinical effectiveness

4.1.1 The assessment report reviewed data from 1 systematic review and 10 randomised controlled trials (RCTs) that examined frequency of application of topical corticosteroids of the same potency. No RCTs or clinical controlled trials of mild topical corticosteroids were identified. One RCT examined moderately potent corticosteroids, 8 RCTs examined potent corticosteroids and 1 RCT examined very potent corticosteroids.

4.1.2 The study setting was hospital or secondary care for 4 of the 10 trials but was not reported in the remaining studies. The duration of treatment for the trials ranged from 7 days to 4 weeks. Quality of life and patient preference were not reported by any of the included trials.

4.1.3 The assessment group concluded the systematic review was of good methodological quality. The systematic review included 3 RCTs (2 trials examining potent topical corticosteroids and 1 examining very potent topical corticosteroids), all of which were included in the assessment report. The authors of the systematic review found that in none of the studies was more frequent application superior to once-daily application. They concluded that point estimates suggest that a small difference in favour of more frequent application cannot be excluded.

4.1.4 The assessment group did not consider meta-analysis to be appropriate because of the clinical and statistical heterogeneity of the trials.

Moderately potent preparations

4.1.5 One RCT was identified that examined the frequency of application in moderately potent topical corticosteroids for atopic eczema; the study population was children. The assessment report stated that the study was small and the duration of treatment was 7 days; the study did not report the setting, how allocation to treatment groups occurred, blinding of either outcome assessors or patients, or the number of patients responding to the treatment. There was no statistically significant difference in severity of symptoms following treatment with once-daily versus twice-daily application of topical corticosteroids. Adverse effects were not reported.

Potent preparations

4.1.6 Eight RCTs were identified that examined frequency of application in potent topical corticosteroids for atopic eczema. Five of these compared the same active compound administered once and twice daily (4 of these trials examined fluticasone propionate [ointment and cream]). Three trials investigating potent topical corticosteroids compared different active compounds; these all compared a once-daily-only product, mometasone furoate, with other topical corticosteroids administered twice daily.

4.1.7 Apart from 2 trials within this potency class, the assessment report considered the quality of reporting and the methodology of the included RCTs to be generally poor.

4.1.8 For 4 of the studies, the study setting was hospital or secondary care but the setting was not reported in the remaining studies. Duration of treatment in the studies was up to either 3 or 4 weeks. Where reported, the studies included people who had moderate to severe atopic eczema, apart from one study that included adults with mild to moderate eczema. One other study did not report the minimum severity of eczema of the study population.

4.1.9 Studies included children and adults, people aged over 12 years or 16 years, or adults only. Subgroup analyses of children aged 12 years or younger were reported for 2 trials.

Response to treatment

4.1.10 The studies measured effectiveness of the treatments using a variety of different outcome measures, most of which were subjective assessments by the investigator and/or patient. All studies apart from 1 reported the number of patients responding to treatment. However, response to treatment was defined in different ways by the studies. Two outcomes were considered in the assessment report: the number of patients with at least a good response or 50% improvement, and the number of patients whose eczema was rated cleared or controlled.

4.1.11 Seven studies reported the number of patients with at least a good response, assessed by the investigator and/or patient, or at least 50% improvement by the end of 3 or 4 weeks. Six studies reported the number of patients with eczema that was rated as cleared and controlled or excellent after 3 or 4 weeks.

4.1.12 Overall, studies found little difference in response to treatment between once-daily and twice-daily application of potent corticosteroids. Some statistically significant differences favouring twice-daily treatment were identified, but these were inconsistent between outcome assessors (physicians versus patients) and outcomes selected for analysis. Subgroup analysis of patients aged 12 years or younger produced similar findings to the main analysis.

4.1.13 One study compared success rates between morning and evening application in the once-daily group (67% versus 78%, difference 11.3%; 95% confidence interval [CI] -4.6 to 27.2, p=0.17). Despite finding a statistically significant difference between once-daily and twice-daily application, when assessed by the physician (but not when assessed by the patient), the difference between once-daily evening treatment and twice-daily application was not statistically significant (78% versus 84%, difference 5.9%; 95% CI -6.6 to 18.4, p=0.33).

Severity of signs and symptoms

4.1.14 None of the studies reported the use of a validated severity scale, and the clinical relevance of a change in severity is not clear. However, in 1 study, once-daily use of mometasone furoate, which is a once-daily-only product, was found to result in a greater percentage improvement in total atopic eczema scores than twice-

daily betamethasone valerate at each assessment (p<0.01). Another study found an improvement in pruritus (p=0.007) only, following mometasone furoate, compared with twice-daily hydrocortisone 17-butyrate. A third study comparing once-daily use of mometasone furoate with betamethasone dipropionate found no statistically significant differences in percentage reduction of severity for erythema, induration or pruritus. However, the assessment group stated that these 3 trials were all of poor quality because they were described as single-blind (investigators blinded), but the trials did not give details of methods or procedures, or use of placebo treatment in the once-daily group. Two of these trials also failed to report whether comparison groups were similar at baseline.

4.1.15 A greater reduction in severity scores demonstrated at 2 weeks (p=0.04) for twice-daily compared with once-daily use of hydrocortisone 17-butyrate was not maintained at 4 weeks (p=0.08) in 1 trial, and although the twice-daily group showed more pronounced reductions in rating for erythema at 4 weeks (p=0.03), this was not the case for the other symptoms assessed. No confidence intervals were available for these trials.

4.1.16 One trial found total severity scores to be similar between once-daily and twice-daily application of fluticasone propionate ointment at each visit, although logistic regression analysis of total severity score (adjusting for age and baseline total severity score) favoured twice-daily application at the last visit attended (odds ratio [OR] 1.72; 95% CI 1.05 to 2.82, p=0.033). However, the odds ratio for the treatment effect in the subgroup analysis of patients aged 12 years or younger was not statistically significant (OR 1.85; 95% CI 0.88 to 3.89, p=1.03).

4.1.17 None of the other studies comparing potent topical corticosteroids found a statistically significant difference in severity of atopic eczema following once-daily application compared with more frequent applications.

Adverse effects

4.1.18 The quality and extent of reporting of adverse effects was variable among studies. There appeared to be little difference in the frequency or severity of adverse events between once-daily and twice-daily application of topical corticosteroids, although data were limited because of the short duration of the

studies.

4.1.19 One study did report potential differences in sleep disturbance, finding sleep to be "as good as ever has been" or better by 37% of patients following once-daily application of fluticasone propionate compared with 55% of patients following twice-daily application. No p-value or confidence intervals were available for this outcome.

Very potent preparations

4.1.20 One RCT compared once-daily application of halcinonide cream (0.1%) with three-times-daily application of the same product.

4.1.21 The trial was double-blind, but the concealment of allocation was not reported. The duration of the study was a maximum of 3 weeks, or shorter if complete remission was obtained. The age range of patients, the study setting and the minimum severity of eczema for the included patients were not reported in the study.

4.1.22 The study compared the response of similar lesions on each side of the patient. A better response (slightly superior or markedly superior) was observed following three-times-daily application. Overall, 32% of patients had a better clinical response to three-times-daily application, 21% had a better clinical response to once-daily application, and 47% had an equal response ($p<0.05$), but no statistically significant difference was found in the number of patients with at least a good absolute therapeutic response.

4.1.23 The authors of the study stated that the side effects were generally of a mild nature, the most common being burning, pruritus and erythema, with no difference in incidence between once-daily and three-times-daily regimens, and that no systemic effects were observed. However, the assessment report pointed out that no data was presented on adverse effects.

Summary

4.1.24 Overall, the assessment report did not identify any clear differences for any of the potency classes in outcomes between once-daily and more frequent application of topical corticosteroids. For potent preparations, 1 study indicated a statistically significant difference in favour of the twice-daily application of fluticasone propionate (ointment) in response rates between the different regimens (at least a good response rate or 50% improvement), when patients were assessed by physicians; however, this was not the case for patient assessment. For a response of cleared or controlled atopic eczema, 1 trial indicated a significant difference in favour of twice-daily treatment of hydrocortisone 17-butyrate when patients were assessed by a physician. Two studies, considered by the assessment group to be of poor quality (as described in 4.1.14), favoured once-daily treatment of mometasone furoate over twice-daily use of other products (depending on severity of certain symptoms). The trial of a very potent corticosteroid reported a statistically significant difference in clinical response, favouring more frequent application, but no significant difference in the number of patients with at least a good response.

4.2 Cost effectiveness

4.2.1 The assessment group did not identify any published economic evaluations that examined frequency of use of same-potency topical corticosteroids.

4.2.2 No economic evaluations were identified or submitted by the manufacturers or other consultees. No quality-of-life or patient preference outcomes were included in any of the studies in the systematic review.

4.2.3 The assessment group concluded that there was no basis to draw firm conclusions over the relative effectiveness of once-daily versus more frequent use of same-potency topical corticosteroids for atopic eczema. Consequently, the economic analysis assumes equivalent effectiveness of once-daily application and more frequent application of topical corticosteroids, and cost-minimisation analysis was undertaken.

4.2.4 The cost per application of topical corticosteroids varies depending on the

quantity used per application. Evidence was derived from 2 of the included RCTs and 4 additional studies that were identified. The assessment group stated that, although it would be reasonable to assume that the actual amount of topical corticosteroid used in a once-daily regimen is less than that used for more frequent applications (especially when referring to the same product), it is not possible to estimate accurately the quantity of medication used according to frequency of application. Another consideration was that topical corticosteroids are applied when people experience flare-ups, rather than continuously over time. Consequently, extrapolation over longer periods of time was not straightforward.

4.2.5 The assessment group provided a cost-minimisation analysis for 9 of the 10 included clinical trials. In this, once-daily use was the least costly option on 6 occasions and twice-daily use the least costly on 3 occasions. The wide range of topical corticosteroid products available and their varied prices means that there are many possible prescribing scenarios. The availability of specifically marketed once-daily topical corticosteroids, which are priced much higher than other generic and proprietary products, makes a once-daily regimen more costly when these products are used. For example, where fluticasone propionate cream (£4.59) or mometasone furoate (£4.22) once daily is substituted for betamethasone valerate (£1.31), betamethasone dipropionate (£2.05) or hydrocortisone butyrate (£2.38) twice daily, the once-daily regimen would be expected to cost more than the twice-daily regimen.

4.2.6 The trial examining fluticasone propionate (ointment) showed a benefit associated with twice-daily use in terms of physician assessment (but not for patient assessment) of patients' target area of atopic eczema. Consequently, a simple estimate of cost effectiveness was made. This found the additional cost per treatment success to be £76.50. The assumptions underlying this analysis were generous and a more realistic estimate of the treatment cost per additional successfully treated flare-up would probably be half that value. The assessment group concluded that the greater likelihood of treatment success (that is, successfully treated flare-up) would be of sufficient value (in terms of patient benefit, and avoided GP consultations, referrals to specialists or prescribing of more expensive products) to regard twice-daily application as cost effective.

4.3 Consideration of the evidence

4.3.1 The committee reviewed the data available on the clinical and cost effectiveness of the frequency of application of topical corticosteroids for atopic eczema, having considered evidence on the nature of the condition and the value placed on the benefits of different frequencies of application of topical corticosteroids by people with atopic eczema, those who represent them, and clinical experts. It was also mindful of the need to take account of the effective use of NHS resources.

4.3.2 The committee considered the various factors that might influence the frequency of application of topical corticosteroids for atopic eczema. These included the clinical presentation, factors influencing concordance with treatment, and patient choice. It heard from the experts that the potency of corticosteroid was not a relevant factor in determining the frequency of application.

4.3.3 Additionally, the committee appreciated that people with eczema may have considerable fear of the use of corticosteroids, and also need to use a number of other measures to manage their condition on a daily basis. On the basis of expert testimony, concordance with once-daily or twice-daily application of topical corticosteroids is not of particular concern to patients because of the fact that they have to apply emollients regularly to manage their condition. The committee was informed that good-quality patient education on the use of topical corticosteroids was a significant factor in ensuring the success of therapy. The committee was also informed that there was a clear need for continuing education of healthcare professionals to ensure that correct advice on the use of topical corticosteroids is given to people with atopic eczema.

4.3.4 The committee reviewed the evidence related to the frequency of application of topical corticosteroids in atopic eczema. It considered that the RCTs available were, in general, of poor methodological quality, and it was advised by the experts that longer follow-up (months, not weeks) would be required of trials to assess fully any potential differences in long-term efficacy and adverse effects between once-daily and more frequent applications of topical corticosteroids. The committee additionally appreciated that there may be differences in the pharmacokinetics of the individual topical corticosteroids, but it was persuaded that these differences, if of clinical significance, would be reflected in the clinical

effectiveness evidence.

4.3.5 The committee was informed that differences exist in clinical practice, between clinicians, in the prescription of once-daily or more frequent use of topical corticosteroids. However, it was agreed by the experts that, where once-daily application of a topical corticosteroid was initially advised, clinicians would have to increase either the potency or the frequency of the topical corticosteroid, if there was no improvement in the condition. Alternatively, if twice-daily application was advised initially for a flare-up, it would be expected that people would reduce the frequency of application of the same product once their condition began to improve.

4.3.6 Having considered the results from the RCTs, as well as the testimony from the expert witnesses, the committee concluded that there was no compelling evidence of a clinically significant difference between once-daily application and more frequent application of topical corticosteroids in terms of their effectiveness, patient satisfaction, adverse events, concordance with therapy or the number of follow-up visits required. It was persuaded that current clinical practice would therefore support a recommendation for the use of topical corticosteroids no more frequently than twice daily.

4.3.7 The committee concluded that, on the basis of the consideration in 4.3.6, where more than one alternative topical corticosteroid is considered clinically appropriate within a potency class, the product with the lowest acquisition cost (taking into account pack size and frequency of application) should be used in preference to more expensive alternatives. From the cost-minimisation analysis presented, the committee noted that because of the acquisition cost of some products licensed solely for once-daily application, in some product comparisons, twice-daily application of other products was less costly than once-daily application.

5 Recommendations for further research

5.1 The trial literature is dominated by comparisons of differing frequency of use of fluticasone propionate (4 trials) and comparisons of mometasone furoate with more traditional twice-daily treatment options (3 trials).

- Trials are needed to establish whether once-daily use of the older (twice-daily) products is equivalent to more frequent use.
- Trials are also required to establish whether once-daily use of the older twice-daily products is equivalent to the once-daily-only products.
- Trials are required for all the potency classes, in particular for mild potency preparations, because no trials examining frequency of application of topical corticosteroids exist for this group.

5.2 Robust trials are required that report quality-of-life data and patient preferences.

5.3 Long-term follow-up is required in trials to assess adverse effects such as skin atrophy.

5.4 The experts informed the committee that there was a lack of support for people with the condition and inadequate information about the management of atopic eczema and the risks associated with the use of topical corticosteroids. Research should therefore be conducted to establish the most suitable method of conveying high-quality information to people with atopic eczema.

6 Implications for the NHS

6.1 Information is not readily available on current prescribing patterns of topical corticosteroids in patients with atopic eczema. There is also limited information on the quantity of product used per treatment regimen. Consequently, it is not possible, with any certainty, to establish baseline information on which to base estimates of the resource impact of changes in prescribing between preparations of different acquisition costs. Furthermore, such cost savings will be relatively small at the patient level, and issues related to pack size and product waste can easily erode any potential cost saving. However, given the large patient group with atopic eczema, there may be opportunities for significant savings to the NHS on products prescribed, particularly at a primary care level, because this is where most prescribing of topical corticosteroids is likely to occur.

6.2 An illustrative scenario is explored below. The estimate is based on a number of assumptions used in the calculations, and so should be interpreted cautiously. The underlying assumptions are that patients have 2 to 4 flare-ups a year, that they throw away any unused products after each flare-up, and that patients applying topical corticosteroids once daily would use either 50% or 75% of the amount they would use if they were applying the product twice daily. These potential savings assume that all the patient prescription costs are met by the NHS. In practice, however, many patients may receive only 1 prescription per year, because they may not discard their unused products. Consequently, the figures in the scenario below are likely to be an estimate of the maximum cost savings to the NHS.

6.3 Where a prescribing practice of one of the newer once-daily-only products can appropriately be altered to twice-daily use of one of the older, cheaper topical corticosteroids of the same potency, cost savings have been estimated to range from £300,000 to £600,000 (excluding VAT) for a patient group of 100,000 people with atopic eczema.

7 Implementation and audit

7.1 All clinicians who care for people with atopic eczema should review their current practice and policies to take account of the guidance set out in section 1.

7.2 Local guidelines or care pathways for people with atopic eczema should incorporate the guidance.

7.3 To measure compliance locally with the guidance, the following criteria could be used. Further details on suggestions for audit are presented in appendix A.

7.4 Topical corticosteroids for atopic eczema are prescribed for application only once or twice daily.

7.5 If more than one alternative topical corticosteroid is considered clinically appropriate within a potency class, the drug with the lowest acquisition cost is prescribed.

7.6 Local clinical audits could also include measurement of compliance with recognised guidelines for the management of atopic eczema and the effectiveness of patient education on the use of topical corticosteroids.

8 Appraisal committee members

The appraisal committee is a standing advisory committee of NICE. Its members are appointed for a 3-year term. The committee meets twice a month except in December, when there are no meetings. The committee membership is split into three branches, with the chair, vice-chair and a number of other members attending meetings of all branches. Each branch considers its own list of technologies and ongoing topics are not moved between the branches.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each appraisal committee meeting, which include the names of the members who attended and their declarations interests, are posted on the NICE website.

The following is a list of the committee members who took part in the discussions for this appraisal.

Dr A E Ades
Senior Scientist, MRC Health Services Research Collaboration, University of Bristol

Dr Tom Aslan
General Practitioner, Stockwell, London

Professor David Barnett (Chair)
Professor of Clinical Pharmacology, University of Leicester

Professor Rosamund Bryar
Professor of Community and Primary Care Nursing, St Bartholomew School of Nursing and Midwifery

Dr Rodney Burnham
Consultant Physician and Gastroenterologist, Oldchurch Hospital, Romford

Dr Gary Butler
Consultant Paediatrician, Endocrinologist, Leeds Teaching Hospitals NHS Trust

Dr Karl Claxton
Health Economist, University of York

Dr Christopher Eccleston
Director, Pain Management Unit, Department of Psychology, University of Bath

Ms Bethan George
Interface Liaison Pharmacist, Mile End Hospital, London

Mr John Goulston
Director of Finance, Barts and the London NHS Trust

Mr Adrian Griffin
Health Outcomes Manager, Johnson & Johnson Medical Ltd

Judith Paget
Chief Executive, Caerphilly Local Health Board

Dr Katherine Payne
Research Fellow, Health Economics, University of Manchester

Mrs Kathryn Roberts
Nurse Practitioner, Hyde, Cheshire

Ms Anne Smith
Lay Representative, Trustee, Long-Term Medical Conditions Alliance

Professor Andrew Stevens (Vice-Chair)
Professor of Public Health, University of Birmingham

Dr Cathryn Thomas
General Practitioner, and Senior Lecturer, Department of Primary Care, General Practice, University of Birmingham

Dr Norman Vetter
Reader, Department of Epidemiology, Statistics and Public Health, College of Medicine, University of Wales, Cardiff

Dr Paul Watson
Medical Director, Essex Strategic Health Authority

NICE Project Team

Each appraisal of a technology is assigned to a Health Technology Analyst and a Technology Appraisal Project Manager.

Joanna Richardson
Health Technology Analyst

Kathleen Dalby
Project Manager

9 Sources of evidence considered by the committee

The following documentation was made available to the committee:

- Assessment report, prepared by Southampton Health Technology Assessment Centre: Green C, Colquitt JL, Kirby J, et al. (2003) Clinical and cost-effectiveness of once daily versus more frequent use of same potency topical corticosteroids for atopic eczema: a systematic review and economic evaluation.

The following organisations accepted the invitation to participate in this appraisal. They were invited to make submissions and comment on the draft scope, assessment report and the appraisal consultation document (ACD). Consultee organisations are provided with the opportunity to appeal against the final appraisal determination:

Companies or sponsors:

- Dermal Laboratories
- GlaxoSmithKline
- Novartis
- Pliva Pharma
- Schering-Plough
- Stiefel Laboratories (UK)
- Typharm
- Waymade Healthcare
- Yamanouchi

Professional or specialist, patient or carer and other groups:

- British Association of Dermatologists
- British Generic Manufacturers' Association

- Department of Health
- Hounslow Primary Care Trust
- National Eczema Society
- Primary Care Dermatology Society
- Royal College of General Practitioners
- Royal College of Nursing
- Royal College of Physicians
- Royal Pharmaceutical Society of Great Britain
- Skin Care Campaign
- Welsh Assembly Government

Commentator organisations (without the right of appeal):

- NHS Confederation
- NHS Purchasing and Supply Agency
- NHS Quality Improvement Scotland
- Skin Treatment and Research Trust.

The following individuals were selected from clinical expert and patient advocate nominations from the professional or specialist, and patient or carer groups. They participated in the appraisal committee discussions and provided evidence to inform the appraisal committee's deliberations. They gave their expert personal view on the frequency of application of topical corticosteroids for atopic eczema by attending the initial committee discussion and/or providing written evidence to the committee. They were also invited to comment on the ACD.

- Ms Sandra Lawton, Nurse Consultant Dermatology, Queen's Medical Centre, Nottingham.
- Dr Celia Moss, Consultant Dermatologist, Birmingham Children's Hospital.
- Ms Sue Ward, Information and Education Manager, National Eczema Society.

Appendix A Detail on criteria for audit of the frequency of application of topical corticosteroids for atopic eczema

Possible objectives for an audit

An audit could be carried out to ensure the appropriateness of prescription of topical corticosteroids for atopic eczema.

Possible patients to be included in the audit

An audit could be carried out on all patients seen for atopic eczema in a reasonable period for audit, for example, 6 months, who are prescribed topical corticosteroids but not those topical agents that combine corticosteroids with other active agents (for example, antimicrobials or salicylic acid).

Table 1 Measures that could be used as a basis for an audit

Criterion	Standard	Exception	Definition of terms
Topical corticosteroids for atopic eczema are prescribed for application only once or twice daily	100% of people for whom topical corticosteroids for atopic eczema are prescribed	None	The diagnosis of atopic eczema is established by the person having an itchy skin condition in the past 12 months plus three or more of the following: history of flexural involvement (that is, affecting the bends of the elbow or behind the knees); history of a generally dry skin; personal history of other atopic disease (in children younger than 4 years, history of atopic disease in a first-degree relative may be included); visible flexural dermatitis as defined by a photographic protocol; and onset before the age of 2 years (not used in children younger than 4 years). For a list of preparations of topical corticosteroids that are relevant for this measure, see appendix B
If more than one alternative topical corticosteroid is considered clinically appropriate within a potency class, the drug with the lowest acquisition cost is prescribed	100% of people who are prescribed topical corticosteroids for atopic eczema	None	Clinicians will need to agree locally on how the lowest acquisition cost is determined for audit purposes, taking into account pack size and frequency of application. See appendix B for a list of preparations by potency class

Calculation of compliance

Compliance (%) with each measure described in table 1 is calculated as follows:

Numerator divided by the denominator, multiplied by 100.

Numerator: Number of patients whose care is consistent with the criterion plus number of patients who meet any exception listed.

Denominator: Number of patients to whom the measure applies.

Clinicians should review the findings of measurement, identify whether practice can be improved, agree on a plan to achieve any desired improvement and repeat the measurement of actual practice to confirm that the desired improvement is being achieved.

Appendix B Topical corticosteroids for the treatment of atopic eczema, grouped by potency

Tables 2 to 5 list the topical corticosteroids in each potency category. The net cost is taken from BNF 47 (March 2004), using the largest pack sizes available (for example, where 100 g is the largest pack size, the cost is calculated using the 100 g price multiplied by 0.3).

Table 2 Topical corticosteroids of mild potency

BNF chemical name	Manufacturer	Product name	Posology from summaries of product characteristics (SPCs), where available	Net cost per 30 g/ 30 ml for each strength (does not include VAT or dispensing fee)
Hydrocortisone	• Alpharma • BCM Specials • Bell Sons & Co. (Druggists) • Bioglan Laboratories • Bioglan Pharmaceuticals • Biorex Laboratories • Co-Pharma • Diomed Developments • Galpharm Healthcare • Lagap Pharmaceuticals • Norton Pharmaceuticals • Novartis • Pinewood Laboratories • Reckitt	Generic hydrocortisone cream 0.5%, 1%, ointment 0.5%, 1%	N/A	£0.66, £0.74, £0.65, £0.76

BNF chemical name	Manufacturer	Product name	Posology from summaries of product characteristics (SPCs), where available	Net cost per 30 g/ 30 ml for each strength (does not include VAT or dispensing fee)
	Benckiser Healthcare (UK) • Roussel Laboratories • Thornton & Ross • Waymade			
Hydrocortisone	GlaxoSmithKline	Efcortelan cream or ointment 0.5%, 1%, 2.5%	2 to 3 times daily	£0.66, £0.81, £1.83
Hydrocortisone	Yamanouchi	Mildison Lipocream 1%	2 to 3 times daily	£2.63
Hydrocortisone	Dermal	Dioderm cream 0.1%	Twice daily	£2.69
Fluocinolone acetonide	GP Pharma	Synalar cream 1/10, 0.0025%	2 to 3 times daily	£1.15

Table 3 Topical corticosteroids of moderate potency

BNF chemical name	Manufacturer	Product name	Posology from summaries of product characteristics (SPCs), where available	Net cost per 30 g/30 ml for each strength (does not include VAT or dispensing fee)
Alclometasone dipropionate	Pliva	Modrasone cream or ointment 0.05%	2 to 3 times daily	£1.69

BNF chemical name	Manufacturer	Product name	Posology from summaries of product characteristics (SPCs), where available	Net cost per 30 g/30 ml for each strength (does not include VAT or dispensing fee)
Betamethasone valerate	GlaxoSmithKline	Betnovate RD cream or ointment 0.025%	2 to 3 times daily	£1.08
Clobetasone butyrate	GlaxoSmithKline	Eumovate cream or ointment 0.05%	Up to 4 times daily	£1.70
Desoximetasone	Stiefel	Stiedex LP oily cream 0.05%	2 to 3 times daily	£2.46
Fluocinolone acetonide	GP Pharma	Synalar cream or ointment 1/4, 0.00625%	2 to 3 times daily	£1.22
Fluocortolone	Meadow	Ultralanum Plain cream or ointment 0.25%	N/A	£1.77
Fludroxycortide	Typharm	Haelan cream or ointment 0.0125%	2 to 3 times daily	£1.63

Table 4 Potent topical corticosteroids

BNF chemical name	Manufacturer	Product name	Posology from summaries of product characteristics (SPCs), where available	Net cost per 30 g/30 ml for each strength (does not include VAT or dispensing fee)
Beclometasone dipropionate	GlaxoSmithKline	Propaderm cream or ointment 0.025%	Twice daily	£1.74

BNF chemical name	Manufacturer	Product name	Posology from summaries of product characteristics (SPCs), where available	Net cost per 30 g/ 30 ml for each strength (does not include VAT or dispensing fee)
Betamethasone dipropionate	Schering Plough	Diprosone cream or ointment 0.05%, lotion 0.05%	1 to 2 times daily	£2.05, £2.61
Betamethasone valerate	GlaxoSmithKline	Betnovate cream or ointment 0.1%, lotion 0.1%, scalp application 0.1%	2 to 3 times daily	£1.31, £1.57, £1.71
Betamethasone valerate	Celltech	Bettamousse foam 0.12%	Twice daily	£2.25
Betamethasone valerate	Dermal	Betacap scalp application 0.1%	Twice daily	£1.27
Betamethasone valerate	Dowelhurst, Futuna	Generic betamethasone valerate cream 0.1%, ointment 0.1%	N/A	£1.54, £1.69
Diflucortolone valerate	Meadow	Nerisone cream or ointment 0.1%, oily cream 0.1%	N/A	£1.59, £2.56
Fluocinolone acetonide	GP Pharma	Synalar cream or ointment 0.025%, gel 0.025%	2 to 3 times daily	£1.74, £2.57
Fluocinonide	GP Pharma	Metosyn FAPG cream 0.05%, ointment 0.05%	3 to 4 times daily	£1.54, £1.52
Fluticasone propionate	GlaxoSmithKline	Cutivate cream 0.05%	Once daily	£4.59
Fluticasone propionate	GlaxoSmithKline	Cutivate ointment 0.05%	Twice daily	£4.59

BNF chemical name	Manufacturer	Product name	Posology from summaries of product characteristics (SPCs), where available	Net cost per 30 g/ 30 ml for each strength (does not include VAT or dispensing fee)
Hydrocortisone butyrate	Yamanouchi	Locoid Lipocream 0.1%	2 to 3 times daily	£2.38
Hydrocortisone butyrate	Yamanouchi	Locoid cream or ointment 0.1%, scalp lotion 0.1%	2 to 4 times daily	£2.27, £3.15
Hydrocortisone butyrate	Yamanouchi	Locoid Crelo 0.1%	2 to 3 times daily	£2.72
Mometasone furoate	Schering Plough	Elocon cream or ointment 0.1%, scalp lotion 0.1%	Once daily	£4.22, £4.88

Table 5 Very potent topical corticosteroids

BNF chemical name	Manufacturer	Product name	Posology from summaries of product characteristics (SPCs), where available	Net cost per 30 g/30 ml for each strength (does not include VAT or dispensing fee)
Clobetasol propionate	GlaxoSmithKline	Dermovate cream or ointment 0.05%, scalp application 0.05%	1 to 2 times daily	£2.48, £3.27
Diflucortolone valerate	Schering Health/Meadow	Nerisone Forte ointment or oily cream 0.3%	N/A	£4.18
Halcinonide	Bristol–Myers Squibb	Halciderm cream 0.1%	2 to 3 times daily	£3.40

ISBN: 978-1-4731-5620-3