COMPASS Therapeutic Notes on the Primary Care Pharmacological Management of Atopic Eczema

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— changes highlighted as ***'updated 2016'***

In this issue:

Glossary of terms

Anti-mitotic	Inhibiting or preventing cell division.
Intertriginous	Where opposing skin surfaces touch and may rub, such as skin folds of the groin, axillae and breasts.
Lauromacrogols	Chemical substances reputed to have skin-soothing and anti-itch properties.
Molluscum contagiosum	A common, benign, usually self-limited viral infection of the skin and occasionally the conjunctivae by a molluscum virus.
Tachyphylaxis	A rapid decrease in the response to a drug after repeated doses over a short period of time. Increasing the dose of the drug will not increase the pharmacological response.
Telangiectasia	Permanent dilation of pre-existing blood vessels creating small focal red lesions, most commonly in the skin or mucous membranes. It is characterised by the prominence of skin blood vessels.
Xerosis	Abnormal dryness of a body part or tissue (e.g. the skin or conjunctiva).

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Introduction and Background

Atopic eczema (also known as atopic dermatitis) is a chronic inflammatory skin condition characterised by intense itching, dry skin, erythema, inflammation and sometimes exudation.[1-3] It is typically an episodic disease of exacerbations and remissions.[1] In some cases it may be continuous.[1] Acute lesions are itchy +/- painful and erythematous; there may be tiny vesicles that ooze and crust. The subsequent chronic inflammatory phase is characterised by scaling, excoriations, skin thickening and enhancement of skin markings (lichenification).[4,5]

Atopic eczema affects mainly the flexor surfaces of the elbows and knees, as well as the face and neck,[3] although patterns of localisation can differ depending on the age of the patient. In babies and small children eczema is common on the cheeks, forehead and extensor surfaces of the limbs.[6]

The impact of atopic eczema

Although atopic eczema may not always be recognised as being a serious medical condition, the impact of atopic eczema on quality of life can be considerable, and varies according to disease severity.[3] The effects of atopic eczema vary in complexity from a minor irritating rash to a complex, long-term condition which can be a major challenge to living a "normal" life. In addition to the burden imposed by daily treatment, the condition affects everyday activities such as work, school and social relationships.[3] People with atopic eczema may also experience anxiety, depression and other psychological problems.[3] Sleep disturbance is common, especially during flares, which in turn can lead to problems with irritability and lack of concentration.[3] In children, sleeplessness and irritability could be perceived as hyperactivity.[7]

Prevalence of atopic eczema

Estimates of the prevalence of atopic eczema vary but it is thought that the condition:

- is the most common inflammatory skin disease of childhood[2,8-10]
- accounts for 30% of all dermatological consultations in general practice[11]
- is increasing in prevalence in most industrialised countries[12]
- has a prevalence of around 15-20% in children and 2-10% in adults[2,3,11,13-17]
- has no difference in prevalence based on gender or ethnicity[1,19]
- typically starts early in life, with about 80% of cases starting before the age of 5 years[2,8-11,20-22]
- is mild in around 80% of cases; only around 2-4% of people with eczema have a severe form of the disease.[3]

Aetiology of eczema (updated 2016)

The pathophysiology of atopic eczema is not fully understood but is thought to involve a complex interaction of genes, environmental triggers, skin barrier defects and immunologic responses.[23] Raised immunoglobulin E (IgE) levels are seen in atopic eczema, but the exact role of IgE in the disease is unclear.[24] Atopic eczema is present in about 80% of children where both parents are affected and in 60% if only one parent is affected.[28] There has therefore been a lot of research in recent years into the genetic component attributable to atopic eczema.[25-27] Loss-of-function mutations in the skin barrier protein filaggrin (FLG) is thought to contribute towards skin barrier dysfunction and are therefore a major risk for atopic eczema.[122]

This is now widely considered a key mechanism contributing to eczema pathogenesis. Exposure to certain environmental factors such as pets and certain foods can contribute to exacerbations. [23]

Is there any evidence that children "grow out" of eczema in later life?

About 60% of children outgrow the disease or experience milder symptoms as they get older, however, the tendency towards dry and irritable skin is probably lifelong and the condition can recur in adults, often as hand eczema.[2,29-31] See **Table ONE**.

Table ONE: Diagnostic criteria for atopic eczema [1,3,18]

Itchy skin (or parental report of scratching) in the last 12 months, *plus* three or more of the following:

- A history of involvement of skin creases (elbows, knees, ankles, neck, or around eyes).
- A personal history of asthma or hay fever (or history of atopic disease in a first -degree relative if a child is less than 4 years of age).
- A history of a generally dry skin in the last year.
- Onset under the age of 2 years (not used if a child is less than 4 years of age).
- Visible flexural eczema (or eczema affecting cheeks or forehead and outer aspects of limbs in children less than 4 years of age).

Managing Atopic Eczema

Although atopic eczema cannot be cured, symptoms can be alleviated with good skin care and lifestyle measures. It is also important to identify the factors that exacerbate the condition and avoid them where possible. The aims of treatment are to heal skin and keep it healthy, prevent flare-ups and treat symptoms as soon as they occur and so improve quality of life.[32]

Where are patients with atopic eczema managed?

Most patients with atopic eczema can be managed by the primary care team.[2,3] Referral to a specialist is advised if the condition is severe and has not responded to appropriate therapy.[1,13] About 4% of children with atopic eczema are referred to a dermatologist.[33]

Community pharmacists

Community pharmacists are well placed to be a source of support and advice for the majority of children who are diagnosed by their GP and never see a dermatologist or specialist nurse. Community pharmacists are the healthcare professionals likely to:[34]

- have contact with the child or parent in the early stages of the condition
- see patients every time they pick up their prescriptions or buy an over-the-counter preparation.

NICE Guidance on atopic eczema

There is a NICE clinical guideline concerning the management of atopic eczema in children from birth up to the age of 12 years.[1] It has been developed with the aim of providing guidance on:[1]

- diagnosis, assessment and impact
- management during and between flares
- information and education for children and their parents or carers.

NICE propose a stepped care plan approach to treatment. This is where treatment is stepped up or down according to the physical severity of the eczema. See **Table TWO**.

Although the scope of the NICE guideline is limited to children under the age of 12 years, the recommendations can be reasonably extrapolated to the management of older children and adults with atopic eczema, because although atopic eczema is predominantly a disorder of childhood,[29] there is no evidence that the pathology of the condition is different in adulthood compared with childhood, and there is no suggestion that it does not respond to the same interventions.

There are currently no authoritative UK guidelines on the management of eczema in older children or adults.

Hence this paper uses the NICE guideline as the basis for most recommendations for all-groups, with additional information added where available.

What is meant by a "flare" of atopic eczema?

A "flare" is a worsening of eczema that results in escalation of treatment or seeking additional medical advice.[35]

NICE pragmatically defines a flare of eczema as "an increase in clinical severity (redness, oedema, or itching) of the condition".[1]

Why is early identification of a flare important?

Early identification and treatment of a flare can reduce the severity of the flare and allow for more conservative treatment measures (such as emollients alone and so reduce the need to use topical corticosteroids).[11] Scratching is thought to be a major component of flare progression; it physically damages the skin and can delay healing or facilitate infection. Emollients are believed to ease itching and thus may have a role in breaking the itch-scratch cycle.[36] Early application of topical corticosteroids may prevent the flare from worsening, and thus lead to reduced use of corticosteroids in the longer term.[11]

Healthcare professionals should offer children with atopic eczema and their parents or carers information on how to recognise flares.[1] They should give clear instructions on how to manage flares according to the stepped-care plan, and prescribe treatments that allow patients and/or carers to follow this plan.[1]

Table TWO: NICE stepwise approach to management of atopic eczema[1]

Mild atopic eczema	Moderate atopic eczema	Severe atopic eczema
Emollients	Emollients	Emollients
Mild potency topical corticosteroids	Moderate potency topical corticosteroids	Potent topical corticosteroids
	Topical calcineurin inhibitors*	Topical calcineurin inhibitors*
	Bandages*	Bandages*
		Phototherapy†
		Systemic therapy‡

* Usually only prescribed by a specialist (e.g. a GP with specialist interest in dermatology, dermatologist, or paediatrician).
† Available in secondary care only
‡ Oral corticosteroids can be prescribed short-term in primary care for severe flares. Other systemic treatments suitable for maintenance of severe eczema (e.g. methotrexate, ciclosporin or azathioprine) require referral to secondary care.

Emollients

Emollients have been used in the treatment of eczema for many decades and are almost universally recommended as first-line treatment. However there is actually very little evidence of effectiveness from controlled trials.[2,11,36]

What is the role of an emollient in atopic eczema? (updated 2016)

Dry skin is an important feature of atopic eczema, but the rationale for reversing this dryness with emollients is less clear. One rationale is simply to relieve the feeling and appearance of "dryness" which many eczema sufferers choose to do. Another rationale is that emollients have soothing effect on itching and soreness and can have other useful properties; they can be exfoliative (especially when combined with products such as salicylic acid), and may have anti-inflammatory, and anti-mitotic effects especially when combined with other excipients such as lauromacrogols.[37,38]
There is currently research looking into whether or not the use of emollients from birth could prevent eczema in babies with a strong family history.[120]

How do emollients work?

To many people, the terms "emollient" and "moisturiser" are synonymous. However, technically emollients and moisturisers are different; an emollient being something that smoothes and softens the skin, usually via occlusion, and a moisturiser being something that actively adds moisture to the skin. In this document the word "emollient" is used as an inclusive term to define substances whose main actions are to:

1. **Occlude the skin surface** – by utilising greasy substances (e.g. white soft paraffin) to trap water in the stratum corneum, thus preventing transepidermal water loss by evaporation.
2. **Encourage build up of water within the stratum corneum**.[39] This involves the active movement of water from the dermis to the epidermis. Emollients that have this effect contain substances known as "humectants" (e.g. urea or glycerine). These have a low molecular weight and water-attracting properties[40] and as they penetrate the epidermis they draw water in from the dermis.

Some emollients contain a mixture of occlusive and humectant substances.

Which emollient? (updated 2016)

Given the lack of evidence of comparative effectiveness of the various available emollients, **the correct emollient is the one that the patient will use**. It is generally considered that giving patients a choice of emollient is likely to result in their choosing one that they will use frequently and regularly.[11,13,41] Adherence to emollient treatment is the key to successful therapy for atopic eczema.[1]

Emollients can be applied to the skin in a number of ways, including wash products (e.g. bath additives, soap substitutes and skin cleansers) or topical preparations (e.g. creams, ointments and lotions).
Often, several different emollients will be required. The severity of the condition, patient preference and site of application will often guide the choice of emollient:[41]

- **Lotions** are used for the scalp and other hairy areas and for mild dryness on the face, trunk and limbs.
- **Creams** are used when more emollience is required on these latter areas.
- **Ointments** are prescribed for drier, thicker, scalier areas. They have less additives / potential allergens (so are often better tolerated) and are lipid based, so generally more effective.[119] Ointments are usually a first line option for patients presenting to secondary care (i.e. the more moderate and severe cases). However, they are not acceptable to all patients as some people find them too greasy[39] and ointments may stain clothes.

Often the best way to choose an emollient is to provide samples and ask the patient to choose the one or ones they feel suit their skin. Patients may use a thinner, less messy, lotion in the morning when getting dressed and then a thicker cream or ointment at night on retiring to bed.
NICE believe that ointments are preferable for dry skin because they are more effective than creams, but creams are preferable on red, inflamed skin because the evaporation of water-based products cools the skin.[1] This recommendation is based on clinical experience, rather than evidence from controlled trials or studies.

See **Table FIVE** for advice on using emollients.

How should emollients be prescribed?

Emollients are probably under-used in general practice, with many patients not using an emollient at all before being prescribed a topical corticosteroid.[42] Once the preferred choice of emollient(s) is known, **prescribe large quantities, frequently**.[11] The amount of emollient prescribed will vary depending on the size of the person and extent and severity of the eczema[11] (see **Table THREE**). The amount of emollient used should far exceed other topical treatments (i.e. corticosteroids), by a factor of at least ten.[11] Where possible, pump-dispensers should be prescribed if large quantities of cream or lotion are required.[11]

Why should emollients <u>not</u> be rubbed into the skin?

- Rubbing emollients into the skin should be discouraged because it:
- introduces air into the emollient and reduces absorption
- occludes or physically aggravates hair follicles, which may cause folliculitis (especially with ointments)
- stimulates blood circulation, which generates heat and may cause itch.

Can emollients have adverse effects?

Emollients are generally thought to be safe, with limited adverse effects. However, the following have been reported:

Sensitivity to some of the ingredients (more common in children than adults) - The most common adverse effect seen with emollients is a rash caused by sensitivity of the skin to one or more of the ingredients in the product.[11] The skin shows an immediate and dose-dependent inflamed response.[11] The ingredients that have been reported to cause sensitisation reactions in skin are listed in **Table FOUR**. If a skin reaction occurs, stop the product and use a different emollient. If the person has had previous skin reactions to emollients:

- test a small quantity first (e.g. on the skin of the inner arm) before widespread application.[11]
- the chance of a further reaction is reduced by prescribing an ointment (these do not require preservatives and generally have fewer excipients).[11]

Folliculitis
Use of very greasy ointments can block the hair follicles, which can lead to irritation and inflammation. This can usually be avoided by stroking, rather than rubbing, the emollient into the skin following the directional lie of the hair and/or using a lighter, less occlusive product. Occasionally blockage of the hair follicle may lead to painful pustules and infection, causing folliculitis. Antibiotics may be needed. However, stopping the product is often sufficient to resolve the problem.

Slip hazard (bath additives)
Bath emollients can pose a slip hazard.[11]

! Fire Hazard with paraffin-based emollients[41,45]

Emulsifying ointment or Liquid Paraffin and White Soft Paraffin in contact with dressings and clothing are easily ignited by a naked flame. The risk is greater when these preparations are applied to large areas of the body, and clothing or dressings become soaked with the ointment. Patients should be told to keep away from fire or flames, and not to smoke when using these preparations.

Table THREE: Quantities of emollients that should be prescribed for <u>adults*</u> with eczema, per week [39]

Area affected	Creams and ointments (grams)	Lotions (ml)
Face	15-30	100
Both hands	25-50	200
Scalp	50-100	200
Both arms or both legs	100-200	200
Trunk	400	500
Groin and genitalia	15-25	100

* For children, about half these amounts are suitable

Table FOUR: Potential sensitising ingredients found in emollients [39,41]

Beeswax
Benzyl alcohol
Butylated hydroxytoluene
Cetostearyl alcohol
EDTA
Fragrances
Hydroxybenzoates
Imidurea
Isopropyl palmitate
N-(3-Chloroallyl) hexamine chloride
Polysorbates
Propylene glycol
Sodium metabisulphite
Sorbic acid
Wool fat and related substances (including lanolin)*

* Although lanolin has often been reported in the literature as a potent sensitiser; newer more highly refined (hypo-allergenic) types of lanolin rarely cause adverse reactions.[43]

What are "soap substitutes"?

These are used like soap, being applied over the body (using hands or a wash cloth) and then rinsed off to aid the removal of organic matter and enhance the lipid coating on the skin. They have the advantage of being non-drying. Preparations such as aqueous cream or emulsifying ointment can be used as soap substitutes for hand washing and in the bath.[41] Branded soap substitutes are also available.

What is the purpose of a bath emollient/ additive?

As well as being advised to apply emollient creams or ointments directly to the skin, people with atopic eczema are commonly prescribed bath emollients. Each year in Northern Ireland, we spend over £620,000 on bath emollients on prescription.[46] Bath emollients are sometimes used in the belief that it is an easier way of applying an emollient to a large skin surface area, particularly for children who may not co-operate with having topical emollients applied frequently. This advice also aims to encourage people to change from using potentially irritant preparations such as bubble baths.

How should a bath additive be used?

Bath emollients/additives can be used in several ways:[41]

- They can be added to bath water – some authors recommend that any supplement must be added 5 minutes after the patient is sitting in the water so the skin can absorb a maximum of water before it is "sealed" by the oil.[47] Hydration can be improved by soaking in the bath for 10-20 minutes.
- Some bath emollients can be applied to wet skin undiluted and rinsed off.
- Some can be applied to dry skin.

If used, it is essential that they should not replace standard emollients, and the person should be advised to continue using these in addition to any bath emollient product.[11]

Is there proven evidence of effectiveness?

The Drug and Therapeutics Bulletin has called the use of bath emollients "questionable",[48] pointing out that there are no published RCTs that have investigated the use of bath emollients, and, unlike emollients designed to be left on the skin, there is no universal consensus on their benefit.[48]

Several emollient bath preparations are available on prescription.[41] The main ingredients in most are liquid paraffin together with another emollient, most commonly wool fat or isopropyl myristate. Some bath emollients (e.g. Dermol® 600 Bath Emollient, Emulsiderm®, Oilatum® Plus) also contain antimicrobials. However, such products should not be used regularly unless infection is widespread or recurrent.[13,41] A few preparations contain lauromacrogols (e.g. Balneum Plus® bath oil), the inclusion of which is claimed to help break the itch-scratch cycle.[13] There is no published evidence to confirm this.[48]

What is "complete emollient therapy"?

"Complete emollient therapy" (CET) involves the use of a topical emollient cream or ointment, emollient bath oil and emollient soap substitute, backed up with education on how to use them. (Soaps and detergents, including so-called "moisturising soaps" and bubble baths, must be avoided at all times). CET is based on the premise that the patient's skin should be protected from soap and detergents as far as possible and treated with emollients as frequently as possible.

Is the use of emollients steroid-sparing?

Effective use of emollients can have a steroid-sparing effect; that is to say the beneficial effects of the steroid treatment are achieved at a lower dose than if the steroid product had been used alone.[36,49,50] This may be a useful point to make to patients as many of them are concerned about the long-term effects of using steroids.

Prescribing point: Aqueous cream

Aqueous cream was originally devised as a soap substitute, not a topical emollient. When applied directly to the skin as an emollient, aqueous cream causes significantly more stinging than other emollients.[44] It has also been shown to increase transepidermal water loss.[119] Thus, **use of aqueous cream as a topical emollient should be avoided**.[11,44] As a soap substitute it is generally well tolerated.

Prescribing point: BRAND prescribing of multi-ingredient creams and ointments

It is considered *inappropriate* to prescribe products with multi-ingredients generically. Creams, ointments, bath oils, lotions etc which contain many active ingredients should be prescribed by *brand name*.[51]

Table FIVE: Advice on using emollients [11,41]

The effects of emollients are short-lived, and will depend on several factors such as the dryness of the skin and the type of emollient used (products with higher water content lose effectiveness faster). **Use emollients liberally and frequently, even when the skin appears improved or is clear.**

- For very dry skin, application of an emollient every 2-3 hours should be considered normal.
- The amount and frequency of emollient used will need to increase at the first sign of any worsening of the condition.
- Even if other treatments such as topical corticosteroids are being used, regular use of emollients should continue.
- To facilitate frequent application, the person should consider keeping packs of emollients at work or school.

Applying emollients:

- Healthcare professionals should demonstrate to patients or their carers how to apply emollients.
- Apply by smoothing them into the skin in the direction of hair growth (rather than rubbing them in).

Washing:

- Avoid using soaps, detergents and bubble bath. Instead use a suitable soap substitute, for example an ointment dissolved in hot water or lotion in warm water.
- Dry the skin gently after washing and apply the emollient straight away while the skin is still moist.
- Use of emollient bath additives and shower gels can be considered in people with extensive areas of dry skin. However, their use should supplement, not replace, emollients designed to be left on the skin.
- Bathing hydrates and cleanses the skin and emollient based soap substitutes moisturise the skin. Bathing is therefore usually recommended once a day.[119] ***(updated 2016)***

Emollients should not be shared with other people.

Wait 10-15 minutes after application of an emollient before applying a topical corticosteroid.

Topical corticosteroids

Many patients with atopic eczema need to use topical corticosteroid preparations intermittently when the condition flares and a few patients need to use them long-term.

Topical corticosteroids are the first-line treatment for flare-ups of atopic eczema.[3] They do not cure the condition but they will control it via anti-inflammatory and immunosuppressive effects.[3] Topical corticosteroids reduce inflammation and relieve itching, although the mechanism by which they do this is largely unclear.

Evidence of the effectiveness of topical steroids in atopic eczema.

Topical corticosteroids have been a vital component of treatment for atopic eczema since the development of hydrocortisone in 1952. The development of the early topical corticosteroids preceded the use of high-quality RCTs to determine clinical effectiveness. As a result, evidence from controlled trials for effectiveness of this group of drugs is limited.[2] Clinical experience has shown that topical steroids improve atopic eczema over a two to four week period.[52] Initial improvement should be seen within 3-7 days of starting topical steroids.[53]

Relative potency of topical steroids

The BNF categorises topical corticosteroids for the skin as "mild", "moderately potent", "potent" or "very potent".[41] **Table SIX** shows the potency of various corticosteroid preparations. The potency of each corticosteroid is measured by its ability to cause vasoconstriction, rather than its clinical effectiveness.[11] "Very potent" topical corticosteroids are up to 600 times as potent as mild topical corticosteroids.[11] Potency is also affected by the formulation and other ingredients, for example, propylene glycol, urea or salicylic acid may enhance absorption of steroids.[54] The salt of the steroid may also affect potency, e.g. hydrocortisone is a mild steroid, while hydrocortisone butyrate is classified as potent [54] (see **Table SIX**).

How do I decide which topical corticosteroid to prescribe?

The choice of topical corticosteroid is based on potency of the preparation and the site and severity of the condition. Use:[1]

- Mild potency for mild atopic eczema
- Moderate potency for moderate atopic eczema
- Potent for severe atopic eczema
- Mild potency for the face and neck, except for short-term (3-5 days) use of moderate potency for severe flares
- Moderate or potent preparations for short periods only (7-14 days) for flares in vulnerable sites such as axillae or groin.

Do not use very potent preparations without specialist dermatological advice.
NICE recommends 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.[3]

Formulation aspects of topical corticosteroid preparations

It is important to consider the base in which the corticosteroid is supplied.[11,41]
Corticosteroid creams are more suitable for skin which is:

- moist or weeping (ointments are difficult to apply to wet areas)
- infected so that the infected area is not occluded.
- visible, such as the face and hands

Corticosteroid ointments are more suitable for:

- dry lichenified or scaly lesions
- when a more occlusive effect is required

Corticosteroid lotions are more suitable for:

- minimal application to a large or hair-bearing area
- treatment of exudative lesions.

OTC sale of topical corticosteroids

Creams and ointments containing **hydrocortisone 1%** (alone or with other ingredients) can be sold to the public for the treatment of allergic contact dermatitis, irritant dermatitis, insect bite reactions and mild to moderate eczema, to be applied sparingly over the affected area 1-2 times a day for a maximum of one week.[41] OTC hydrocortisone preparations should not be sold without medical advice for children under 10 years or for pregnant women;[41] they should not be sold for application to the face, anogenital region, or broken/infected skin. Pack size is limited to 15 grams.

Clobetasone butyrate 0.05% cream may be sold for the short-term treatment and control of small patches of atopic eczema in adults and children over 12 years of age provided the pack does not contain more than 15 grams.

Prescribing point: Hydrocortisone cream — note strength ***(updated 2016)***
When prescribing hydrocortisone, some GP clinical systems automatically default to the 0.1% strength. Ensure that the intended strength of hydrocortisone is selected.

What adverse effects are associated with the use of topical steroids?

The adverse effects of topical corticosteroids are well recognised but often exaggerated. Side-effects generally only occur following the incorrect use of potent steroids over a long period of time. The following factors can influence the likelihood of adverse effects:

- Site of treatment - absorption is greatest from intertriginous areas.
- Skin thickness - absorption is greatest where the skin is thin
- Skin condition - greater absorption occurs when the skin is damaged.
- Patient age - children, especially infants, are particularly susceptible to side-effects.[41]
- Potency of preparation - mild and moderately potent topical corticosteroids are associated with few side-effects but care is required in the use of potent and very potent corticosteroids.
- Duration of treatment

Local side-effects include:[41]

- Transient burning or stinging is common and may necessitate changing the product.[11]
- Spread and worsening of untreated infection.
- The skin can become thin and easily bruised.[3] It is particularly common in the skin of the elbow creases and behind the knees.[11] Studies in healthy volunteers showed skin thinning at 6 weeks, which completely reversed after treatment was stopped[52] but the original skin structure may never return.
- Irreversible striae atrophicae - prolonged or excessive use of potent steroids causes the dermis to lose its elasticity and stretch marks (striae) to appear, which are permanent.[3]
- Telangiectasia - especially on the cheeks.
- Steroid-induced dermatitis - contact sensitivity can develop not only to preservatives within steroid preparations, but also to the steroid molecule itself.[55]
- Perioral dermatitis.
- Acne.
- Mild depigmentation - may be reversible.
- Hypertrichosis.
- Rebound flare – if topical steroids are stopped abruptly.[54,56]
- Cataracts and glaucoma – following application of topical corticosteroids on the eyelid region.[57]

When topical corticosteroids are used correctly, **systemic adverse effects** are very rare but include adrenal suppression that can result in symptoms of Cushing's syndrome and growth retardation in children.[57] However, a study of children using topical corticosteroids for atopic eczema for a median of 6.9 years found evidence of HPA axis suppression only in those using potent or very potent topical corticosteroids or those who had received corticosteroids from other routes (inhaled, intranasal, or oral).[58]

What can be done to minimise the risk of adverse effects?

In order to minimise the side-effects of a topical corticosteroid, it is important to:[41]

- Apply it thinly to affected areas only
- Apply it no more frequently than twice daily,
- Use the least potent formulation which is fully effective.

Check for signs of adverse effects at review, such as areas of thin skin or striae.[11] In children who are using large amounts of topical corticosteroid, monitor height.[11]

Prescribing point: Monitor large quantities of topical steroids
Patients persistently using large quantities of topical corticosteroids should be monitored. There is no definition of what is meant by "large quantities", but **an adult using more than 100 grams of potent corticosteroid per month, for several months, should trigger a review**.[11]

Table SIX: Topical Corticosteroid Preparation Potencies [41]		
With the exception of hydrocortisone 0.1% - 2.5%, topical corticosteroid preparations should be prescribed by BRAND name. This is to avoid confusion between products, and because potency of topical corticosteroid preparations is a result of the formulation as well as the corticosteroid. ***(updated 2016)***		
Potency	**Examples – steroid alone**	**Steroid plus antimicrobial**
MILD	• Hydrocortisone 0.1% - 2.5% (non-proprietary) **NIF** • Synalar 1 in 10 dilution® (fluocinolone 0.0025%)	• Canestan HC® (hydrocortisone, clotrimazole) **NIF** • Daktacort® (hydrocortisone, miconazole) **NIF** • Econacort® (hydrocortisone, econazole) • Fucidin H® (hydrocortisone, fusidic acid) **NIF** • Nystaform-HC® (hydrocortisone, nystatin, chlorhexidine) • Timodine® (hydrocortisone, nystatin, benzalkonium chloride) **NIF**
MODERATE	• Betnovate-RD® (betamethasone 0.025%) **NIF** • Eumovate (clobeta**sone**) **NIF (1st choice)** • Haelan® (fludroxycortide) • Modrasone® (alclometasone) **NIF** • Synalar 1 in 4 dilution® (fluocinolone) **NIF** • Ultralanum Plain® (fluocortolone)	• Trimovate® (clobeta**sone**, oxytetracycline, nystatin) **NIF**
POTENT	• Betacap®, Bettamousse®, Betnovate® **NIF**, Diprosone® (betametasone 0.1%) • Cutivate® (fluticasone) • Elocon® (mometasone) **NIF** • Locoid®, Locoid Crelo® (hydrocortisone butyrate 0.1%) • Metosyn® (fluocinonide) • Nerisone® (diflucortolone) • Synalar® (fluocinolone) **NIF**	• Aureocort® (triamcinolone, chlortetracycline) • Fucibet® (betametasone, fusidic acid) **NIF** • Lotridern® (betametasone, clotrimazole) • Synalar C® (fluocinolone, clioquinol) • Synalar N (fluocinolone, neomycin)
VERY POTENT	• Clarelux®, Dermovate® **NIF** , Etrivex® (Clobeta**sol** 0.05%) • Nerisone Forte® (diflucortolone)	
* **NIF** Northern Ireland Formulary choice http://niformulary.hscni.net		

Dispensing note: Topical corticosteroids[1]

NICE guidance indicates that healthcare professionals who dispense topical corticosteroids should apply labels to the container (for example, the tube), not the outer packaging. The label should also state the potency class of the preparation [1]

Concern about the safety of topical steroids should not result in the patient being under-treated. The aim is to control the condition as well as possible; inadequate treatment will perpetuate the condition.[41] Healthcare professionals should discuss the benefits and harms of treatment with topical corticosteroids with patients or carers, emphasising that the benefits outweigh possible harms when they are used correctly.[1]

What is "steroid-phobia"?

Many patients are reticent about using topical steroids because of the fear of side-effects.[31] Steroid phobia is a real phenomenon with some people being so frightened that they will not use steroids, even when they have been prescribed. Furthermore, confusion about potency is common. Surveys and questionnaires of dermatology outpatients with atopic eczema have shown:[59,60]

- 72% of patients (or their carers) are worried about using topical steroids.
- 24% admitted to not having used prescribed topical steroids because of worries about side-effects.
- 9.5% of patients were worried about systemic absorption of the steroid.
- 42% of patients who used potent topical corticosteroids perceived it to be moderate or weak. This could lead to inappropriate use and increased risk of side-effects.[61]
- 44% incorrectly graded hydrocortisone as moderate or potent and may have used it inadequately because of worries about potential side effects.[61]

Avoiding steroid phobia / communicating to patients ***(updated 2016)***

Framing the very small risk of side effects in context with plenty of reassurance about the safety and benefit of appropriate treatment could relieve steroid phobia and prevent it from occurring.[124]

Topical corticosteroids – apply once or twice a day?

Once-daily application of topical corticosteroids is widely endorsed[2,3,41,62,63] and should be used as a first-step in all patients with atopic eczema. If necessary, use can be increased to twice daily to bring the condition under control before stepping down again to once-daily.

Topical corticosteroids – duration of treatment? (updated 2016)

Use mild potency for the face and neck, except for short-term (3 to 5 days) use of moderate potency for severe flares. Use moderate or potent preparations for short periods only (7 to 14 days) for flares in vulnerable sites such as axillae and groin.[1] Exclude secondary bacterial or viral infection if a mild or moderately potent topical corticosteroid has not controlled the atopic eczema within 7-14 days.[1]

Where should topical corticosteroids be applied?

Topical corticosteroids should only be applied to areas of active atopic eczema (or eczema that has been active within the past 48 hours); this may include areas of broken skin.[1]

If a topical steroid and an emollient are to be applied, which should be applied first?

Advise the person to use their emollient first, then wait 10-15 minutes before applying the topical corticosteroid (after the emollient has been absorbed).[11,41]

Table SEVEN: Suitable quantities of steroid cream/ointment to be prescribed for specific areas[41]	
Face and neck	15 to 30 grams
Both hands	15 to 30 grams
Scalp	15 to 30 grams
Both arms	30 to 60 grams
Both legs	100 grams
Trunk	100 grams
Groins and genitalia	15 to 30 grams
These amounts are usually suitable for an adult for once-daily application for 2 weeks.	

Can topical corticosteroids be used as "maintenance" treatment in atopic eczema? (updated 2016)

Intermittent treatment with a moderate or potent topical corticosteroid is as effective as continuous treatment with a mild corticosteroid.[65] In practice, twice weekly treatment with a moderate steroid is usually sufficient and this would be the standard maintenance therapy in local paediatric dermatology units. Some patients will require twice weekly potent corticosteroids.[120]

Healthcare professionals should consider treating problem areas of atopic eczema with topical corticosteroids for two consecutive days per week (so-called "weekend therapy") to prevent flares, instead of treating flares as they arise, in people with frequent flares (two or three per month), once the eczema has been controlled.[1] This strategy should be reviewed within 3 to 6 months to assess effectiveness.[1] A different topical corticosteroid of the same potency should be considered as an alternative to stepping up treatment if tachyphylaxis to a topical corticosteroid is suspected.[1]

Fingertip units

Patients are often advised to apply topical corticosteroids "sparingly" or "thinly". This rightly recognises the potential for side-effects that have been associated with inappropriate, prolonged and/or excessive use of topical corticosteroids, especially the more potent agents. However, the advice to apply "sparingly" or "thinly" carries with it messages of economy, caution and even danger. Certainly, there is good evidence that patients interpret this warning in a negative way, giving rise to steroid phobia, with accompanying poor adherence to treatment.[60,66] The "finger-tip-unit", first introduced in the early 1990s,[67] is a simple tool to help health professionals and patients obtain a better understanding of the amount of topical products, they should use on different parts of the body.[67]

One "fingertip unit" (FTU) is the quantity of cream or ointment required to go from the tip of the patient's index finger to the first joint as it is squeezed out of the tube and is equivalent to 0.5 grams of cream or ointment. Topical steroids should be applied in the amounts shown in **Table EIGHT**.

Table EIGHT: Fingertip units (FTUs) required [64]

Body site	Adults	Child (3-6 mths)	Child (1-2 years)	Child (3-5 years)	Child (6-10 years)
Face and neck	2.5	1	1.5	1.5	2
Arm and hand	4	1	1.5	2	2.5
Leg and foot	8	1.5	2	3	4.5
Trunk (front)	7	1	2	3	3.5
Trunk (back) & buttocks	7	1.5	2	3.5	5

Note: Some topical steroid creams are available in pump dispensers, in which case one action of the pump is equivalent to **two** FTUs.

Topical calcineurin inhibitors

Two topical calcineurin inhibitors are available to treat atopic eczema: **tacrolimus** (Protopic® ointment) and **pimecrolimus** (Elidel® cream).

How do tacrolimus and pimecrolimus work?

Tacrolimus and pimecrolimus are topical immunomodulators classified as calcineurin inhibitors. Although they also act on other cells playing a role in atopic eczema (mast cells, Langerhan's cells, B-lymphocytes), their action on T-lymphocytes seems to be the most important.[71-73] Although tacrolimus and pimecrolimus have similar mechanisms of action, they have different licensed indications (see later).

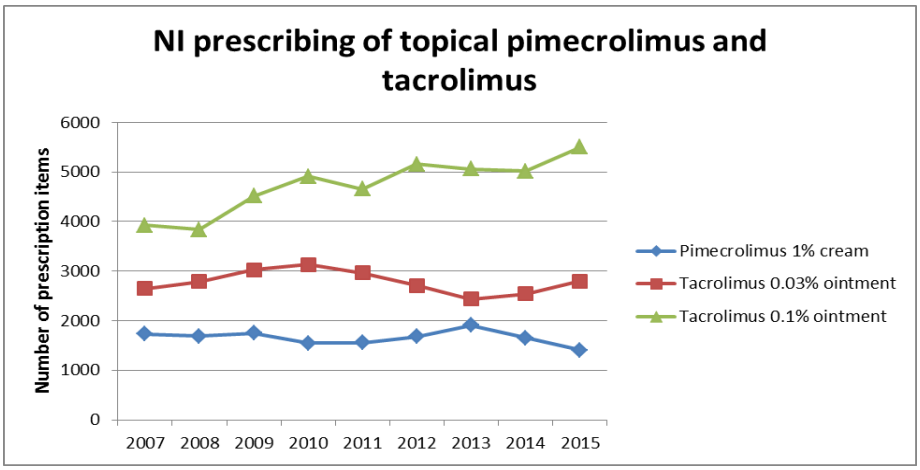
What is the place of topical calcineurin inhibitors in the management of atopic eczema?

In its appraisal of these agents,[74] NICE recommends that, within their licensed indications:

- Topical tacrolimus is an option for the second-line treatment of *moderate to severe* atopic eczema in adults and children aged 2 years and older.
- Topical pimecrolimus is an option for the second-line treatment of *moderate* atopic eczema on the face and neck in children aged 2–16 years.

In either case, the atopic eczema will not have been controlled by topical corticosteroids or there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy.[74]

Treatment with tacrolimus or pimecrolimus should be initiated only by physicians (including general practitioners) with a special interest and experience in dermatology, and only after careful discussion with the patient about the potential risks and benefits of all appropriate second-line treatment options.[68-70,74] See **Table TEN**.



How much tacrolimus and pimecrolimus are prescribed in primary care in Northern Ireland?

See chart of prescribing data.

Efficacy of tacrolimus and pimecrolimus

Tacrolimus and pimecrolimus have been shown to be effective in the treatment of atopic eczema.[75,76] Trials have shown a rapid reduction of symptoms within a few days of therapy; they are effective in both the short- and long-term, and in adults and children.[20,77-85]

When compared to topical steroids:

- Tacrolimus is more effective than mild topical steroids[86] and equally effective to moderately potent topical steroids.[87,88]
- Pimecrolimus has been found to be equivalent in efficacy to mild topical steroids and less effective than moderately potent topical corticosteroids.[87]

Although less effective than potent topical corticosteroids, pimecrolimus has value in the long-term maintenance and steroid-sparing effect in atopic eczema. This is particularly true if pimecrolimus is used early in the disease course.[87] In moderate to severe atopic eczema, application of pimecrolimus cream regularly for 6 months resulted in significantly fewer flares of eczema and significant reduction of the use of topical corticosteroids.[87]

What are the advantages of tacrolimus and pimecrolimus?

Unlike topical corticosteroids, tacrolimus and pimecrolimus do NOT interfere with collagen synthesis or induce skin atrophy.[89-91] This could be a major advantage for long-term use and for use on the face and neck.[92]

Pimecrolimus is minimally absorbed even when the drug is applied to large areas of inflamed skin.[93]

How should tacrolimus or pimecrolimus be used?

See **Table NINE**.

Adverse effects of tacrolimus

Application site reactions:

In studies, approximately 50% of patients applying topical tacrolimus experienced some type of skin irritation at the site of application. A burning sensation and pruritus were very common, usually mild to moderate in severity and tended to resolve within one week of starting treatment.[94,95] Patients/carers should also be told to avoid application after bathing as this will enhance the discomfort.

Erythema was also a common adverse skin reaction. Sensations of warmth, pain, paraesthesia and rash at the site of application were also commonly observed.[68,69] Patients may be at an increased risk of folliculitis, acne and herpes viral infections.[68,69]

Systemic reactions:

In trials, the most common systemic adverse events were:

- flu-like symptoms
- headache
- alcohol intolerance (facial flushing or skin irritation after consumption of alcohol).

As with topical corticosteroids, tacrolimus treatment is suppressive and discontinuation of treatment frequently leads to recurrence of eczema.[47]

Adverse effects of pimecrolimus

Local side effects include a burning sensation, pruritus, erythema, skin infections (including folliculitis, impetigo, herpes simplex and zoster, and molluscum contagiosum), papilloma (rarely) and local reactions such as pain, paraesthesia, peeling, dryness, oedema and worsening eczema.[74] Skin reactions to pimecrolimus are usually mild and transient, however, if the application site reaction is severe, the risk/benefit of treatment should be re-evaluated.[70]

Malignancies (updated 2016)

The MHRA issued a warning in 2012 that topical tacrolimus may be associated with a possible risk of malignancy: cases of lymphomas and skin cancers have been reported. In addition, findings from epidemiological studies have suggested a possible increased risk of cutaneous T-cell lymphoma in patients treated with topical calcineurin inhibitors, including tacrolimus ointment.[118]

A systematic review and meta-analysis has since reviewed the risk of lymphoma in patients with atopic eczema: the review found a slightly increased risk of lymphoma in patients with atopic eczema. Severity of atopic eczema appeared to be a significant risk factor; the role of topical calcineurin inhibitors was unlikely to be significant.[123] The safety profiles of calcineurin inhibitors are overall reassuring to date, with no causal link with cancer shown. However, longer term data is needed.[119]

Until further data is available the following cautions apply:

- do not prescribe Protopic® to patients younger than 2 years,
- use of Protopic® in children aged 2 to 16 years is restricted to the lower strength 0.03% ointment only.
- do not apply Protopic® to lesions that are considered to be potentially malignant or pre-malignant,
- do not use Protopic® in patients with congenital or acquired immunodeficiencies, or in patients on therapy that causes immunosuppression.[118]

Table TEN: NICE Guidance on tacrolimus and pimecrolimus in atopic eczema [74]

►Topical tacrolimus and pimecrolimus are not recommended for the treatment of mild atopic eczema or as first-line treatments for atopic eczema of any severity.

►Topical tacrolimus is recommended, within its licensed indications, as an option for the second-line treatment of moderate to severe atopic eczema in adults and children aged 2 years and older that has not been controlled by topical corticosteroids, where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy.

►Pimecrolimus is recommended, within its licensed indications, as an option for the second-line treatment of moderate atopic eczema on the face and neck in children aged 2-16 years that has not been fully controlled by topical corticosteroids, where there is a serious risk of important adverse effects from further topical corticosteroid use, particularly irreversible skin atrophy.

►"atopic eczema that has not been controlled by topical corticosteroids" refers to disease that has not shown a satisfactory clinical response to adequate use of the maximum strength and potency that is appropriate for the patient's age and the area being treated.

►It is recommended that treatment with tacrolimus or pimecrolimus be initiated only by physicians (including general practitioners) with a special interest and experience in dermatology, and only after careful discussion with the patient about the potential risks and benefits of all appropriate second-line treatment options.

Can tacrolimus or pimecrolimus be used in infected eczema?

The safety and efficacy of tacrolimus or pimecrolimus has not been evaluated in clinically infected atopic eczema. Hence, before beginning treatment with tacrolimus or pimecrolimus, clinical infections at treatment sites should be cleared.[68-70]

Table NINE: Using tacrolimus and pimecrolimus [68-70]

	Application	Use in an acute flare	Use as maintenance	Notes
Tacrolimus ointment	Apply as a thin layer to affected areas. Can be used on any part of the body, including face, neck and flexure areas, but NOT on mucous membranes.	Apply at the first sign of disease flare. Apply twice daily for up to 3 weeks. Frequency of application should then be reduced to once a day. If no signs of improvement are seen after 2 weeks of treatment, consider other treatment options.	As maintenance, apply once a day, twice weekly (e.g. Monday and Thursday) to areas commonly affected to prevent progression to flares. Adults should use tacrolimus 0.1% ointment; children should use 0.03% ointment. If signs of a flare reoccur, twice daily treatment should be re-initiated. After 12 months, review the patient's condition and decide whether to continue maintenance treatment.	Do not apply under occlusion. Emollients should not be applied to the same area within 2 hours of applying tacrolimus ointment.
Pimecrolimus cream		Apply at the first sign of disease flare. Apply twice daily until the area is clear then stop when signs and symptoms resolve. If no improvement occurs after 6 weeks pimecrolimus should be stopped.	Can be used intermittently in the long term for the prevention of progression to flares. Pimecrolimus should be applied twice daily. Data from clinical studies support intermittent treatment with pimecrolimus for up to 12 months.	Do not apply under occlusion. No restrictions on the body surface area that can be treated or the duration of treatment. Emollients CAN be applied immediately after using pimecrolimus.

Systemic therapy of atopic eczema

In a subgroup of patients with moderate to severe atopic eczema, the disease cannot be sufficiently controlled with conventional topical treatments[96,97] and systemic treatments become necessary.[98]

Ciclosporin

Ciclosporin is an immunosuppressant prodrug that acts by inhibiting T-cell function.[99,100] The role of ciclosporin in severe, recalcitrant atopic eczema is well established. In patients in whom atopic eczema cannot be controlled by standard topical therapies, ciclosporin significantly decreases symptom scores, disease extent, pruritus and sleep deprivation, and has been shown to improve quality of life.[99] In a recent meta-analysis,[97] consistent evidence was found that short-term use of ciclosporin effectively decreased disease severity. The mean clinical improvement after 6-8 weeks was calculated as being approximately 55%. Withdrawal of ciclosporin can lead to rapid flaring of the acute atopic eczema,[101,102] so slow dose reduction is required.[103] Even with this, 80% of patients will relapse within 6 weeks of ciclosporin withdrawal.[97]

Adverse effects of ciclosporin

The most common adverse effects of ciclosporin are hypertension, renal dysfunction, headache, hypertrichosis, gingival hyperplasia and paraesthesia.[99] Ciclosporin requires careful monitoring.

Azathioprine

Azathioprine is a long-known systemic immunosuppressive agent affecting purine nucleotide synthesis and metabolism.[98] Azathioprine has been shown to be useful in both adults and children with severe atopic eczema.[104,105] It is safer than ciclosporin for long-term use, though it does have several side-effects, including myelosuppression, nausea, fatigue, myalgia and liver dysfunction.[29] Although it is effective and can be used continuously,[106] it is not always well tolerated.[104]

Methotrexate (updated 2016)

Methotrexate has anti-inflammatory effects and reduces allergen specific T-cell activity.[119] It is increasingly used in the management of atopic eczema.[120] Evidence for the use of methotrexate in eczema is limited, but trials in the UK are underway. One RCT suggests that methotrexate and azathioprine are equally effective in treating eczema in the short term, but larger adequately powered studies with longer follow-up are needed.[119]

Alitretinoin capsules (Toctino®)

Alitretinoin is a derivative of retinoic acid that binds to and activates intracellular retinoid receptors. These receptors regulate cellular differentiation and proliferation.[107] Alitretinoin capsules are indicated for use in adults who have severe chronic hand eczema that is unresponsive to treatment with potent topical corticosteroids.[41,107]

How big a problem is hand eczema?

Hand eczema affects about 10% of the general population and up to 30% of high risk occupational groups, such as healthcare workers and workers in manufacturing industries. Approximately 7% of people with hand eczema are thought to have a severe, chronic form.[108]

How is oral alitretinoin used?

The recommended dosage is 30 milligrams once daily for 12-24 weeks. The dosage can be reduced to 10 milligrams once daily if there are unacceptable adverse effects. The SmPC specifies that if a person still has severe disease after the first 12 weeks, stopping the treatment should be considered. In the event of relapse, further treatment courses may be of benefit. Alitretinoin should be prescribed only by, or under the supervision of, a consultant dermatologist.[41]

What adverse effects have been associated with alitretinoin?

The most frequent adverse effects seen with alitretinoin include headache, dry mouth, anaemia, flushing and erythema. Increases in cholesterol and triglyceride levels have also been observed.[107] Adverse effects are generally dose related and reversible.[107] **Alitretinoin is teratogenic and is contraindicated in women of childbearing potential unless all of the conditions of the Pregnancy Prevention Programme (as outlined in the SmPC) are met.[107]**

Prescribing points: Red / Amber issues

► In Northern Ireland, ciclosporin and azathioprine are on the **amber list** of specialist medicines and as such are initiated on the recommendation of a specialist within a shared care arrangement.

► Alitretinoin is a **red list** agent and should only be prescribed in the hospital setting by a specialist.

► See www.ipnsm.hscni.net

Antihistamines

The most common and least tolerated symptom of atopic eczema is itching. It is usually worse at night and frequently disrupts sleep. Patients with atopic eczema have a reduced threshold for pruritus and its control allows an important improvement in quality of life for both patients and caregivers.

For decades, elevated histamine levels measured in the skin of patients with atopic eczema were considered responsible for inflammation and itching. This led to the concept that antihistamines would be of potential benefit in the management of pruritus.[109] However, recent studies revealed that histamine does not appear to be the only crucial agent inducing pruritus in atopic eczema.[110] Other mast cell mediators such as tumour necrosis factor and interleukins play a more important role in the aetiology of itching. However, if itch is a dominant feature, NICE recommend that clinical experience still supports the use of antihistamines in some situations, although this should not be routine. To assess whether treatment is of benefit, it is worth considering a short trial on an individual basis:

- a 1 to 2 week trial of a **sedating antihistamine** during an acute flare if sleep disturbance has a significant impact.[1,41] This can be repeated during subsequent flares if successful.[1]
- a 1-month trial of a **non-sedating antihistamine** for patients with severe atopic eczema or patients with mild or moderate disease where there is severe itching or urticaria.[1,41] Treatment can be continued, if successful, while symptoms persist, and reviewed every 3 months.[1]

Prescribe **cetirizine, fexofenadine** ***(updated 2016)*** or **loratadine** once daily if a non-sedating antihistamine is required (both are available generically).[11] **Chlorphenamine** is recommended if a sedating antihistamine is required.[11]

Oral corticosteroids

Oral corticosteroids are rarely used except for an acute flare with body surface area involvement over 40%.[111]

What issues should be considered before prescribing an oral corticosteroid in atopic eczema?

Prescribe only a short course of an oral corticosteroid; 30 milligrams of prednisolone taken each morning for one week should be sufficient.[112] Consider referring a patient if:

- More than very occasional use of oral corticosteroids is needed (e.g. more than one course in a year).
- The patient is aged less than 16 years.

It should be explained to the patient that the oral corticosteroid will have an immediate impact on the eczema, but steroids are for exceptional use and cannot be prescribed very often. Advise that the use of topical corticosteroids is NOT NECESSARY while oral prednisolone is being used (although emollients should still be used). However, they should use potent topical corticosteroids on the affected areas when the oral course has finished, as there is a risk of rebound eczema occurring after discontinuation of prednisolone.[23,112] The topical corticosteroids can then be tapered.

Phototherapy

Phototherapy can be considered for the treatment of severe atopic eczema when other management options have failed or are inappropriate and where there is a significant negative impact on quality of life.[1] Treatment should be undertaken only under specialist dermatological supervision.[1]

Dry bandages and medicated dressings including wet wrap therapy

Localised medicated dressings or dry bandages can be used with emollients as a treatment for areas of chronic lichenified atopic eczema in children.[1] They can also be used for short-term treatment of flares (7 –14 days). Such treatments should not be used as first-line treatment for atopic eczema and should only be initiated by a healthcare professional trained in their use.[1]

Wet dressings are useful in children with severe widespread eczema.[113] This is essentially an inpatient procedure but can be used for short periods at home. A water-based emollient is applied all over; a corticosteroid cream is applied to the areas of active eczema. The creams are covered with a double layer of wrapping, the innermost of which is wetted with tepid water. The wet wraps are usually left on overnight.

Complementary therapies

The use of Chinese herbal medicine in the management of atopic eczema became popular a few years ago, but evidence of benefit is mixed.[2] Patients should be informed that the effectiveness and safety of therapies such as homeopathy, herbal medicine, massage and food supplements for the management of atopic eczema have not yet been adequately assessed in clinical studies.[1] In addition:[30,114]

- they should be cautious with the use of herbal medicines and be wary of any 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 in atopic eczema
- liver toxicity has been associated with the use of some Chinese herbal medicines intended to treat eczema.

Patients should inform their healthcare professionals if they are using or intend to use complementary therapies.

Infection & the role of antimicrobials (updated 2016)

Infection is a common complication of atopic eczema. Bacterial infection (commonly with *Staphylococcus aureus* and occasionally with *Streptococcus pyogenes*) can exacerbate eczema and requires treatment with topical or systemic antibacterial drugs along with topical corticosteroids.[11,41] People with atopic eczema (or their carers) should be offered information on how to recognise the symptoms and signs of bacterial infection (weeping, pustules, crusts, atopic eczema failing to respond to therapy, rapidly worsening atopic eczema, fever and malaise).[1] Healthcare professionals should provide clear information on how to access appropriate treatment if infection is suspected.[1]

Topical antimicrobials

Topical preparations for infection are available, including fusidic acid (Fucidin® cream or ointment) and mupirocin (Bactroban® cream or ointment). Some preparations are also combined with a steroid, e.g. fusidic acid and betametasone (Fucibet® cream). However, despite their widespread use, there is no evidence that topical antimicrobials are of any benefit.[116] Given the risk of development of bacterial resistance, they should only be considered for use on single small lesions for short periods of time (maximum two weeks).[1] Mupiricin should be reserved for MRSA infection.[117] Where necessary, topical fusidic acid (cream or ointment) applied three times daily for 5 days is suggested.[117]

Tips for living with eczema (National Eczema Society)

The following simple tips can make a huge difference to the lives of people with eczema and may improve compliance with, what can be, a complicated treatment regime:

- Find the right emollient – patients are more likely to use it frequently.
- Always do a patch test for any new product. Apply the new product to a small area of skin on the inner arm and leave for 24 hours to check for adverse reactions.
- Ensure the patient has small packs of their creams to carry around and apply frequently.
- Large tubs can be kept at home. Pump packs will help to avoid contamination.
- Emollients should be dabbed onto the skin then stroked lightly in the direction of the hair growth.
- If the skin is particularly hot and itchy, it may be helpful to cool creams or lotions in a fridge before applying them to the skin. This cannot be done with most ointments which will become too hard to use.
- Advise patients to have extra supplies of emollients to be kept wherever they may need them, e.g. at work.
- Apply emollient before doing anything which could aggravate the eczema to help act as a barrier and to prevent skin drying out.
- Many people with eczema find that man-made fibres and wool irritate the skin.

Systemic antimicrobials

Systemic antibiotics that are active against *Staphylococcus aureus* and streptococcus should be used to treat widespread bacterial infections of atopic eczema.[1] For adults, guidelines suggest flucloxacillin orally 500 milligrams four times daily for 7 days. Erythromycin 250mg four times a day for seven days or clarithromycin orally 250-500 milligrams twice daily for 7 days[117] are alternatives (for corresponding doses for children see BNF).

How can further episodes of infection be prevented?

Topical preparations should be discarded after the infection has cleared, as pathogens can contaminate them and survive in product packaging; this applies particularly to creams packaged in tubs and tubes, although is probably less with pump-dispensers.[1]

'Bleach baths' (where a mild bleach and water solution is used to decrease bacteria on the skin) now forms part of the standard management of recurrent infection in eczema in local paediatric dermatology units.[120,121]

Infection with herpes simplex and eczema herpeticum

Healthcare professionals should consider infection with herpes simplex (cold sore) virus if a child's infected atopic eczema fails to respond to treatment with antibiotics and an appropriate topical corticosteroid.[1] If a lesion is suspected to be infected with herpes simplex virus, treatment with oral aciclovir should be started even if the infection is localised.[1] Topical corticosteroids should be stopped but antiseptics such as povidone iodine can be used and treatment with topical aciclovir may also be considered.

If eczema herpeticum (widespread herpes simplex virus) is suspected, treatment with systemic aciclovir should be started immediately and the person should be referred for **same-day specialist dermatological advice**.[1] If secondary bacterial infection is also suspected, treatment with appropriate systemic antibiotics should also be started.[1] If eczema herpeticum involves the skin around the eyes, the person should be treated with systemic aciclovir and should be referred for same-day ophthalmological and dermatological advice.[1]

Patients with atopic eczema (or their carers) should be offered information on how to recognise eczema herpeticum.[1] Signs of eczema herpeticum are:

- Areas of rapidly worsening, painful eczema
- Clustered blisters consistent with early-stage cold sores
- Punched-out erosions (circular, depressed, ulcerated lesions) usually 1-3 millimetres that are uniform in appearance (these may coalesce to form larger areas of erosion and crusting)
- Possible fever, lethargy or distress.

Prescribing points: Infected atopic eczema

►NICE advises that people with atopic eczema (or their carers) should obtain new supplies of their usual topical atopic eczema medications after treatment for infected atopic eczema because products in open containers can become contaminated with micro-organisms and act as a source of infection.[1]

►Continue treatment with topical corticosteroids and emollients while taking antibiotics.

►Healthcare professionals should only take swabs from infected lesions of atopic eczema if they suspect micro-organisms other than Staphylococcus aureus to be present, or if they think antibiotic resistance is relevant.[1]

►The Commission on Human Medicines has advised that flucloxacillin has been associated with a very small increased risk of hepatic disorders (hepatitis and cholestatic jaundice). Hepatic reactions may occur up to two months after treatment with flucloxacillin has stopped. Risk factors include treatment for more than 14 days and increasing age. The dose and route of administration do not appear to affect this risk.[115] Avoid flucloxacillin in people with hepatic impairment, or a history of hepatic dysfunction associated with flucloxacillin.

Summary: Managing Atopic Eczema			
	Description	**Managing an acute flare**	**Maintaining skin between flares**
Mild Eczema	• Areas of dry skin • With or without small areas of redness • Infrequent itching	Emollients are the mainstay of treatment for mild flares. Prescribe generous amounts and advise frequent and liberal use. Consider prescribing topical hydrocortisone for areas of red skin. Continue treatment for 48 hours after the flare has been controlled.	
Moderate eczema	• Areas of dry skin • Frequent itching • Redness (with or without excoriation and localised skin thickening)	Advise frequent and liberal use of emollients (i.e. more than usual). A moderate potency topical corticosteroid should be used on inflamed areas. Treatment should be continued for 48 hours after signs and symptoms have resolved.	Encourage the frequent and liberal use of emollients, even during periods when the skin is clear.
Severe eczema	• Widespread areas of dry skin • Incessant itching • Redness (with or without excoriation, extension skin thickening, bleeding, oozing, cracking, and alteration of pigmentation).	• Advise frequent and liberal use of emollients (i.e. more than usual). • A potent topical corticosteroid should be used on inflamed areas. • Treatment should be continued for 48 hours after signs and symptoms have resolved. • Consider prescribing a sedating antihistamine if itching is severe and affecting sleep (maximum 2 week course). • Consider prescribing a short course of oral corticosteroids if there is severe, extensive eczema causing psychological distress.	Avoid trigger factors where possible, and give advice on preventing infection. • Encourage the frequent and liberal use of emollients during periods where the eczema appears controlled, even if the skin is clear. • Prescribe corticosteroids to control areas of skin prone to flares. Consider: a step down approach (prescribe the lowest potency and amount of steroid necessary to control the condition) or, weekend therapy (use of topical corticosteroids on two consecutive days, once a week) • Topical calcineurin inhibitors are a second-line option. • Provide education on recognising the early signs and symptoms of a flare. Should this occur, advise immediate and aggressive treatment, using an agreed stepped-care plan.
Infected eczema	Most common causative organisms are *Staphylococcus aureus* or Streptococcus species. Characteristics include weeping, pustules, crusts, failure to respond to treatment, rapidly worsening eczema, and fever or malaise.[11] If infected eczema co-exists with a flare, concomitant treatment at the appropriate treatment step will be required. See above.	Extensive areas of infected eczema require an oral antibiotic: • Flucloxacillin is the first-line choice. • A macrolide, e.g. clarithromycin, if penicillins are contraindicated. If localised areas of infection, consider a topical antibiotic: • Creams or ointments containing antibiotics can be used as separate products or combined with a corticosteroid. • Topical antibiotics should not be used for longer than 2 weeks.	

Websites

National Eczema Society – www.eczema.org

British Association of Dermatologists – www.bad.org.uk

Primary Care Dermatology Society - www.pcds.org.uk

British Dermatology Nursing Group - www.bdng.org.uk

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COMPASS THERAPEUTIC NOTES ASSESSMENT
Management of Atopic Eczema in Primary Care

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1	**In the management of atopic eczema:**			
	a	Mild atopic eczema can sometimes be managed with topical emollients alone for the most part.	T	F
	b	Early application of topical steroids may prevent a flare from worsening.	T	F
	c	The majority of patients can be managed successfully in primary care.	T	F
	d	Liberal use of topical emollients is the cornerstone of the management of atopic eczema.	T	F
2	**Emollients:**			
	a	Patients can cease to use their emollient when their eczema is well controlled.	T	F
	b	An emollient is applied by rubbing a generous amount of the product into the affected area(s).	T	F
	c	An adult whose both legs are affected by atopic eczema will require about 200 grams of emollient per week.	T	F
	d	Use of emollients in atopic eczema is underpinned by a robust evidence base.	T	F
3	**Topical corticosteroids in atopic eczema**			
	a	The potency of a topical steroid is a measure of its ability cause vasoconstriction rather than its clinical effectiveness.	T	F
	b	Clobetasol is a topical corticosteroid of moderate potency.	T	F
	c	Topical corticosteroids should be applied before emollients so the steroid is not diluted on the skin.	T	F
	d	It is usually adequate to apply a topical corticosteroid once a day.	T	F
4	**Topical calcineurin inhibitors (tacrolimus and pimecrolimus)**			
	a	Tacrolimus is as effective as moderately potent topical steroids.	T	F
	b	Pimecrolimus is as effective as moderately potent topical steroids.	T	F
	c	Tacrolimus can be applied within 10-15 minutes of applying an emollient.	T	F
	d	Pimecrolimus can be applied immediately after applying an emollient.	T	F
5	**Infection and atopic eczema**			
	a	Failure to respond to treatment, pustules, crusts, fever, or malaise may be signs that eczema is infected.	T	F
	b	Use of a topical antimicrobial cream or ointment could be considered for localised areas of infected eczema.	T	F
	c	Once a patient commences an oral antibiotic, their topical corticosteroids should be stopped.	T	F
	d	If infection co-exists with a flare of atopic eczema consider stepping up the topical corticosteroid potency until the flare is controlled.	T	F