Continuing Professional Development

CPD

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60 Second Summary

Eczema often occurs concurrently in patients with other atopic diseases such as asthma, allergic rhinitis and food allergy. Each of these conditions share a common pathogenesis, often presenting together in the same individual and family.

The most important and basic requirement of eczema therapy is emollient use as a moisturiser or soap substitute. They come as lotions, ointments and creams that need to be used several times a day in order to ease dry, itchy skin and to repair the skin barrier.

Patients and even healthcare professionals sometimes can be hesitant to use a topical corticosteroid cream due to the side effects associated with them. The phrases "topical steroid phobia" or "corticophobia" have been used to describe this scenario.

The most common side effect of topical corticosteroid use is skin atrophy, the skin becomes thinner and easily bruised. It is more likely to occur when topical corticosteroids are applied to the face or the flexures.

The risk of experiencing systemic side effects of topical steroids is higher when patients use higher potency products or a long duration of treatment with topical glucocorticosteroids of any potency.

The NICE guidelines recommend that topical steroids for use in atopic eczema should be prescribed for once or twice daily application only. With that being said, it is important to signpost that the recommended dosing pattern and duration of treatment in the product licence of a topical corticosteroid formulation may vary to a number of published clinical guidelines for this disease.

1. REFLECT - Before reading this module, consider the following: Will this clinical area be relevant to my practice?

2. IDENTIFY - If the answer is no, I may still be interested in the area but the article may not contribute towards my continuing professional development (CPD). If the answer is yes, I should identify any knowledge gaps in the clinical area.

3. PLAN - If I have identified a knowledge gap - will this article satisfy those needs - or will more reading be required?

4. EVALUATE - Did this article meet my learning needs - and how has my practise changed as a result?Have I identified further learning needs?

5. WHAT NEXT - At this time you may like to record your learning for future use or assessment. Follow the 4 previous steps, log and record your findings.

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Atopic Eczema: Topical Corticosteroid Therapy and Patient Counselling

The term "Eczema" originates from the Greek word "ekzein" which means "to boil out or to boil over." Eczema (also called 'atopic dermatitis' or 'atopic eczema') is a chronic inflammatory skin condition, characterised by dry itchy skin with eczematous lesions that typically fluctuates between periods of relative quiescence and flares, although some patients may have a chronically active disease.

Eczema often occurs concurrently in patients with other atopic diseases such as asthma, allergic rhinitis and food allergy. Each of these conditions share a common pathogenesis, often presenting together in the same individual and family. 'Atopy' refers to the genetic tendency to produce immunoglobulin E (IgE) antibodies in response to common environmental proteins such as pollen, house dust mite, and food allergens.

The Irish Skin foundation reports that 15-20% of all GP consultations a year are dedicated to investigating skin related concerns. In Ireland, eczema approximately affects 1 in 5 children and 1 in 10 adults. Children can outgrow this condition when branching into adulthood, however they are likely to present with life-long sensitive skin and may experience an exacerbation of symptoms of eczema following lengthy intervals.

The most important and basic requirement of eczema therapy is emollient use as a moisturiser or soap substitute. They come as lotions, ointments and creams that need to be used several times a day in order to ease dry, itchy skin and to repair the skin barrier. When emollient use alone cannot control an eczema flare, a topical steroid may be prescribed for short-term use.

Topical corticosteroids have been a part of the mainstay treatment of atopic eczema for over 40 years. Hydrocortisone was the original topical steroid used to treat eczema and other dermatoses. Now, over 30 additional corticosteroids have been licensed for the treatment of atopic eczema. These formulations are typically used for the treatment of an eczema flare-up when emollient therapy alone has proven to be insufficient. Their anti-inflammatory and anti-proliferative effects deliver a dramatic improvement to an exacerbated patch of skin within a short period of time. They exert their immunosuppressive activity through in a number of different ways including; inhibiting the late phase allergic reaction process by decreasing the density of mast cells, decreasing chemotaxis, lessening the activation of eosinophils, reducing cytokine production and preventing the metabolism of arachidonic acid.

Patients and even healthcare professionals sometimes can be hesitant to use a topical corticosteroid cream due to the side effects associated with them. The phrases "topical steroid phobia" or "corticophobia" have been used to describe this scenario. One of the important roles of pharmacists and pharmacy staff is to counsel patients how to use medication safely. Patient counselling can provide an excellent opportunity to stimulate a positive perception towards the use of topical steroids and advise patients how to use the dispensed preparation safely in order to avoid unwanted side effects.

The side effects of topical steroids

- The side effects of topical corticosteroid use include:
- Thinning of the skin (skin atrophy)
- Stretch marks (striae)
- Easy bruising or tearing of the skin (Senile/solar purpura)
- Enlarged blood vessels (Telangiectasia)
- Localised increased hair thickness and length (Hypertrichosis)
- Pigmentation changes to the skin
- Perioral dermatitis
- Steroid rosacea or acne
- Pustular psoriasis
- Contact dermatitis

- Masking and exacerbation of fungal infections
- Hypercortisolisim (Cushing's syndrome)
- Hypothalamic-pituitary-adrenal axis suppression
- Growth retardation in young children
- Topical steroid withdrawal syndrome

The most common side effect of topical corticosteroid use is skin atrophy, the skin becomes thinner and easily bruised. It is more likely to occur when topical corticosteroids are applied to the face or the flexures. The thin skin on the face and the flexures, allows for a high delivery of product absorption which may progress to cause skin atrophy. When it is possible, patients should be counselled to avoid application of topical steroids to these areas. When it is unavoidable, the SPC of the chosen product can be an excellent source of information for the recommended dose and duration of treatment to avoid unwanted side effects. Cessation of topical therapy to the affected area may lead to a gradual recovery, however this is not guaranteed. The resulting loss of elasticity of the dermis following the prolonged or excessive use of potent steroids could potentially create permanent stretch marks. Pharmacists should counsel patients using topical corticosteroids to avoid their use in the periocular region as they can contribute to the development of cataracts and glaucoma.

Topical corticosteroid preparations vary greatly in potency. There are four different classes of potency: mild, moderately potent, potent and very potent. The potency of a compound is determined by the degree of vasoconstriction a topical corticosteroid can produce and the subsequent inhibition of inflammation that results. The more potent a product is, the greater its' ability to suppress the inflammatory pathway.

The risk of experiencing systemic side effects of topical steroids is greater when patients use higher potency products or a long duration of treatment with topical glucocorticosteroids of any potency. The extended use of high-potency steroids may place the patient at risk of a "rebound" flare-up of eczema after stopping the use of a topical steroid preparation. In some cases, where a higher potency product has been used for an extended period of time, it may be necessary to reduce treatment gradually or switch to a lower potency product to complete the course.

Potency	Medicine	Strength	Licensed product examples
Very Potent	Clobetasol propionate	0.05%	Dermovate 0.05% w/w Ointment® Dermovate 0.05% w/w Cream® Dermovate Scalp Application 0.05% w/v Cutaneous solution® Etrivex 500mcg/g shampoo®
Potent	Betamethasone valerate	0.1%	Betnovate 0.1% w/w Cream® Betacap Scalp Application 0.1% w/w cutaneous solution® Betnovate 0.1% w/w Ointment® Betnovate Scalp Application 0.1% w/v cutaneous solution® Betnovate-C 0.1%/3% w/w Cream® Bettamousse 1mg/g (0.1%) cutaneous foam Eczibet 20mg/g and 1mg/g Cream® (with fusidic acid) Fucibet 20mg/g and 1mg/g Cream® (with fusidic acid) Fucibet Lipid 20mg/g and 1mg/g Cream ® (with fusidic acid)
	Hydrocortisone butyrate	0.1%	Locoid Cream 0.1% w/w® Locoid Lipocream 0.1%w/w Cream®
	Mometasone fumoate	0.1%	Elocon 0.1% w/w Cream® Elocon 0.1% w/w Ointment® Elocon 0.1% w/w Scalp Lotion® Monovo 1mg/g Cutaneous Emulsion® Monovo 1mg/g Cream®
	Betamethasone dipropionate	0.05%	Diprosalic 0.05% and 2% w/w Scalp Application® (with salicylic acid)
Moderate	Betamethasone Valerate	0.025%	Betnovate RD 0.025% w/w Cream® Betnovate RD 0.025% w/w Ointment®
	Clobetasone butyrate	0.05%	Eumovate 0.05% Cream® Eumovate 0.05% Ointment®
Mild	Hydrocortisone Acetate	1%	Fucidin H 20mg/g and 10mg/g Cream® (With fusidic acid) HC45 Hydrocortisone Acetate Cream 1%w/w®
	Hydrocortisone	1%	Calmurid HC 10%/5%/1% w/w Cream® (with urea and lactic acid) Canesten HC 1%w/w and 1%w/w Cream® (with clotrimazole) Cortopin 1% w/w cream® Daktacort 2% w/w and 1% w/w Cream® (with miconazole nitrate) Hydrocortisone 1% w/w cream® Hydrocortisyl 1% w/w skin cream®

The systemic absorption of topical corticosteroids involves the passage of the drug through epidermis, dermis into the blood stream. The extent of percutaneous absorption of these compounds is determined by many different factors that will be discussed throughout this article.

Topical medicinal formulations typically have a slow and poor extent of absorption, topical steroids are no exception to this.

Absorption is directly proportional to the mass or concentration of topical steroid applied to the skin up to a critical point. The rubbing motion increases the surface area of the skin being treated and augments the local blood supply in the area to facilitate systemic absorption. The more frequency the application of a topical corticosteroid treatment is the greater the contact period and overall absorption.

A study was conducted to determine to determine the absorption of a once daily application of hydrocortisone 1% cream. Following a 24 hour period, less than 2% of the steroid was found to be systemically

absorbed. When the absorption of topical corticosteroids is higher, the patient is at a higher risk of experiencing unwanted systemic side effects. The systemic side effects of topical glucocorticosteroids include: hypercortisolism, hypothalamic-pituitary-adrenal axis suppression or growth retardation in young children.

The risk factors for experiencing systemic effects include:

- Higher potency products
- Duration of exposure
- Application to a large surface area of the skin
- The use of the occlusive dressings prior to administration
- The use of the product on intertriginous areas of the skin
- Increased hydration of the stratum corneum
- Use on the face and flexures
- Use on broken or an impaired skin barrier
- Age: Children and infants have a higher rate of absorption than adults

When topical corticosteroids are absorbed into the bloodstream, the steroid is metabolised primarily in the liver by the enzyme CYP 3A4, followed by excretion through the kidneys or as their metabolites in bile. Patients with decreased hepatic or renal function or those who concomitantly use medication that are potent inhibitors of CYP 3A4 are placed at an increased the risk of experiencing the unwanted effects of these products.

The most vulnerable cohort of patients to experience these side effects are children and infants, as they have a higher surface area to body mass ratio than adults. Special care should be taken to avoid the use of potent topical steroids or the prolonged use of topical steroids in these groups. For breastfeeding mothers, the use of topical corticosteroids is not recommended unless the benefits to the mother outweigh the potential risk to the infant. It is not known whether the topical administration of topical corticosteroids in breastfeeding mothers could result in sufficient systemic absorption to produce detectable amounts in breast milk.

What is the correct dose, frequency of application and duration of treatment?

The guidelines recommend that topical steroids for use in atopic eczema should be prescribed for once or twice daily application only. With that being said, it is important to signpost that the recommended dosing pattern and duration of treatment in the product licence of a topical corticosteroid formulation may vary to a number of published clinical guidelines for this disease. For example, The British Association of Dermatologists suggest that topical corticosteroids should be used twice daily for 10-14 days, followed by a "holiday period" of emollients only. In contrast, the product licence of Dermovate 0.05% w/w ointment directs once or twice daily application of the product for up to 4 weeks until an improvement in the condition is noted, followed by a reduction in the frequency of application or switching to a less potent preparation for continuing drug therapy. The license also states that as an alternative Dermovate 0.05% w/w ointment could be used to treat exacerbations of the disease in multiple short bursts of treatment.

Considering the economic impact of eczema

Eczema has the potential to have a detrimental impact on the quality of life of a patient, especially for those with moderate to severe eczema. The cost of topical treatments such as emollients, steroids or immunomodulators can be expensive and repetitive. In the effort of optimising accessibility for to healthcare for patients, pharmacist should consider the economic burden of this disease by taking the relative cost of different preparations of equal potency into account upon dispensing in combination with the amount of product that will be required based upon the product pack size, treatment area, frequency of application and prescribed treatment length.

The fingertip unit system: How much do I need?

A fingertip unit (FTU) is the amount of topical steroid that is squeezed from a tube of topical corticosteroid with a standard 5mm nozzle onto an adult's fingertip (from the end of the finger to the first crease of the finger). One FTU provides a sufficient amount of the preparation to treat an area of the skin twice the size of the flat of an adult's hand with the fingers closed beside one another. The body is divided into five distinct areas and each area, depending on the age of the patient, has a recommended amount of steroid to cover that entire area. Two fingertip units are approximately the equivalent of 1g of the topical steroid. The FTU system can be used to estimate the amount of product required for a course of topical steroid treatment and subsequently, the appropriate product size for the patient.

Choosing the appropriate formulation

The "five rights" of medication use include: the right patient, the right drug, the right time, the right dose, and the right route. There is often more than one formulation available for topical corticosteroid products of equal strength. When dispensing a topical corticosteroid formulation, the nature of the skin or site of the eczema on the skin to be treated can be taken into consideration in order to choose the most appropriate product.

What is the nature of the skin to be treated

- For wet skin (presence of blisters or pus): cream and lotion formulations are most suitable.
- For dry, scaly skin: ointment formulations are most suitable.
- For inflamed skin: cream or ointment formulations, occlusion of the skin several hours before the application of topical corticosteroid formulations may be of benefit. These two treatments should be spaced apart appropriately as occlusion can enhance the systemic absorption of topical corticosteroids by up to 10 times.
- Cracks and sores – treatment with topical corticosteroids on broken skin can increase the risk of systemic side effects. Their use should be avoided where possible and should be completely avoided if there is an underlying skin infection which has not been treated. The use of a moisturiser free from alcohol or acid is more suitable.

What site of skin is to be treated

- Palms and soles: ointment or cream
- Skin fold: Cream or lotion
- Hairy areas: lotion, shampoo, solution, gel or foam

Patient counselling for topical corticosteroid use

Patients should be educated about the side effects of topical steroid formulations to highlight the importance of using these products correctly. As the saying goes, knowledge is power, it can help patients and healthcare professionals alike to overcome the barriers of topical steroid phobia. A counselling session should include the steps patients can take to overcome or avoid the risks of experiencing the side effects of topical corticosteroid preparations. These counselling points may include:

1. Wash your hands before the handling or application of a topical product to the skin.

Area of skin to be treated (adults)	Size	FTUs each dose (adults)
A hand and fingers (front and back)	2 adult hands	1 FTU
Front of chest and abdomen	14 adult hands	7 FTUs
Back and buttocks	14 adult hands	7 FTUs
Face and neck	5 adult hands	2.5 FTUs
An entire arm and hand	8 adult hands	4 FTUs
An entire leg and foot	16 adult hands	8 FTUs

2. A patch test should be recommended to all patients before using any new topical product on their skin. A pea sized amount of the new ointment, lotion or cream should be applied to the pulse of a wrist or the crook of an elbow for 24-48 hours without washing. After this time period has lapsed, ensure there are no signs of an allergic reaction in the specified area. Typical signs of an allergic reaction include; redness, itchiness, pain, flaking and/or a rash. If any traces of an allergic reaction have developed on the skin, the patient should be counselled to avoid using this new product.

3. Only apply a topical corticosteroid preparation to the affected area of the skin at the frequency prescribed by your doctor for a specified length of time.

4. Explain the FTU system and how this can be used by the patient to apply the appropriate amount of steroid on the affected area of the skin.

5. Apply your regular emollient or moisturiser 30 minutes after the application of the topical corticosteroid.

6. Avoid the use of this product on areas of the body where the skin is thinner and may absorb more product, potentially resulting in unwanted side-effects. This may include the face, the genitals, the skin folds, broke, raw or thick skin, areas of the skin that rub together i.e. beneath the breasts or between the buttocks or thighs.

7. Once the inflammation of the skin has come under control following the use of a topical corticosteroid, stop using this product, in line with the instructions given to you by your doctor. If the inflammation of the skin has not resolved by the end of a treatment course, consult your doctor for the next step.

8. Some topical products may contain flammable ingredients such as paraffin. Patient's using products that contain flammable ingredients should be directed to avoid smoke or naked flames due to the risk of severe burns. Fabric such as clothing, bedding, dressings that have been in contact with this product can burn more easily, making them a serious fire hazard. When using these products, washing clothing and bedding regularly should be recommended but washing may not totally remove the absorbed product.

9. Wash your hands after the handling or application of a topical product to the skin.

New treatments on the market for atopic dermatitis: Dupixent® (dupilumab)

Dupilumab is a fully human monoclonal antibody that acts against interleukin (IL)-4 receptor alpha to inhibit IL-4/IL-13 signalling, produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology. This product has a number of therapeutic indications including; atopic dermatitis, asthma and chronic rhinosinusitis with nasal polyposis (CRSwNP). It may be of interest for patients who have tried and tested the topical corticosteroids and immunosuppressants for their atopic dermatitis, receiving poor results.

On the 2nd of March 2021, The Medication Management Programme (MMP) released a Managed Access Protocol (MAP) to provide conditional reimbursement for the confined use of Dupixent® in patients aged 12 years and over for systemic treatment of moderate-to severe atopic dermatitis. Eligible applicants include patients who have previously tried immunosuppressant therapies which have failed, were poorly tolerated or otherwise contraindicated. The reimbursement for this new product can be applied for by the prescriber on an individual patient basis. As part of the application process, the prescriber must confirm the patient is receiving best supportive care for atopic dermatitis, the patient's current Eczema Area and Severity Index (EASI) score (equal to 16 or more) and the Children's Dermatology Life Quality Index (CDLQI) score or Dermatology Life Quality Index (DLQI) score.

The product is available as a pre-filled pen in two different strengths: Dupixent® 200 mg solution for injection in pre-filled pen and Dupixent® 300 mg solution for injection in pre-filled pen. The recommended dosing schedule as outlined by the product's SPC is listed in the table below.

Following a 16 week treatment period, the patient should notice a dramatic improvement in their skin condition. An adequate response may be measured as; a minimum of 50% reduction in the EASI score or an at least a 4-point reduction in the DLQI score recorded at the beginning of treatment. The NICE guidelines and the MAP recommend that dupilumab should be stopped at 16 weeks if a patient's atopic dermatitis has not responded adequately to treatment.

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Patient Population	Initial dose	Subsequent doses (every other week)
Adults	600mg	300mg
Adolescents (age 12-17 years)		
>60 years	600mg	300mg
<60 years	400mg	200mg