A RESEARCH REVIEW™
PRODUCT REVIEW

Methylprednisolone aceponate 0.1% ointment/cream [Advantan®]

Making Education Easy 2021

About the expert

Dr Jennifer Pilgrim
MB ChB (Otago), FRACP

A graduate of Otago University, Dr Jennifer Pilgrim undertook post-graduate training at Wadsworth VA-UCLA, California and St John's Hospital, London. She practices as a specialist dermatologist at Bowen Hospital, Wellington and at Kew Hospital in Invercargill. Jennifer has extensive experience in a wide range of dermatological areas including paediatric and adolescent dermatology, minor surgery, tattoo removal, vulval disorders and some cosmetic procedures.

Abbreviations used in this review
DLQI = Dermatology Life Quality Index
EASI = Eczema Area and Severity Index
FTU = fingertip unit
HR = hazard ratio
IV = intravenous
MPA = methylprednisolone aceponate
NICE = National Institute for Health and Clinical Excellence
TIX = Therapeutic Index

ABOUT RESEARCH REVIEW

Research Review is an independent medical publishing organisation producing electronic publications in a wide variety of specialist areas. Product Reviews feature independent short summaries of major research affecting an individual medicine. They include a background to the particular condition, a summary of the medicine and selected studies by a key New Zealand specialist with a comment on the relevance to New Zealand practice. Research Review publications are intended for New Zealand medical professionals.

New Zealand Research Review subscribers can claim CPD/CME points for time spent reading our reviews from a wide range of local medical and nursing colleges. Find out more on our **CPD page**.

Privacy Policy: Research Review will record your email details on a secure database and will not release them to anyone without your prior approval. Research Review and you have the right to inspect, update or delete your details at any time.

RESEARCH REVIEW™
Making Education Easy — Since 2006

This review discusses the evidence in support of the use of methylprednisolone aceponate (MPA) 0.1% ointment/cream [Advantan®], a fourth-generation, non-halogenated topical corticosteroid approved for use in New Zealand for the management of eczema. MPA exhibits a fast and effective itch relief profile in infants and children with atopic eczema. MPA has the advantage of once-daily dosing, providing benefits in terms of patient compliance, and has an optimised efficacy/safety profile with minimal local or systemic adverse effects. This agent is suitable for use in adults and children and also for short-term use on the face. The choice of 2 topical MPA formulations allows tailored treatment for a variety of eczema types and locations. MPA 0.1% ointment/cream is fully funded. This review is sponsored by an educational grant from Leo Pharma Limited.

Atopic eczema

Atopic eczema (also known as atopic dermatitis) is a chronically relapsing, intensely pruritic inflammatory skin disease that favours flexural skin and is characterised by periods of acute worsening ("flares") alternating with periods of relative quiescence following treatment.[1,2] The condition typically develops in childhood, with approximately 80% of cases developing before the age of 5 years.[3] In the acute phase of the disease, erythema, vesicles, papules, crusts and weeping may be present, while in the chronic phase, lichenification and scaling of the skin are the predominant features.[4]

Prevalence

The overall prevalence of atopic eczema is 2-5%, with a prevalence of approximately 10-20% in children and young adults, thus making it the most common skin disease.[1,5-9] A survey of NZ children and adolescents between 2001 and 2003 revealed current eczema prevalence rates of 15% for children aged 6-7 years and 8.8% for adolescents aged 13-14 years, with corresponding rates for severe eczema of 1.8% and 1.3%, and for 'eczema ever' of 31.5% and 26.1%, respectively.[10] The survey also revealed that Māori and Pacific children and adolescents had a greater prevalence of severe eczema than European/Pakeha.[10]

Diagnosis

The diagnosis of atopic eczema is a clinical one based on itching, redness and often skin crease involvement, and takes into account the atopic stigmata of the condition.[1,5] The UK National Institute for Health and Clinical Excellence (NICE) guidelines recommend specific criteria for diagnosing atopic eczema in children.[11] The guidelines, which have taken into account all available severity tools (including the Eczema Area and Severity Index [EASI]), recommend that healthcare professionals adopt a holistic approach when assessing the severity of a child's atopic eczema (**Table 1**).[11,12] This assessment should guide treatment decisions.

Table 1: Assessing the severity of atopic eczema (Adapted from UK NICE guidelines[11])

Skin/physical severity		Impact on quality of life and psychosocial wellbeing
Clear	Normal skin, no evidence of active atopic eczema	No impact on quality of life
Mild	Areas of dry skin, infrequent itching (with or without small areas of redness)	Little impact on everyday activities, sleep and psychosocial wellbeing
Moderate	Areas of dry skin, frequent itching, redness (with or without excoriation and localised skin thickening)	Moderate impact on everyday activities and psychosocial wellbeing, frequently disturbed sleep
Severe	Widespread areas of dry skin, incessant itching, redness (with or without excoriation, extensive skin thickening, bleeding, oozing, cracking and alteration of pigmentation)	Severe limitation of everyday activities and psychosocial functioning, nightly loss of sleep

Treatment options

As with other chronic conditions, the management plan for atopic eczema requires a multidisciplinary approach directed at long-term stabilisation, the prevention of flares and the avoidance of adverse effects.[5] International guidelines recommend that a stepped approach to management be employed, with treatment tailored to the severity of the condition (**Table 2**).[11-13] Treatment should be stepped up or down according to clinical response. Always use emollients as maintenance, even when the skin is clear. Add other treatments as required, with specialist advice where recommended (see page 5 – 'When should I refer to a specialist dermatologist?') Patients and their caregivers should be given advice on the quantities and frequency of treatments to be used and informed about recognising symptoms of bacterial and viral infection. A useful personal eczema management plan for patients with eczema is available from: http://www.dermnetnz.org/dermatitis/pdf/eczema-management-plan.pdf

Table 2. Treatment options for atopic eczema recommended in the NICE clinical guidelines (Adapted from UK NICE clinical guidelines[11])

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
	Systemic antihistamines**	Phototherapy
		Systemic therapy including antihistamines**

* Pimecrolimus cream [Elidel® is the only topical calcineurin inhibitor approved for use in NZ for atopic eczema. The NICE guidelines state that oral antihistamines should not be routinely used in the management of atopic eczema in children, but a 1-month trial of a non-sedating antihistamine should be offered to children with severe atopic eczema or those with mild or moderate eczema where there is severe itching or urticaria; if treatment is successful it can be continued while symptoms persist. A 7-14 day trial of an age-appropriate sedating antihistamine can be offered to children aged over 6 months during acute flares where sleep disturbance is a significant issue, and if successful, can be repeated during subsequent flares.

Emollient therapy is crucial for maintaining skin hydration and improving skin barrier function, and is ideally used at least twice daily.[5] The use of emollients has been shown to significantly reduce the amount of topical corticosteroids used in infants with atopic eczema.[14] The NICE guidelines recommend that where emollients and other topical products are used at the same time of day, they should be applied one at a time with several minutes between applications.[11] Guidelines from Starship Child Health, recommend that corticosteroids be applied first and emollients afterwards.[15]

Topical corticosteroids

Mild atopic eczema may be managed sufficiently with emollients, but topical corticosteroids are required for moderate-to-severe symptoms resulting from acute flares and possibly for maintaining remission (when used intermittently). Topical corticosteroids, which are divided into four groups according to their strength (Class 1-4, **see Table 3**), have been the gold standard in the treatment of atopic eczema for more than five decades.

The topical corticosteroids shown in **Table 3** are available in NZ (some are available in combination with antibacterial or antifungal agents). Creams may be more suitable if the problem area is weeping, while ointments are recommended for drier areas. Lotions are more suitable for hairy areas. Continuous use for less than 1 month is considered short-term use, while use for greater than 3 months is considered long-term use.

In treating atopic eczema, the weakest possible steroid that will be effective should be used. However, at times it may be necessary to use a more potent corticosteroid to clear the skin. Speed of anti-pruritic effect should also be considered when choosing an appropriate corticosteroid, as early anti-pruritic interventions to disrupt the itch-scratch cycle are imperative, especially in children who find it much more difficult not to scratch than adults.[16,17] Short 'bursts' of treatment with a potent topical corticosteroid may be more effective than a longer treatment with a mild preparation.[18] These agents are considered to be effective and safe when used correctly.[1]

Table 3. Topical corticosteroids grouped according to their potency

Class	Potency	Corticosteroid
Class 1	Very potent	Clobetasol propionate Betamethasone dipropionate*
Class 2	Potent	Methylprednisolone aceponate Mometasone furoate Betamethasone valerate Betamethasone dipropionate Diflucortolone valerate Hydrocortisone 17-butyrate
Class 3	Moderate	Clobetasone butyrate Triamcinolone acetonide
Class 4	Mild	Hydrocortisone

*In optimised vehicle

Therapeutic index

MPA has been awarded an excellent therapeutic rating by the German Society of Dermatology which has published a Therapeutic Index (TIX) for several topical corticosteroids.[19] The TIX describes the balance between the potency of a topical corticosteroid and its adverse effects (see **Table 4**).

Table 4. The benefit-to-risk ratio as assessed by the Therapeutic Index (TIX) for a selection of Class 1 and 2 topical corticosteroids (Adapted from Ruzicka et al 2006)[16,19]

Topical corticosteroid	Efficacy score	Toxicity score	TIX rating
Methylprednisolone aceponate	**18.0**	**9.0**	**2.0**
Mometasone furoate	18.0	9.0	2.0
Clobetasol propionate	27.0	17.0	1.5
Hydrocortisone butyrate	14.0	10.0	1.4
Betamethasone valerate	18.0	15.0	1.2

Duration of topical corticosteroid use

Mild atopic eczema may respond to low-potency topical corticosteroids within a few days, with symptoms clearing within 1-2 weeks.[20] Moderate disease may require more potent topical corticosteroids, and these may need to be used for several weeks to clear symptoms.[20] Severe disease may only partially respond to potent topical corticosteroids after several months.[20]

Consider 'weekend therapy'

NICE guidelines suggest considering treating problem areas with topical corticosteroids for two consecutive days per week (often referred to as 'weekend therapy') in order to prevent flares in children experiencing 2-3 flares per month (this strategy should be reviewed for effectiveness within 3 to 6 months).[11]

Treatment compliance issues

Poor compliance with therapy is a major issue in treating patients with atopic eczema. Interestingly, the strongest predictor of treatment compliance is a good patient-doctor relationship.[12,21,22] Furthermore, a survey has shown that steroid phobia is a major contributor to poor treatment compliance and while the majority of patients receive topical corticosteroids to treat flares, 49% are concerned about using these agents.[23,24] Therefore, it is crucial that patients and their families are provided with simple, clear, unambiguous information on the management of this disease and are adequately educated regarding the risks and benefits of corticosteroid use.[8,23,25] Do not advise them to 'use sparingly' as this creates confusion and may result in inadequate use and poor symptom control.[18] Using topical corticosteroids that are dosed once daily as opposed to twice daily provides benefits in terms of patient compliance. One of the major predictors of poor compliance is caregiver misconception and concern regarding the use of topical corticosteroids in children, and clinicians should be familiar with typical concerns and what the evidence says in this regard (see **Table 5)**.[18]

Table 5. Caregiver misconceptions and concerns associated with the use of topical corticosteroids in childhood eczema and evidence-based responses [Adapted from Bpac 2017[18]]

Misconception or concern	What does the evidence say?
Topical corticosteroids should only be used for severe symptoms	Topical corticosteroids can and should be used for all severities of eczema, including mild symptoms
Regular use of topical corticosteroids causes adverse effects such as skin thinning	Topical corticosteroids are unlikely to cause skin thinning or other long-term harm if used appropriately
The percentage of topical corticosteroid is its strength	The % value of different formulations of topical corticosteroids does not indicate their potency, e.g. 1% hydrocortisone is a weaker formulation than hydrocortisone butyrate 0.1%
Corticosteroids are confused with anabolic steroids	Clarify the meaning of the word "steroid" - "steroid" is a classification used for a wide group of hormones and medicines with different functions, including corticosteroids and anabolic steroids
Topical corticosteroids should not be applied to broken skin	The consensus of New Zealand and Australian paediatric dermatologists is that topical corticosteroids can be applied to areas of eczema with broken skin
Topical corticosteroids are not "natural"	Corticosteroids mimic the effects of hormones produced by the adrenal glands, despite being "man-made"

About methylprednisolone aceponate

MPA 0.1% topical ointment or cream [Advantan®] is a fourth-generation, non-halogenated corticosteroid, used for the topical management of eczema in both adults and children.[26] The agent is fully funded at NZ$4.46 per 15g tube. Clinicians may prescribe as many 15g tubes as deemed necessary for up to 3 months of treatment (see Prescribing Advantan® section, page 4) for advice on determining the amount required).

Contraindications

Contraindications to the use of MPA include most viral diseases (e.g. varicella/herpes zoster, vaccinia) and the presence of tuberculous or syphilitic processes and post-vaccination skin reactions in the area to be treated.[26]

Pharmacological properties

MPA has a methyl group at C-6 and both of the alcohol residues attached to the five-membered ring (a propionate group at C-17 and an acetate group at C-21) are esterified.[4] The methyl group at C-6 is associated with a high intrinsic activity (drug-receptor binding), while the lipophilic diester grouping allows for good penetration into the stratum corneum.[27] The degree of penetration depends on the state of the skin and the conditions of application (open/occlusion).[26] Within the epidermis and dermis, MPA is rapidly metabolised by esterases to the active metabolite methylprednisolone-17-propionate, which binds 3-fold more strongly to glucocorticoid receptors than MPA.[4] Inflamed skin, with its higher concentration of esterases has been found to concentrate this active metabolite.[4] Within the skin, methylprednisolone-17-propionate is converted to methylprednisolone-21-propionate, which is hydrolysed and rendered relatively inactive.[4] Glucuronic acid rapidly inactivates any methylprednisolone-17-propionate entering the systemic circulation.[4] These metabolites are eliminated via the kidneys with a half-life of approximately 16 hours.[26]

Unlike other potent corticosteroids, MPA does not have a halogen at C-9 and this feature allows for the high degree of dissociation between topical and systemic effects; non-halogenated corticosteroids appear to preserve the function of the circadian rhythm of cortisol secretion even when used on large areas (40-60% of the skin surface).[26-28]

Dosage and administration[26]

One gram of cream or ointment contains 1mg (0.1%) MPA. The agent is for external topical use only. Generally, the formulation deemed most appropriate to the skin conditions is applied thinly once daily and should be used for no more than 12 weeks in adults and no more than 4 weeks in children.

- Advantan® cream has a high water content and a low fat content and is particularly suitable for acute and subacute weeping stages of eczema, and for use on exposed or hairy parts of the body.
- Advantan® ointment has balanced proportions of fat and water and is used where skin is very dry and not in a weeping state.

When being applied to the face, the agent should only be used for short periods and must not come into contact with the eyes. If signs of hypersensitivity occur the agent should be discontinued. Use in children should be limited to the least amount required for therapeutic effect. Prolonged use in intertriginous areas is undesirable. If fungal or bacterial infections are present, additional specific therapy is required.

NZ Bpac recommendations point out that underuse of topical corticosteroids is far more common than overuse.[29] They recommend using 'fingertip units' (FTUs) as a measure for dosing, with one FTU being the amount of product that can be squeezed onto the top third of an adult finger (approximately 2.5cm) and equating to approximately 0.5g.

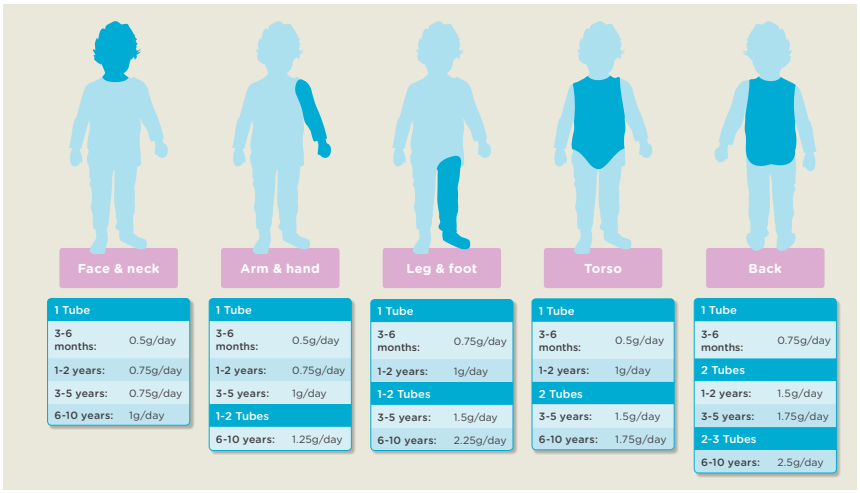
Methylprednisolone aceponate 0.1% ointment/cream [Advantan®]

How much should I prescribe?

The graphic below has been been designed as a convenient Advantan® dosing guide to help determine an individual's needs based on the extent of their skin disease. The individual tubes should not be dispensed into a single container as it has an unknown effect on the efficacy and safety of the product.

Optimal dosing guide for children

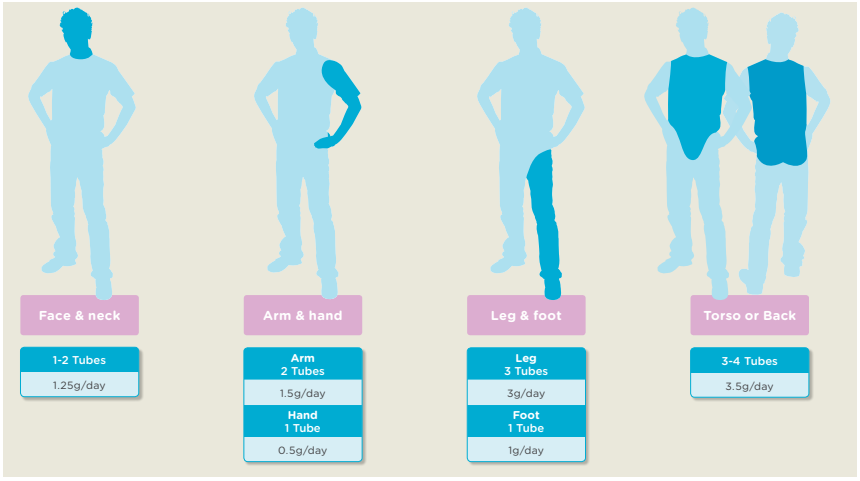
2 week supply



As an example, a 6-10-year-old child who has the ointment or cream applied to their torso once daily, will require 1.75g per day (3.5 FTUs per day), equating to 12.25g of product per week. For this child, it would be appropriate to prescribe two tubes of Advantan® for 2 weeks supply or one tube of Advantan® per week for up to 4 weeks.

Optimal dosing guide for adults

2 week supply



An adult patient would require 4g per day (8 FTUs) to cover their leg and foot once daily and would thus require 28g of product per week, or four tubes of Advantan® for a 2-week course, or 2 tubes per week for up to 12 weeks; these amounts are for one limb and so would need to be doubled for a bilateral presentation.

Evidence for the use of methylprednisolone aceponate for atopic eczema

Efficacy data

Methylprednisolone aceponate, dosed once daily, is considered to be a safe and effective acute and maintenance treatment choice for children (including infants) and adults with moderate-to-severe atopic eczema requiring fast and effective relief from their symptoms.[4,16,27,28,30-32] Its onset of activity is very rapid, with 50-80% of patients experiencing complete or distinct symptom improvement within 1 week of starting treatment and 90% experiencing such improvement within 3 weeks.[4] This is also true for patients with severe symptoms, who have been shown to experience fast and effective relief from reddening and itching.[5]

Fast relief from symptoms including itch

A study demonstrated relief of symptoms (especially itching and redness) within 2-3 days in 65% of children receiving MPA 0.1% and significant improvement or cleared symptoms by the end of treatment in 97% of patients.[33] It is clear from multiple other studies, that treatment with MPA results in very rapid symptom improvement, with 50-80% of patients with atopic eczema experiencing complete or distinct improvement within days of starting treatment and the majority of patients achieving complete remission within 2-3 weeks.[4,17]

Single arm studies

A Swiss multicenter phase IV study investigating the use of MPA in 830 eczema patients ranging in age from 6 months to 97 years (average duration of treatment 5 weeks) demonstrated symptom cure or significant improvement in 87.4% of patients, with a response that was classified as fast or very fast onset in 79.4%.[32]

In a large observational trial involving 408 dermatologists and 2059 patients aged between 2 months and 87 years (mean age 37.6 years) with acute and chronic eczema (atopic eczema 38.6%, acute contact eczema 26.7%), treatment with MPA ointment or cream resulted in 74% of patients exhibiting distinct improvement in their symptoms after 5.5 days of treatment and approximately 40% being completely symptom free after 12.5 days.[34]

The symptoms, reddening and itching, rated as mainly severe or moderately severe at baseline, showed distinct regression, with the percentage of patients showing severe reddening decreasing from 48% to 1% and those with moderate reddening decreasing from 42% to 7%. Furthermore, the percentage of patients with severe itching decreased from 57% to 1% and those with moderate itching decreased from 31% to 5.5% following treatment.

Head-to-head trials in children and adults

Several comparator trials have demonstrated that MPA compares favourably with other corticosteroids in its class and to tacrolimus.[4,16,27,28,30-32]

The clinical efficacy of 0.1% MPA cream and ointment once or twice-daily for a maximum of 21 days was compared with that of 0.25% prednicarbate (not available in NZ, but similar in potency to 0.1% hydrocortisone) in two double-blind, multicentre clinical studies performed in children aged ≤14 years suffering from atopic dermatitis.[31] In these trials, there was no significant difference in response rates between MPA (once daily 96.3%; twice daily 97.4%) and prednicarbate (once daily 98.1%; twice daily 100%) in the efficacy trials.

The efficacy of once- or twice-daily 0.1% MPA cream or ointment was compared to that of twice-daily betamethasone valerate cream in six, multicentre, double-blind controlled trials involving a total of 1723 eczema patients (mean age approx. 45 years) over a period of up to 3 weeks.[35] All regimens were found to be equally effective; >90% of patients were asymptomatic (erythema, vesiculation, weeping, crusting, scaling, lichenification) or greatly improved after 3 weeks. MPA in cream and ointment formulations performed equally well and a once-daily application of MPA was equally effective as a twice-daily application of MPA or betamethasone valerate.

Comparing the efficacy of MPA 0.1% ointment once-daily (n = 129) with that of the calcineurin inhibitor tacrolimus 0.03% ointment applied twice-daily (n = 136) in children and adolescents with severe-to-very severe flares of atopic eczema, a randomised, double-blinded comparative study revealed a successful therapy rate in both groups of 67%.[30] Notably, an approximate 70% reduction in itch was seen with MPA after 7 days and once-daily MPA was superior to twice-daily tacrolimus for EASI, itch and sleep measures. The differences between MPA and tacrolimus were statistically significant and consistently in favour of MPA.

For use in infants

MPA is approved for use in infants, because of its effectiveness and safety profile.[36] Studies of MPA in the paediatric population have involved infants as young as 4-6 months of age, with successful responses and very good tolerability.[31,32] One such study, involving 20 children under 3 years of age treated with once-daily MPA 0.1%, exhibited a response (complete healing or distinct improvement) in 100% of patients.[31]

For use on the face

The tolerability of MPA cream and/or ointment once daily for a maximum of 4 weeks was examined in a multicentre, post-marketing surveillance study in 575 patients (aged 3 months to 87 years) with eczematous dermatitis of the face (including 46.4% atopic dermatitis, 24.6% contact eczema, 15% seborrhoeic eczema and 1.7% photodermatoses) and revealed no reports of perioral dermatitis or atrophy.[37] MPA was generally well tolerated, no skin infections were reported and "very good tolerability" was experienced by 86% of patients and 89% of doctors. MPA demonstrated excellent efficacy and doctor's assessment at the end of therapy reported symptoms to be "asymptomatic" in 66.3% of patients, with "distinct improvement" in 32.9%.

For maintenance 'weekend therapy' during remission

The long-term efficacy (16 weeks) of MPA 0.1% cream twice-weekly, in addition to an emollient was examined in a multicentre, randomised, double-blind, controlled study involving 249 patients who had been treated with MPA alone to stabilise an acute severe or very severe flare of atopic dermatitis.[38] Time to relapse (primary endpoint) of atopic dermatitis was longer in the MPA group than in the emollient only group, and the probability of being relapse free at 16 weeks was 87.1% in the MPA group versus 65.8% in those receiving emollient only. MPA twice-weekly induced a 3.5-fold lower risk of relapse than emollient alone (HR 3.5, 95% CI 1.9-6.4; $p < 0.0001$). MPA was also superior to emollient for all other efficacy endpoints (relapse rate, disease status, patient's assessment of intensity of itch, the EASI, Investigator's Global Assessment score, affected body surface area, Dermatology Life Quality Index [DLQI] and children's DLQI, patient's and investigator's global assessment of response and patient's assessment of sleep quality). Both treatments were well tolerated, with the frequency of adverse events with the emollient alone being higher than with the study drug (24% vs 15%); none of the adverse events reported during the maintenance phase were considered to be due to the study drug, and no serious adverse events were reported.

The findings of this study demonstrated that the combination of MPA with emollient provides an effective and safe maintenance treatment regimen to control atopic eczema in patients ≥12 years of age. In particular, the improvement in itching and the reduced risk of relapse may have important implications for physicians when considering strategy options for patients who need long-term treatment. NICE guidelines for the management of atopic eczema recommend the continued use of a topical corticosteroid (1-2 times per week) after disease stabilisation, to previously involved skin in order to reduce subsequent flares or relapses.[11]

Safety data

The safety profile of methylprednisolone in terms of local tolerability and systemic effects is well documented.[16] The overall incidence of adverse effects associated with MPA is approximately 5% and this agent exhibits a low incidence of systemic adverse effects.[4] When adverse effects do occur they are almost always mild-to-moderate in severity and do not usually result in the discontinuation of treatment.[4] The most commonly seen adverse effects are mild erythema, dryness and a sensation of burning, scaling and rash.[4,32]

A number of studies have demonstrated that the incidence and severity of adverse effects with MPA are similar to those of less potent corticosteroids and significantly lower than those of other corticosteroids in the same class.[4] One such study was undertaken by Kecskés comparing MPA and mometasone furoate.[39] Their study revealed equal anti-inflammatory activity of the two agents and similar cortisol suppression, but significantly fewer local adverse effects with MPA than mometasone furoate.

Regarding potential systemic effects, studies in all age groups (including infants) have revealed minimal effects of suppression of the hypothalamic-pituitary axis after up to 4 weeks of treatment.[16] Furthermore, the use of topical MPA in infants and children aged 6 months to 10 years (mean age 25 months) with atopic eczema and between 5% and 20% involved skin surface area, showed no changes in plasma cortisol values after 7 days of treatment.[31] An additional trial compared the systemic safety (endogenous cortisol production after 7 days application over a large skin area [mean 12% of skin surface]) of 0.1% MPA and 0.1% hydrocortisone 17-butyrate and found that cortisol levels were unchanged after 7 days of exposure to either MPA or 0.1% hydrocortisone 17-butyrate.[31]

The favourable safety profile of MPA renders it a suitable agent for use in facial eczema.[37] The development of perioral dermatitis is unlikely if use of the agent beyond clinical healing is avoided.[37]

When should I refer to a specialist dermatologist?

- Immediate (same-day) if eczema herpeticum is suspected
- Urgent (within 3 weeks) if severe eczema is unresponsive to 2 weeks of optimal topical therapy
- Paediatric patients in whom the diagnosis is uncertain, the eczema is severe with frequent flares and/or it is not responding to appropriate treatment, facial atopic eczema is present and not responding to appropriate topical therapy, there is severe psychosocial impact, the family needs guidance and support for management of the child's eczema, and for patients where employment is at risk
- If patients require oral corticosteroids on a regular basis (more than two courses yearly) or if large amounts of topical corticosteroids are being required and the patient is not compliant with ancillary measures (medicated baths, emollients).

Methylprednisolone aceponate 0.1% ointment/cream [Advantan®]

THE PAEDIATRIC PERSPECTIVE WITH REMARKS *by Georgina Harvey*

Atopic dermatitis (AD), or eczema, is a common disease in NZ children, with a prevalence of 15-20%.[40] The consequences of AD in children can be significant, with severe AD impacting on a child's daily ability to learn and develop, further exacerbated by sleep disturbance due to nocturnal itch. Children may feel self-conscious regarding their skin changes, and may require time off school due to severe AD flares. The necessary skin care required as treatment of AD is generally performed by parents; the on-going, and at times challenging, nature of this can be time-consuming and stressful.

It is essential that AD is diagnosed and managed appropriately to reduce the consequences of this disease. This involves minimising exposure to potential irritants and allergens, regular application of emollients and suitable use of topical corticosteroids, in addition to prevention and treatment of secondary infection.

Given the increased skin surface area to volume ratio in infants and young children compared to adults,[28] consideration of the potency and quantities of topical corticosteroids is required, to minimise the risk of systemic corticosteroid toxicity (although this is extremely rare).

MPA 0.1% is a fourth-generation topical corticosteroid, which has been shown to have a low side effect profile for its potency. The active metabolite of MPA has a high binding affinity for the corticosteroid receptor; upon completion of binding, the active metabolite is rapidly deactivated and excreted, leading to low systemic exposure to MPA and its metabolite.[17] It is suitable to use as treatment of moderate-severe flares of AD. However, like all potent topical corticosteroids, care should be taken when using MPA on the face in children due to the risk of periorificial dermatitis; for this reason, short courses only are recommended for treatment of facial AD. When MPA is used to treat AD on the body and limbs, daily application to settle the flare is recommended, followed by a weaning schedule, or reduction in steroid potency to an alternative less-potent agent.

From a practical perspective, prescribers should be mindful of the size of tubes of MPA. In New Zealand, MPA is available in 15g tubes. Thus, when prescribing MPA to treat large surface areas, it is important to prescribe adequate quantities, or consider an alternate topical corticosteroid that is available in larger tube sizes.

In summary, MPA can be considered for treatment of moderate-severe AD in children, in conjunction with other AD management strategies.

Dr Georgina Harvey MBBS, FACD

Georgina is a Fellow of the Australasian College of Dermatologists, who has recently undertaken a Fellowship in Paediatric Dermatology at Starship Hospital. She is currently completing her FRACP Dermatology training in Auckland.

CONCLUDING COMMENTS *by Jennifer Pilgrim*

Managing atopic eczema requires a multifaceted approach. Simple measures including regular emollients of acceptable consistency, medicated baths and avoidance of harsh soaps are an integral part of this. The role of bacterial colonisation in both chronic and particularly acute eczema flares is often poorly recognised. It must be considered and managed appropriately.

Systemic antihistamines may also be invaluable in reducing repeated scratching. Both sedating and non-sedating medications may be required. In spite of these measures, topical corticosteroids will be required in many patients for acute situations as well as maintenance therapy.

Topical corticosteroid therapy has been shown to be effective and safe. However, it is essential that the steroid selected is appropriate for the age of the patient and the sites being treated, that guidelines for the quantity and duration of use are provided, as are sufficient quantities. Reassurance on the safety of the steroid being used is essential and realistic time frames for benefit must be provided. The need for ongoing management must be emphasised and must be made both simple and achievable.

MPA has been shown to be an effective and safe product in both cream and ointments formulations. Both formulations have a consistency that makes application easy and, importantly, acceptable to patients. MPA has been shown to be effective in a wide range of age groups with differing types of eczema. It has a relatively rapid onset of effect and can be used for acute flares as well as maintenance therapy. The additional benefit of once-daily application increases compliance, which is essential in managing any long-term medical condition.

TAKE-HOME MESSAGES

- MPA is a useful agent in the management of atopic eczema in paediatric and adult populations
- MPA has a high efficacy to safety ratio compared with topical corticosteroids of similar potency
- MPA has a rapid onset of itch relief, to assist in breaking the itch-scratch cycle
- The increased compliance with once-daily, as opposed to twice-daily application, is also significant (time taken to apply products repeatedly is acknowledged by patients as a reason for treatment failure)
- Twice-weekly application of MPA 'weekend therapy' has been shown to reduce the risk of flare development
- Patients are often reluctant to use ointment-based products as they are sticky, harder to apply (so more time consuming) and leave greasy residue on clothing and bedding
- Ointments may be superior in terms of hydration and efficacy
- MPA ointment has the property of an ointment, but the cosmetic acceptability and ease of application of a cream.

REFERENCES

1. Hoare C et al. Health Technol Assess. 2000;4(37):1-191
2. Sidbury R et al. J Am Acad Dermatol. 2014;71(6):1218-33
3. Williams HC and Wüthrich B.. Atopic dermatitis. Cambridge: Cambridge University Press; 2000
4. Luger TA. J Eur Acad Dermatol Venereol. 2011;25(3):251-8
5. Darsow U et al. J Eur Acad Dermatol Venereol. 2010;24(3):317-28
6. Williams HC. Clin Exp Dermatol. 1992;17:385-9
7. Asher MI et al. N Z Med J. 2001;114(1128):114-20
8. Kemp AS. Pharmacoeconomics 2003;21(2):105-13
9. Simpson CR et al. J R Soc Med. 2009;102(3):108-17
10. Clayton T et al. Asia Pac Allergy 2013;3(3):161-78
11. NICE, 2007 Guidelines: Atopic eczema in children http://www.nice.org.uk/CG057 (Accessed July 2018)
12. Lewis-Jones S. Int J Clin Pract. 2006 Aug;60(8):984-92
13. Akdis CA et al. Allergy.2006;61(8):969-87
14. Grimalt R et al. Dermatology 2007;214(1):61-7
15. Starship Clinical Practice Guidelines: Eczema. Available from https://www.starship.org.nz/for-health-professionals/starship-clinical-guidelines/e/eczema/#Outpatient-Management-of-Eczema (Accessed July 2018)
16. Ruzicka T. Int J Clin Pract. 2006;60(1):85-92
17. Garcia Ponte L and Ebert U. J Eur Acad Dermatol Venereol 2012;26(Suppl 6):9-13
18. Bpac. A focus on skin: Childhood eczema: https://bpac.org.nz/BPJ/2017/April/BPJ78.pdf (Accessed July 2018)
19. Luger TA. Guidelines of the German Dermatology Society. AWMF 2003
20. DermNet NZ. Treatment of atopic dermatitis. http://www.dermnetnz.org/dermatitis/treatment.html (Accessed July 2018)
21. Ohya et al. J Invest Dermatol 2001;117:852-7
22. Santer M et al. Br J Gen Pract. 2012;62(597):e261-7
23. Zuberbier T et al. J Allergy Clin Immunol. 2006;118(1):226-32
24. Fischer G. Australas J Dermatol. 1996;37 Suppl 1:S10-3
25. Ricci G. Pediatr Dermatol. 2009;26(1):1-5
26. ADVANTAN® Data Sheet:https://www.medsafe.govt.nz/profs/Datasheet/a/Advantanointcrm.pdf (Accessed Feb 2021)
27. Zaumseil RP et al. J Derm Treat. 1992;3 Suppl 2:3-7
28. Blume-Peytavi U and Wahn U. J Eur Acad Dermatol Venereol. 2011;25(5):508-15
29. Bpac BPJ Issue 23 September 2009. Available from: http://www.bpac.org.nz/magazine/2009/september/docs/bpj23_corticosteroids_pages8-13.pdf (Accessed July 2018)
30. Bieber T et al. Allergy 2007;62(2):184-9
31. Rampini E. J Dermatol Treat. 1992;3(Suppl 2):27-9
32. Elsner P. Anktuelle Dermatologie 1995;21(5):3-6
33. Niedner R and Zaumseil R-P. Akt Dermatol. 2004;30:200-03
34. Mensing H and Lorenz B. Zeitschrift für Hautkrankheiten, H + G. 1998;5(73):281-85
35. Fritsch P. J Derm Treat. 1992;3(2):17-19
36. Torrelo A. I J Dermatol. 2017;56:691-97
37. Ruzicka T and Zaumseil RP. H-G Z Hautkr 2002;77(4):185-89
38. Peserico A. Br J Dermatol. 2008;158(4):801-7
39. Kecskés A et al. J Am Acad Dermatol. 1993;29:576–580
40. Odhiambo JA, et al,J Allergy Clin Immunol. 2009, 124(6) 1251-58.e23

This article was sponsored by Leo Pharma Limited. The content is entirely independent and based on published studies and the author's opinions and has not had any input from Leo Pharma. Before prescribing any of the medications mentioned in this article please consult the full datasheets, available at www.medsafe.govt.nz. Treatment decisions based on these data are the full responsibility of the prescribing physician. All trademarks mentioned in this review are the property of their respective owners.