

Methylprednisolone Aceponate: An Evidence-Based Expert Review of its Clinical Role in Inflammatory Dermatology

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ABSTRACT

Methylprednisolone aceponate (MPA) is a non-halogenated fourth-generation topical corticosteroid with a well-established efficacy and safety profile in inflammatory dermatoses. Its molecular design allows selective cutaneous activation and rapid systemic inactivation, resulting in a favorable benefit-risk balance. Clinical studies demonstrate significant efficacy in acute flares of atopic dermatitis, reduction of relapses with proactive therapy, and good tolerability in pediatric populations. This review summarizes pharmacologic properties, clinical evidence, safety data, and current positioning of MPA within modern therapeutic algorithms.

Abbreviations: MPA: Methylprednisolone Aceponate; TCS: Topical corticosteroids; ATC: Anatomical Therapeutic Chemical; AD: Atopic Dermatitis; FTU: Fingertip Unit

Introduction

Topical corticosteroids (TCS) remain a cornerstone in the management of a wide spectrum of inflammatory and immune-mediated dermatoses, including atopic dermatitis, contact dermatitis, radiation-induced dermatitis, psoriasis, vitiligo, lichen planus, and discoid lupus erythematosus. Their therapeutic efficacy is mediated through potent anti-inflammatory, antiproliferative, and immunomodulatory actions [1]. Long-standing concerns regarding cutaneous atrophy and potential systemic adverse effects associated with topical corticosteroid therapy have prompted the development of optimized molecules with enhanced therapeutic indices. Methylprednisolone aceponate (MPA) was specifically designed to maximize local anti-inflammatory activity while minimizing percutaneous absorption and systemic bioavailability [2,3]. This article presents an expert-led, evidence-based appraisal of its pharmacological properties, clinical efficacy, and safety profile within contemporary dermatological practice.

Pharmacology and Mechanism of Action

MPA is a lipophilic diester corticosteroid that functions as a prodrug following topical application, undergoing cutaneous hydroly-

sis to its principal active metabolite, 6 α -methylprednisolone-17-proionate, which has high affinity for intracellular glucocorticoid receptors and exerts its effects locally within the epidermis and dermis [1,4,5]. Binding of the receptor-ligand complex to glucocorticoid response elements in the nucleus modulates transcription, leading to suppression of pro-inflammatory cytokines and effector mediators and upregulation of anti-inflammatory proteins, which underlies the potent anti-inflammatory and immunosuppressive effects observed clinically [4,6].

MPA is classified as a potent topical corticosteroid in both American and European classification systems. In the United States, the 7-class system ranks topical corticosteroids from class 1 (super potent) to class 7 (least potent). MPA is generally placed in class 2 or 3, corresponding to “potent” or “upper mid-strength” depending on the vehicle and concentration, but mostly recognized as “potent”. In Europe, the Anatomical Therapeutic Chemical (ATC) classification and UK systems use a 4-class scale: mild, moderate, potent, and very potent. MPA is consistently categorized as “potent” (category III) in these systems. This classification is based on vasoconstrictor assay and clinical efficacy, with MPA showing activity comparable to other potent corticosteroids. The potency may vary slightly depending

on the formulation (cream, ointment, milk), but all standard topical forms (0.1%) are considered potent [7].

Safety and Tolerability

Methylprednisolone aceponate demonstrates an excellent safety and tolerability profile among potent topical corticosteroids, with minimal risk of local and systemic adverse effects when used as directed. Clinical studies and reviews consistently report a low incidence of skin atrophy, telangiectasia, and hypothalamic-pituitary-adrenal axis suppression, even in pediatric populations and with once-daily application regimens. Compared to other potent corticosteroids such as mometasone furoate, methylprednisolone aceponate is associated with significantly fewer local side effects, including reduced atrophogenicity and telangiectasia formation [8,9].

Systemic absorption is minimal and suppression of serum cortisol is rare, particularly when used on limited body surface areas and for short durations. The therapeutic index is considered highly favorable, especially in children and infants, due to structural modifications that enhance potency without increasing adverse event risk [3,10]. The broad range of formulations (cream, ointment, fatty ointment, milk) allows for tailored therapy, further improving tolerability [3,10,11].

Overall, methylprednisolone aceponate is well tolerated, with a safety profile superior to many other potent topical corticosteroids, making it suitable for both acute and maintenance therapy in adults and children.

Current Therapeutic Positioning

The main clinical indications for methylprednisolone aceponate are the treatment of eczema (including atopic dermatitis and contact dermatitis) and other inflammatory skin disorders such as seborrheic dermatitis, nummular eczema, and lichen simplex chronicus. It is also used for psoriasis (localized plaques) and has demonstrated efficacy in the management of facial and scalp eczema, sunburn, and other steroid-responsive dermatoses [11].

Atopic Dermatitis

MPA is clinically used for the treatment of atopic dermatitis, both in acute flares and for maintenance therapy [2,12,13]. It is suitable for adults, children, and infants, and is available in multiple formulations (cream, ointment, fatty ointment, milk), allowing for tailored therapy based on disease severity and skin site [2,3,11]. The typical regimen is once-daily application of 0.1% formulation for acute flares, and twice-weekly application for maintenance after disease stabilization [3,13-16].

Efficacy is rapid and reliable, with clinical studies demonstrating that methylprednisolone aceponate achieves significant improvement in disease severity scores, pruritus, and sleep quality. It is at least as effective as tacrolimus 0.03% ointment for acute flares in children and adolescents, and superior in reducing itch and sleep

disturbance [12]. Maintenance therapy with twice-weekly methylprednisolone aceponate significantly prolongs time to relapse and reduces relapse rates compared to emollient alone [13]. The safety profile is highly favorable, with minimal risk of local adverse effects such as skin atrophy, telangiectasia, or irritation, and negligible systemic absorption even in infants and children [2,3,11,14]. No significant drug-related adverse events have been reported in clinical trials and the therapeutic index is superior to other potent topical corticosteroids, including mometasone furoate. Methylprednisolone aceponate is well tolerated and its once-daily dosing improves compliance without compromising efficacy [3,9,11,14].

In this era of new treatments for atopic dermatitis, including JAK inhibitors (e.g., upadacitinib, abrocitinib, baricitinib) and biologics (e.g., dupilumab, tralokinumab, lebrikizumab), we might well ask what role topical corticosteroids play. Topical corticosteroids remain the first-line anti-inflammatory treatment and the cornerstone of therapy for all severities of atopic dermatitis (AD), even with the emergence of advanced systemic options. Their primary role is the management of acute flares and, increasingly, proactive therapy to maintain long-term disease control. The guidelines emphasize that, before considering a patient as a candidate for systemic treatment, an adequate trial of optimized topical treatment—including medium- to high-potency topical corticosteroids—should be carried out [17].

The introduction of biologics and oral JAK inhibitors has modified but not eliminated the use of TCS:

- **Synergistic Combination:** Biologics and JAK inhibitors are frequently studied and prescribed in combination with TCS. This approach often results in higher responder rates than monotherapy; for example, adding TCS to dupilumab or tralokinumab significantly increases the percentage of patients reaching clear or almost-clear skin [18].
- **Rescue Therapy:** For patients on systemic treatments who experience breakthrough activity, TCS serve as a vital “rescue” option to manage localized flares without needing to switch systemic medications.

Furthermore, it is necessary to switch from topical corticosteroids to systemic treatment when a patient’s atopic dermatitis (AD) remains uncontrolled despite an optimized topical regimen. The following criteria and steps summarize when this switch should be made:

- Failure of optimized topical treatment.
- High severity and impact of the disease.
- Impact on quality of life.
- Need to reduce the topical steroid dose.

However, before switching to systemic therapy, it is essential that the doctor does the following:

- Confirm the diagnosis: Rule out other conditions that may mimic or exacerbate AD, such as cutaneous T-cell lymphoma or allergic contact dermatitis.
- Check compliance: Ensure that the patient or carers are applying topical treatments correctly and following the recommendations for patient education.
- Manage comorbidities: Assess and treat secondary infections (such as *Staphylococcus aureus*) that may be preventing improvement with conventional topical treatment.

In conclusion, the decision to switch to systemic therapy is an individualized decision shared between the clinician and the patient, based on clinical severity, refractoriness to optimized treatment and the social impact of the disease.

Contact Dermatitis

Methylprednisolone aceponate (MPA) 0.1% is a highly effective topical corticosteroid for contact dermatitis, demonstrating rapid itch relief and clinical improvement with an excellent safety profile [11]. In an experimental model of allergic contact eczema to nickel sulfate, MPA achieved mean time to itch relief of 1.0 day, with 75% reduction in pruritus occurring in 1.7 days and complete resolution in 2.0 days [19].

Seborrheic Dermatitis

Effective management of seborrheic dermatitis requires clearing of symptoms with antifungal and anti-inflammatory treatment, ameliorating associated symptoms such as pruritus, and general scalp and skin health to help maintain remission [20]. MPA is approved for seborrheic dermatitis with severe inflammation [5,21-23].

Key Features and Benefits of MPA

The main advantages of topical methylprednisolone aceponate (MPA) include: once-daily application (vs. twice-daily for most corticosteroids), approval for use in infants from 4 months of age, multiple vehicle formulations for different lesion types, and a favorable safety profile in pregnancy.

Frequency of Application

Once-daily application is the approved posology for MPA, representing a significant advantage:

- Most topical corticosteroids require twice-daily application.
- Once-daily dosing improves patient adherence without compromising efficacy.

It is also important to know the correct amount of corticosteroid to apply; this requires an understanding of the FTU. The fingertip

unit (FTU) system is the standard method for quantifying topical corticosteroid application: One FTU = amount dispensed from the tip of the index finger to the distal interphalangeal crease $\approx$ 0.5 g, covering approximately 2% body surface area in an adult. For example, to treat one hand (both sides), you would need 1 FTU per application, which would amount to 15 grams per month with one daily application of MPA [24].

Use in Children

MPA is licensed for use in infants, children, and adults, including infants as young as 4 months of age. Furthermore, clinical experience in children aged 2 months to 4 years, together with evidence from multiple clinical studies, supports its use in infants and children, demonstrating minimal local or systemic adverse effects. However, it is important to note that children have a higher body surface area-to-weight ratio, which leads to proportionally greater percutaneous absorption. In addition, the systemic effects of corticosteroids are more pronounced (especially suppression of the HPA axis). The optimized safety profile of MPA makes it particularly suitable for this population [2,3].

Different Vehicle Formulations

MPA 0.1% is available in four formulations (cream, ointment, fatty ointment and emulsion) allowing treatment to be tailored to lesion characteristics and individual patient needs [3,5,21-23].

Use in Pregnancy and Lactation

The best evidence currently available suggests that topical corticosteroids are, in general, safe for medical use during pregnancy, provided that certain principles regarding strength and dosage are followed.

The European Forum of Dermatology guidelines emphasize a stepwise approach to treatment to maximize safety: mild or moderate-strength topical corticosteroids should be the first choice for pregnant women, whilst strong or very strong TCS should be reserved as second-line treatment and used for as short a time as possible [25,26]. Topical corticosteroids appear sufficiently safe during breastfeeding [27].

Conclusion

Methylprednisolone aceponate (MPA) is an effective and well-established topical corticosteroid, with a favorable benefit-risk profile supported by extensive clinical evidence. Its prodrug design enables local cutaneous activation and rapid systemic inactivation, contributing to reduced systemic exposure.

In inflammatory dermatoses, particularly atopic dermatitis, MPA has demonstrated consistent efficacy, providing rapid symptom control, reducing disease severity, and being useful both in the management of acute flares and in proactive treatment strategies to prevent relapses.

In addition, it shows excellent tolerability, with a low incidence of local adverse effects and minimal risk of systemic effects, even in sensitive populations such as infants and children, supporting its use in both short and long-term treatment under appropriate conditions.

In the current therapeutic landscape, despite the introduction of advanced therapies such as biologics and JAK inhibitors, topical corticosteroids remain the foundation of treatment. Within this context, MPA stands out as a versatile, reliable, and evidence-based option, both as monotherapy and in combination with systemic treatments.

Overall, MPA maintains a key role in modern dermatological practice, offering a clinically relevant balance between efficacy, safety, and ease of use, and positioning itself as an essential tool in the comprehensive management of inflammatory dermatoses.

Conflicts of Interest

Francisco Javier Vicente Martín reports having received financial support from Italfarmaco related to the development of this manuscript. The author declares no additional conflicts of interest that could have influenced the content, interpretation, or presentation of the findings.

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