1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

MACEPATAN CREAM 1 mg/g

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 g of MACEPATAN CREAM contains 1 mg methylprednisolone aceponate.

Preservative: Benzyl alcohol 1 % *m/m*

Cetostearyl alcohol 60 mg/g

Butyl hydroxy toluene 0,050 mg/g

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cream.

MACEPATAN CREAM is a white to yellowish opaque cream.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

MACEPATAN CREAM is indicated for endogenous eczema (atopic dermatitis, neurodermatitis), contact eczema, dyshidrotic and other eczemas.

4.2. Posology and method of administration

Posology

MACEPATAN CREAM is applied thinly once per day to the diseased areas of skin.

In general, the duration of use should not exceed 12 weeks in adults.

As a low-fat formulation with a high water content, MACEPATAN CREAM is particularly suitable for acute and weeping stages of eczema, for very greasy skin and for use on exposed or hairy parts of the body.
If the skin dries out excessively under protracted use of MACEPATAN CREAM, a switch should be made to a fattier formulation (ointment or fatty ointment).

Paediatric population

The duration of use should not exceed 4 weeks in children.

MACEPATAN CREAM should not be applied to infants and young children (see section 4.3).

Method of administration

For external topical use.

4.3. Contraindications

MACEPATAN CREAM is contraindicated in:

- Patients with hypersensitivity to methylprednisolone aceponate or to any excipients in MACEPATAN CREAM (see section 6.1).

- Tuberculous or syphilitic processes, post-vaccination skin reactions present in the area to be treated.
- Viral diseases (e.g. varicella/herpes zoster, herpes simplex, vaccinia, chickenpox, shingles).
- Pregnancy. Corticosteroids, such as MACEPATAN CREAM, have been shown to be teratogenic in animals following dermal application. As these medicines are absorbed percutaneously, teratogenicity following topical application cannot be excluded.
- Children under four months due to lack of experience.

If rosacea, ulcers, atrophic skin diseases, acne vulgaris or perioral dermatitis are present, MACEPATAN CREAM must not be applied to the face.

4.4. Special warnings and precautions for use

Hypersensitivity

If signs of hypersensitivity develop, MACEPATAN CREAM should be discontinued and appropriate treatment instituted.

Long-term continuous treatment with topical corticosteroids, such as MACEPATAN CREAM, should be avoided as far as possible as this may cause atrophic changes in the skin leading to thinning, loss of elasticity, striae, dilatation of superficial blood vessels, telangiectasiae and ecchymoses.

These changes are particularly likely to occur on the face and when occlusive dressings are used.

Acneiform skin conditions can occur under therapy with potent corticoids such as MACEPATAN CREAM.

Treatment should be discontinued if symptoms such as cutaneous atrophy occur.

Systemic absorption of topically applied corticosteroids may occur, particularly under the following conditions:

- when large quantities are used,
- when application is made to wide areas of the body, or to damaged skin,
- when potent topical corticosteroids are used,
- when the occlusive dressing technique is applied.

Depression of the hypothalamic-pituitary-adrenal axis with consequent suppression of the adrenal gland may occur.

These effects are most likely to be severe in children.

Growth may be retarded and Cushingoid state may be produced.

Benign increased intracranial pressure has been rarely reported.

If a secondary microbial skin infection is present suitable concomitant antimicrobial therapy should be instituted. If fungal infections are present, a topically active antimycotic should be applied.

Any spread of infection requires withdrawal of topical corticosteroid therapy.

Topical corticosteroids should be used with particular caution in facial dermatoses, and only for short periods. A steroid rosacea-like facies may be produced. If rosacea or perioral dermatitis is present, MACEPATAN CREAM must not be applied to the face. MACEPATAN CREAM should not be allowed to come into contact with the eyes when being applied to the face.

MACEPATAN CREAM should not be allowed to come into contact with deep open wounds or mucosae.

Regular review should be made of the necessity for continuing therapy.

The treatment of psoriasis with potent topical corticosteroids may provoke the pustular form of the disease.

MACEPATAN CREAM should not be applied to skin crease areas.

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

As known from systemically administered corticosteroids, glaucoma may also develop from using topical corticosteroids (e.g. after large-dose or extensive application over a prolonged period, application under occlusive dressings, or application to skin around or near the eyes).

Topical steroid withdrawal syndrome

Long term continuous or inappropriate use of topical steroids can result in the development of rebound flares after stopping treatment (topical steroid withdrawal syndrome). A severe form of rebound flare can develop which takes the form of a dermatitis with intense redness, stinging and burning that can spread beyond the initial treatment area. It is more likely to occur when delicate skin sites such as the face and flexures are treated. Should there be a reoccurrence of the condition within days to weeks after successful treatment a withdrawal

reaction should be suspected. Reapplication should be with caution and specialist advise is recommended in these cases or other treatment options should be considered.

Paediatric population

MACEPATAN CREAM should not be used in the nappy areas in infants for flexural eruptions and ideally it should not be applied to infants and young children (see section 4.3).

In infants and children, plastic pants and napkins may act as occlusive dressings and increase absorption. Because of children's larger skin surface area to bodyweight ratio, paediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced HPA axis suppression and Cushing's syndrome than adults. Chronic/long-term corticosteroid therapy may interfere with growth and development of children. Use of topical corticosteroids in children should be limited to the least amount required for therapeutic effect.

Excipients

MACEPATAN CREAM contains benzyl alcohol and cetostearyl alcohol which may cause local skin reactions and irritations (e.g. contact dermatitis) MACEPATAN CREAM also contains butyl hydroxy toluene which may cause irritation to the eyes and mucous membranes in addition to local skin reactions.

4.5. Interaction with other medicines and other forms of interaction

No specific information exists on interactions with other medicines.

4.6. Fertility, pregnancy and lactation

Pregnancy

The use of MACEPATAN CREAM is contraindicated in pregnancy (see section 4.3).

There are no adequate data from the use of MACEPATAN CREAM in pregnant women. Epidemiological studies suggest that there could possibly be an increased risk of oral clefts among newborns or women who were treated with glucocorticosteroids during the first trimester of pregnancy. Reduced placental and birth weight have been recorded in animals and humans after long-term treatment. The possibility of suppression of the adrenal cortex in the newborn baby after long-term treatment must be considered.
Maternal pulmonary oedema has been reported, with tocolysis and fluid overload.

Breastfeeding

MACEPATAN CREAM should be used with caution in nursing mothers.

It is not known whether methylprednisolone aceponate, as in MACEPATAN CREAM, is secreted in breast milk.

Nursing mothers should avoid treatment over large areas, prolonged use or occlusive dressings. MACEPATAN CREAM should not be applied to the chest area during breastfeeding to avoid possible ingestion by infants.

Fertility

No data available.

4.7. Effects on ability to drive and use machines

MACEPATAN CREAM has no or negligible influence on the ability to drive or operate machinery.

Patients should not drive, use machinery or perform any tasks that require concentration until they are certain that MACEPATAN CREAM does not adversely affect their ability to do so safely (see section 4.4 and/or 4.8).

4.8. Undesirable effects

a) Summary of the safety profile

Most frequently observed side effects include application site burning and application site pruritus.

b) Tabulated list of adverse reactions

System organ class	**Frequent**	**Less frequent**	**Frequency unknown** (cannot be estimated from the available data)
Immune system disorders		Hypersensitivity	
Eye disorders			Blurred vision
Skin and subcutaneous tissue disorders			Folliculitis, hypertrichosis, perioral dermatitis,
		Atrophic changes in the skin with long-term continuous use, leading to thinning, loss of elasticity, dilatation of superficial blood vessels, telangiectasiae, ecchymoses,	
		impetigo, skin greasy, pyoderma, skin fissures, fungal infection, acne	
			Withdrawal reactions - redness of the skin which may extend to areas beyond the initial affected area, burning or stinging sensation, itch, skin peeling, oozing

			pustules. (see section 4.4),
General disorders and administrative site conditions	Application site burning, application site pruritus	Application site erythema, application site dryness, application site vesicles, application site irritation, application site eczema, application site papules, peripheral oedema	

c) Description of selected adverse reactions

The following local side effects may occur:

skin atrophy, skin striae, application folliculitis, hypertrichosis, telangiectasia, perioral dermatitis, skin discolouration, and hypersensitivity to any of the ingredients of the formulation. Systemic effects due to absorption may occur when topical medicines containing corticoids are applied.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug Reaction Reporting From”. Found online under SAHPRA’s publications:

SAHPRA: https://www.sahpra.org.za/Publications/Index/8

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

4.9. Overdose

Symptoms

Excessive dosing may occur with prolonged or intensive topical use (see sections 4.4 and 4.8).

Acute toxicity studies with methylprednisolone aceponate (namely oral ingestion, or single dermal application to a large area, under conditions favourable to absorption) do not indicate that any acute intoxication is expected.

Treatment

If any symptoms of overdosage occur, treatment must be discontinued.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Category and Class: A.13.4.1 Corticosteroids without anti-infective agents.

Pharmacotherapeutic group: Corticosteroids, potent (group III)

ATC code: D07AC14

Mechanism of action

After topical application, MACEPATAN CREAM has anti-inflammatory, antipruritic and vasoconstrictive actions.

The mechanism of action of methylprednisolone aceponate is not completely understood. It is known that methylprednisolone aceponate itself binds to the intracellular glucocorticoid receptor and this is especially true for the principal metabolite methylprednisolone-17-propionate, which is formed after cleavage in the skin.

The steroid receptor complex binds to certain regions of DNA, thereby triggering a series of biological effects. Binding of the steroid receptor complex results in induction of macrocortin synthesis. Macrocortin inhibits the release of arachidonic acid and thus the formation of inflammatory mediators such as prostaglandins and leukotrienes.

The immunosuppressive action of glucocorticoids can be explained by inhibition of cytokine synthesis and an antimitotic effect, which so far is not well understood. Inhibition of the synthesis of vasodilating prostaglandins or potentiation of the vasoconstrictive effect of adrenalin finally results in the vasoconstrictive activity of glucocorticosteroids.

5.2. Pharmacokinetic properties

Absorption

Methylprednisolone aceponate is bioavailable. When applied topically the concentration of methylprednisolone aceponate is highest in the outer layer of the epidermis (stratum corneum) and decreases progressively in the deeper strata.

The degree of percutaneous absorption of methylprednisolone aceponate varies according to the state of the skin (intact/inflamed/damaged), and the conditions of application (ope/occlusion). Studies using cream formulation in juvenile and adult patients with neurodermatitis and psoriasis have shown that the percutaneous absorption on open application was slightly (≤ 2,5 %) greater than the percutaneous absorption in volunteers

with normal skin (0,2 % to 1,5 %). Occlusive dressing increased percutaneous absorption. When the superficial horny layer is removed before application of methylprednisolone aceponate, the corticoid levels in the skin are about three times higher than after application to intact skin.

Distribution

The systemic effects of methylprednisolone aceponate are minimal in both man and animals following application of a topically effective dose. After treatment of large areas in patients with skin disorders, the plasma cortisol values remain within the normal range; circadian cortisol rhythm is maintained, and no reduction of cortisol has been ascertained in 24-hour urine.

Biotransformation

Methylprednisolone aceponate is hydrolysed in the epidermis and dermis to the principal metabolite, 6α-methylprednisolone-17-propionate. This metabolite binds to the intracellular glucocorticoid receptor with higher affinity than methylprednisolone aceponate. The binding of 6α-methylprednisolone-17-propionate to the receptor is an indicator of “bioactivation” in the skin.

After absorption into the systemic circulation, the primary hydrolysis product of methylprednisolone aceponate, 6α-methylprednisolone-17-propionate, is rapidly conjugated with glucuronic acid, and as a result, inactivated.

Elimination

The principal metabolites of methylprednisolone aceponate are eliminated primarily via the kidneys. The half-life is about 16 hours. Following intravenous administration, excretion via

the urine and faeces was complete within 7 days. There is no accumulation of methylprednisolone aceponate or metabolites in the body.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Benzyl alcohol, butyl hydroxy toluene, cetostearyl alcohol, decyl oleate, disodium edetate, glycerol, glycerol monostearate, hard fat, macrogol stearate, purified water, Softisan.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

36 months.

6.4. Special precautions for storage

Store at or below 25 °C.

6.5. Nature and contents of container

15 g, 20 g or 50 g packed in lami collapsible tube with polypropylene cap.

Not all pack sizes may be marketed.

6.6. Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8. REGISTRATION NUMBER

56/13.4.1/0423

9. DATE OF FIRST AUTHORISATION

23 January 2024

10. DATE OF REVISION OF TEXT

23 January 2024

Die Afrikaanse Professionele Inligting is op versoek beskikbaar. Mediese Blitslyn: 0800 118 088.

ZA_MACECRM_2401_00