AUSTRALIAN PRODUCT INFORMATION

METVANT® OINTMENT (METHYLPREDNISOLONE ACEPONATE) OINTMENT

METVANT® FATTY OINTMENT (METHYLPREDNISOLONE ACEPONATE) OINTMENT

1 NAME OF THE MEDICINE

Methylprednisolone aceponate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

METVANT® OINTMENT/METVANT® FATTY OINTMENT contain methylprednisolone aceponate 1 mg/g (0.1 %).

For a full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

METVANT® OINTMENT is a white opaque homogenous ointment, with firm consistency and free of agglomerates.

METVANT® FATTY OINTMENT is a white to off-white homogenous greasy ointment.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

METVANT® OINTMENT/METVANT® FATTY OINTMENT are indicated for the topical treatment of eczema and psoriasis in adults and children.

4.2 DOSE AND METHOD OF ADMINISTRATION

METVANT® OINTMENT/METVANT® FATTY OINTMENT is FOR EXTERNAL TOPICAL USE ONLY and NOT FOR OPHTHALMIC USE.

The METVANT® formulation most appropriate to the skin condition should be used.

The duration of use should be less than 12 weeks in adults and less than 4 weeks in children.

Instructions for use

Do not use beyond the expiry date on the package.

Do not use if the pack shows signs of damage or tampering.

METVANT® OINTMENT and METVANT® FATTY OINTMENT

METVANT® OINTMENT/METVANT® FATTY OINTMENT should usually be applied as a thin coating once per day to the affected areas. In the treatment of psoriasis, twice daily application may be required.

Choice of formulation

METVANT® OINTMENT

Skin conditions which are neither weeping nor very dry require a base with balanced proportions of fat and water. METVANT® OINTMENT is suitable for dry, fissured, scaly or hyperkeratinised skin areas. It should not be used in areas such as the axilla, groin or skin folds. METVANT® OINTMENT makes the skin slightly greasy without retaining warmth and fluid.

METVANT® FATTY OINTMENT

Very dry skin and the chronic stage of skin conditions require an anhydrous base. METVANT® FATTY OINTMENT base has an occlusive effect. It is suitable for treatment of areas where the stratum corneum is particularly thick, such as the pressure areas of elbows, knees, palms and soles.

4.3 CONTRAINDICATIONS

METVANT® OINTMENT/METVANT® FATTY OINTMENT is contraindicated in viral diseases (e.g., vaccinia, varicella/herpes zoster) and when tuberculous or syphilitic processes and post-vaccination skin reactions are present in the area to be treated. If rosacea, ulcera, atrophic skin diseases, acne vulgaris or perioral dermatitis are present, METVANT® OINTMENT/METVANT® FATTY OINTMENT must not be applied to the face.

Hypersensitivity to methylprednisolone aceponate or any component of the formulations.

Children under four months due to lack of experience.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

FOR EXTERNAL USE ONLY

METVANT® OINTMENT/METVANT® FATTY OINTMENT should not be allowed to come into contact with deep open wounds, muscosae or the eyes when being applied to the face.

Additional specific therapy is required in skin conditions infected with bacteria and/or fungi. Any spread of infection requires withdrawal of topical corticosteroid therapy.

If signs of hypersensitivity develop, METVANT® OINTMENT/METVANT® FATTY OINTMENT should be discontinued, and appropriate treatment instituted.

Any of the side effects that have been reported following systemic use of corticosteroids, including adrenal suppression, may also occur with topical corticosteroids, especially in infants and children.

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).

Methyleprednisolone aceponate is a potent steroid formulated for topical application. As with all potent corticosteroids, the possibility of hypothalamic-pituitary-adrenal (HPA) axis suppression resulting from percutaneous absorption of methylprednisolone must be considered when initiating or reviewing therapy, as adequate studies are not available to define the degree of risk.

Treatment of large areas has been noted to produce some suppression of cortisol secretion, but plasma levels remain above the lower limit of the normal range and circadian rhythm is maintained. Nevertheless, when treating large areas the duration of use should be kept as brief as possible. Extensive application of topical corticosteroids to large areas of the body or for prolonged periods of time, in particular under occlusion, significantly increases the risk of side effects. This is particularly important in children who may absorb proportionately larger amounts of topical corticosteroid and thus be more susceptible to systemic toxicity. Systemic absorption of topical corticosteroids will be increased if extensive body surface areas are treated or if the occlusive technique is used. Suitable precautions should be taken under these conditions or when long-term use is anticipated.

Local atrophy, telangiectasia and striae may occur after prolonged treatment or excessive application. Treatment should be discontinued if symptoms such as cutaneous atrophy occur (see also Section 4.8 Adverse effects (Undesirable effects)).

There was no sensitising effect or potential in animal studies.

Some of the excipients in METVANT® OINTMENT/METVANT® FATTY OINTMENT may reduce the effectiveness of latex products such as condoms and diaphragms.

Visual disturbance

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.

Use in the elderly

No data available

Paediatric use

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.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

No specific information exists on interactions with other medications.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy

Pregnancy Category C

There are no adequate data from the use of methylprednisolone aceponate ointment and fatty ointment in pregnant women.

Animal studies with methylprednisolone aceponate have shown embryolethal effects in rats dosed subcutaneously during the period of organogenesis at doses greater than 1 mg/kg/day and in rabbits following dermal application at doses greater than 0.25 mg/kg/day. No teratogenic effects were observed in rabbits, but in rats the incidence of ventricular septal defects and of cleft palate were increased at subcutaneous doses greater than 1 and 10 mg/kg/day. 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. In general, the use of topical preparations containing corticoids should be avoided during the first trimester of pregnancy.

Reduced placental and birth weight have been recorded in animals and humans after long-term treatment. Since the possibility of suppression of the adrenal cortex in the newborn baby after long-term treatment must be considered, the needs of the mother must be carefully weighed against the risk to the foetus when prescribing these drugs. Maternal pulmonary oedema has been reported, with tocolysis and fluid overload.

The clinical indication for treatment with methylprednisolone aceponate must be carefully reviewed and the benefits weighed against the risks in pregnant and lactating women.

Treatment of large areas or prolonged use (greater than 4 weeks) must be avoided.

Use in lactation.

It is not known whether methylprednisolone aceponate is secreted in breast milk. Methylprednisolone aceponate should be used during lactation only if benefits outweigh the risks.

Nursing mothers should avoid treatment over large areas, prolonged use or occlusive dressings. METVANT® OINTMENT/METVANT® FATTY OINTMENT should not be applied to the chest area during breast feeding to avoid possible ingestion by infants.

When considering use during lactation, note that after systemic administration, very small amounts of glucocorticoid may be present in breast milk. There is only a slight risk of exposure to methylprednisolone aceponate in breast milk following maternal dermal application at therapeutic doses, because the systemic absorption of methylprednisolone aceponate is minimal.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

In clinical studies, most frequently observed side-effects included application site burning and application site pruritus with methylprednisolone aceponate ointment. For methylprednisolone aceponate fatty ointment, application site folliculitis and application site burning were observed most frequently.

Frequencies of side-effects observed in clinical studies and given in tables 1, 2 and 3 below are defined according to the MedDRA frequency convention: very common (>1/10); common (>1/100, <1/10); uncommon (>1/1,000; <1/100), rare (>1/10,000, <1/1,000); very rare (<1/10,000), not known (cannot be estimated from available data). MedDRA version 12.0 was used for coding.

Table 1 Methylprednisolone aceponate Ointment 0.1%

System organ class	common	uncommon	Not known (cannot be estimated from available data)
General disorders and administration site reaction	application site burning, application site pruritus	application site erythema, application site dryness, application site vesicles, application site irritation, application site eczema, application site papules, edema peripheral	
Skin and subcutaneous tissue disorders		skin atrophy, ecchymosis, impetigo, skin greasy	acne

Table 2 Methylprednisolone aceponate Fatty Ointment 0.1%

System organ class	common	uncommon	Not known (cannot be estimated from available data)
General disorders and administration site reaction	application site folliculitis, application site burning	application site pustules, application site vesicles, application site pruritus, application site pain, application site erythema, application site papules	
Skin and subcutaneous tissue disorders		skin fissures, telangiectasia	acne

As with other corticoids for topical application, 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 formulations. Systemic effects due to absorption may occur when topical preparations containing corticoids are applied.

Post marketing

Eye disorders: vision blurred

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Excessive dosing may occur with prolonged or intensive topical use. Refer to Section 4.8 Adverse effects (Undesirable effects) for further information.

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.

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

After topical application, methylprednisolone aceponate has anti-inflammatory, anti-pruritic and vasoconstrictive actions.

As for all other glucocorticoids, the mechanism of action of methylprednisolone aceponate is not completely understood. It is known that methylprednisolone aceponate binds to the intracellular glucocorticoid receptor as does the principal metabolite 6α-methylprednisolone-17-propionate, which is formed by cleavage in the skin. The steroid-receptor complex binds to certain regions of DNA, inducing anti-inflammatory, anti-pruritic and vasoconstrictive effects.

Binding of methylprednisolone aceponate or its metabolites to the steroid receptor results in the induction of lipomodulin synthesis. Lipomodulin, a protein secondary messenger (also known as lipocortin 1 and macrocortin) inhibits release of arachidonic acid, which in turn inhibits the formation of inflammatory mediators, such as prostaglandins and leukotrienes.

The immunosuppressive action of glucocorticoids can be explained in part by their inhibitory effects on chemotaxis (inhibition of leukotriene synthesis). Glucocorticoids also have anti- mitotic activity, which is not well understood.

The vasoconstrictive activity of glucocorticoids results from the inhibition of prostaglandin synthesis. Prostaglandins have vasodilatory actions. Glucocorticoids also potentiate the vasoconstrictive effect of adrenaline.

Please note that the base formulations of the various METVANT® OINTMENT/METVANT® FATTY OINTMENT presentations influence the therapeutic effects (see Section 4.2 Dose and method of administration).

Clinical trials

No clinical trial information is available on the methylprednisolone aceponate ointment or fatty ointment.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Methylprednisolone aceponate is bioavailable from both ointment and fatty ointment formulations. 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), the formulation (ointment/fatty ointment) and the conditions of application (ope/occlusion). Studies using the ointment, fatty ointment and cream formulations 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 – 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.

Skin was artificially damaged to investigate the percutaneous absorption of methylprednisolone aceponate from the lotion formulation. Intact skin was compared with both artificially inflamed (UV-B erythema) and artificially damaged (removal of horny layer) skin. The absorption through artificially inflamed skin was very low (0.27%) and was only marginally higher than the absorption through intact skin (0.17%). The percutaneous absorption of methylprednisolone aceponate through artificially damaged skin resulted in higher levels of corticoid in the skin (15%).

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.

Metabolism

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.

Excretion

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.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

Methylprednisolone aceponate did not elicit any genotoxic effects or chromosomal damage in in vitro and in vivo assays conducted in bacteria and mammalian cells.

Carcinogenicity

Animal studies to evaluate the carcinogenic potential of methylprednisolone aceponate have not been conducted. Other glucocorticoid drugs have been shown to cause hepatic tumours in rats and it must be assumed that methylprednisolone aceponate would have similar activity.

However, in humans, epidemiological surveys of many years of systemic glucocorticoid therapy have not revealed any evidence for a tumourigenic action of this substance class.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

METVANT® OINTMENT contains the excipients: white soft paraffin, liquid paraffin, white beeswax, Dehymuls E - ARTG PI No. 1786 and purified water.

METVANT® FATTY OINTMENT contains the excipients: white soft paraffin, liquid paraffin, microcrystalline wax and hydrogenated castor oil.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

METVANT® OINTMENT: Store below 25ºC.
METVANT® FATTY OINTMENT: Store below 25°C.

6.5 NATURE AND CONTENTS OF CONTAINER

METVANT® OINTMENT is available in a 15 g aluminium tube fitted with a white HDPE screw cap.

METVANT® FATTY OINTMENT is available in a 15 g aluminium tube fitted with a white HDPE screw cap.

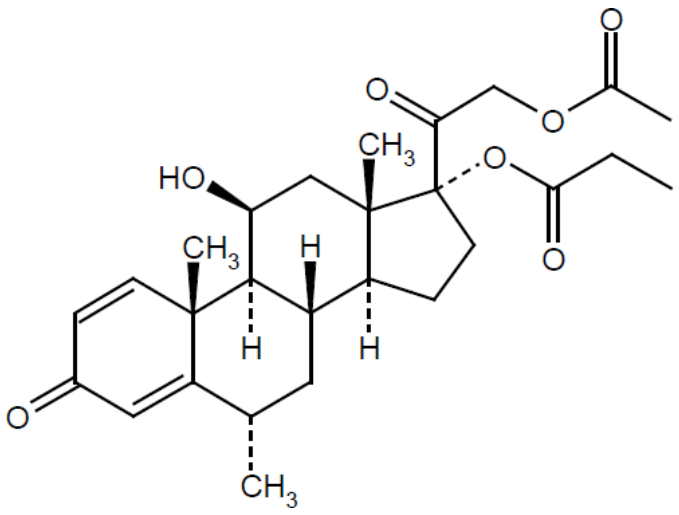
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

The chemical structure is:



The chemical name is 21-acetoxy-11β-hydroxy-6α-methyl-17-propionyloxy-1, 4- pregnadiene-3, 20-dione.

The molecular formula is $C_{27}H_{36}O_7$. The molecular weight is 472.58.

The active ingredient of the METVANT® OINTMENT/METVANT® FATTY OINTMENT formulations is the synthetic corticosteroid Methylprednisolone aceponate (MPA) is a white crystalline powder.

Methylprednisolone aceponate is soluble in methylene chloride, acetone and ethyl acetate and is sparingly soluble in hexane and ether.

CAS number

86401-95-8

7 MEDICINE SCHEDULE (POISONS STANDARD)

SCHEDULE 4 - PRESCRIPTION ONLY MEDICINE

8 SPONSOR

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9 DATE OF FIRST APPROVAL

29 November 2024

10 DATE OF REVISION

N/A

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	New PI