AUSTRALIAN PRODUCT INFORMATION

DIPROSONE® OV (OPTIMISED VEHICLE)

(betamethasone dipropionate)
Cream and Ointment

1 NAME OF THE MEDICINE

Betamethasone dipropionate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

DIPROSONE OV Cream (0.05%): Each g contains 0.64 mg betamethasone dipropionate, equivalent to betamethasone 0.5 mg.

DIPROSONE OV Ointment (0.05%): Each g contains 0.64 mg betamethasone dipropionate, equivalent to betamethasone 0.5 mg.

For the full list of excipients, see **Section 6.1 List of Excipients**.

3 PHARMACEUTICAL FORM

DIPROSONE® OV 0.5 mg/g is supplied as cream and ointment.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

DIPROSONE OV Cream and Ointment are indicated for the relief of the inflammatory and pruritic manifestations of resistant or severe corticosteroid-responsive dermatoses. These include atopic eczema, nummular eczema, contact dermatitis, neurodermatitis, anogenital and senile pruritus, lichen planus and psoriasis.

DIPROSONE OV Ointment is also indicated for the maintenance of remission in chronic psoriasis.

4.2 DOSE AND METHOD OF ADMINISTRATION

DIPROSONE OV Cream and Ointment: Apply a thin film to cover completely the affected area once or twice daily.

Patients with chronic psoriasis who have achieved at least a marked improvement in their psoriatic lesion(s) (i.e., approximately ≥80% improvement) with DIPROSONE OV Ointment may be maintained in remission with a pulse dosing regimen consisting of three consecutive applications of up to 3.5 g each of DIPROSONE OV Ointment, twelve hours apart (e.g., morning, evening, following morning) to the previously affected areas once each week. For this purpose, the DIPROSONE OV Ointment should be applied to the lesion sites previously affected and treated.

Patients on this pulse dose regimen who relapse should be reverted back to the conventional dosing regimen.

4.3 CONTRAINDICATIONS

Hypersensitivity to betamethasone dipropionate, other corticosteroids or any of the components in DIPROSONE OV. Like other topical corticosteroids, DIPROSONE OV is

contraindicated in most viral infections of the skin, such as vaccinia, varicella and Herpes simplex, also tuberculosis and acne rosacea.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

DIPROSONE OV should not be used in or near the eyes.

If irritation or sensitisation develops with the use of DIPROSONE OV, treatment should be discontinued and appropriate therapy instituted.

In the presence of an infection, an appropriate antifungal or antibacterial agent should be administered. If a favourable response does not occur promptly, DIPROSONE OV should be discontinued until the infection has been controlled adequately.

Corticosteroids are known to be absorbed percutaneously, therefore in patients under prolonged and extensive topical treatment, the possibility of systemic effects should be kept in mind.

DIPROSONE OV Cream has been shown to suppress the hypothalamic-pituitary adrenal (HPA) axis with repeated application of 7 g/day. In patients with psoriasis, application of 14 g per day of DIPROSONE OV Cream for eight days produced a depression of adrenocortical hormonal levels in plasma. Shortly after treatment cessation, adrenal output returned to normal.

At 14 g per day for nine days, DIPROSONE OV Ointment was shown to depress the plasma cortisol levels following repeated applications to diseased skin in patients with psoriasis. These effects were reversible upon discontinuation of treatment.

At 7 g per day (applied as 3.5 g twice daily), DIPROSONE OV Ointment was shown to cause minimal inhibition of the hypothalamic-pituitary-adrenal (HPA) axis when applied for two to three weeks in normal patients and in patients with psoriasis and eczematous disorders. With 6 to 7 g of DIPROSONE OV Ointment applied once daily for three weeks, no significant inhibition of the HPA axis was observed in patients with psoriasis and atopic dermatitis, as measured by plasma cortisol and 24-hour urinary 17-hydroxy-corticosteroid levels.

Systemic absorption of topical corticosteroids will be increased if extensive body surface areas are treated. Suitable precautions should be taken under these conditions or when long-term use is anticipated, particularly in infants and children as adrenal suppression may occur. Therefore, patients applying large doses of potent topical corticosteroids over large body surface areas should be evaluated periodically for evidence of HPA axis suppression. If HPA axis suppression occurs, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute with a less potent corticosteroid agent.

Recovery of HPA axis function is generally prompt and complete upon discontinuation of the drug. Infrequently, signs and symptoms of corticosteroid withdrawal may occur, requiring supplemental systemic corticosteroid therapy.

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

DIPROSONE OV is not intended for use under occlusive dressings since this will also increase systemic absorption of the corticosteroid. In infants the napkin may act as an occlusive dressing and increase absorption.

Patients should not use more than 45 g DIPROSONE OV weekly.

Suitable precautions should be taken when using topical corticosteroids in patients with stasis dermatitis and other skin diseases with impaired circulation.

Unless specifically indicated, application to the face is undesirable, as is prolonged use on flexures and intertriginous areas.

Prolonged use of topical corticosteroid preparations may produce striae or atrophy of the skin or subcutaneous tissue. If this occurs, treatment should be discontinued.

As with all highly active topical corticosteroid preparations, treatment should be discontinued when the dermatologic disorder is controlled. According to clinical response, duration of therapy may vary from a few days to a longer period of time. However, treatment should not be continued for more than four weeks without patient re-evaluation.

Visual disturbance may be reported with systemic and topical (including, intranasal, inhaled and intraocular) 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 of visual disturbances 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.

Diprosone OV ointment

Patients who are to use the pulse dosing regimen to maintain remission in chronic psoriasis should be instructed specifically as to where the medication should be applied.

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

Use in the elderly

No data available.

Paediatric use

DIPROSONE OV is not recommended for use in children under 12 years of age.

Chronic corticosteroid therapy may interfere with the growth and development of children.

Paediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced HPA axis suppression and to exogenous corticosteroid effects than mature patients because of greater absorption due to a larger skin surface area to body weight ratio.

HPA axis suppression, Cushing's syndrome, linear growth retardation, delayed weight gain, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include low plasma cortisol levels and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include a bulging fontanelle, headaches and bilateral papilloedema.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

No data available.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy (Category B3)

Topical corticosteroids should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

Use in lactation

Since it is not known whether the components of DIPROSONE OV are excreted in the milk of nursing mothers, caution should be exercised when DIPROSONE OV is administered to nursing women.

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)

The most frequent side effects reported with DIPROSONE OV are mild to moderate transient burning/stinging, dry skin, pruritus, irritation and folliculitis.

Rarely reported adverse effects include tingling, prickly skin, tightening or cracking of skin, warm feeling, laminar scaling and perilesional scaling, follicular rash, skin atrophy, erythema, urticaria, vesiculation and telangiectasia.

Adverse reactions reported with the use of the DIPROSONE OV Ointment pulse dose regimen were mild intermittent hypertension (one case) and paraesthesia (two cases).

Other local adverse reactions that have been reported with the use of topical corticosteroids include: itching, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, striae and miliaria.

Systemic adverse reactions, such as vision blurred, have also been reported with the use of topical corticosteroids.

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 http://www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Symptoms: Excessive prolonged use of topical corticosteroids can suppress pituitary-adrenal function resulting in secondary adrenal insufficiency and produce manifestations of hypercorticism, including Cushing's disease.

Treatment: Appropriate symptomatic treatment is indicated. Acute hypercorticoid symptoms are virtually reversible. Treat electrolyte imbalance, if necessary. In cases of chronic toxicity, slow withdrawal of corticosteroids is advised.

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

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Topical Corticosteroid: DIPROSONE OV is effective because of its anti-inflammatory, antipruritic and vasoconstrictive actions. The optimised vehicle with the propylene glycol component increases penetration and enhances the local effectiveness of the betamethasone dipropionate.

Pharmacology
Betamethasone dipropionate is a potent topically-active corticosteroid, producing prompt, marked and prolonged anti-inflammatory, antipruritic and vasoconstrictive effects.

According to the McKenzie-Stoughton Vasoconstrictor Test, betamethasone dipropionate was demonstrated to be significantly more active ($p<0.05$) than betamethasone valerate, fluocinolone acetonide, fluocortolone caproate plus fluocortolone, and flumethasone pivalate. While the direct applicability of this vasoconstrictor test to clinical situations has not been demonstrated conclusively, the results showed betamethasone dipropionate to be active in a concentration of 0.000016%, the lowest concentration tested which showed activity. To enhance the skin penetration of betamethasone dipropionate, various vehicles were evaluated based on the McKenzie Vasoconstrictor Test. Propylene glycol was determined to be an excellent solvent. The vasoconstrictor potency of the betamethasone dipropionate with propylene glycol (DIPROSONE OV) was demonstrated to be significantly greater than for DIPROSONE as measured by the McKenzie Test.

In controlled clinical trials, patients with moderate to severe chronic psoriasis who had at least a marked improvement in their symptoms (i.e., approximately ≥80% improvement) following 3 to 4 weeks of treatment with DIPROSONE OV Ointment, were entered into a pulse dose regimen (three consecutive applications applied twelve hours apart once each week) for the maintenance of remission. Of these patients, 65% were kept in remission with this regimen of DIPROSONE OV Ointment for a period of 6 months and no significant HPA axis suppression or skin atrophy was observed. Effectiveness and safety of this regimen have been clinically determined for a period of 6 months use.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

The extent of percutaneous absorption of topical corticosteroids is determined by many factors including vehicle, integrity of the epidermal barrier and the use of occlusive dressings. While topical corticosteroids can be absorbed from normal intact skin, dermal inflammation and/or other dermatologic disease processes may increase percutaneous absorption. Occlusive dressings also substantially increase percutaneous absorption.

Distribution

After dermal absorption, topical corticosteroids enter pharmacokinetic pathways similar to those of systemically administered corticosteroids. In varying degrees, corticosteroids are bound to plasma proteins.

Metabolism

Corticosteroids are metabolised primarily in the liver.

Excretion

Corticosteroids are excreted by the kidneys. Some topical corticosteroids and their metabolites undergo biliary excretion.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

DIPROSONE OV Cream (0.05%): is in an optimised vehicle consisting of propylene glycol, carbomer 980, titanium dioxide, sodium hydroxide and purified water.

DIPROSONE OV Ointment (0.05%): is in an optimised vehicle consisting of propylene glycol, white soft paraffin, white beeswax and propylene glycol

DIPROSONE OV Cream and Ointment do not contain preservatives, parabens or lanolin.

6.2 INCOMPATIBILITIES

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

6.3 SHELF LIFE

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

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Cream and Ointment: Store below 25°C.

6.5 NATURE AND CONTENTS OF CONTAINER

DIPROSONE® OV 0.5 mg/g Cream (AUST R 18825) and Ointment (AUST R 18823): 5 g* and 30 g tube.

** Not available in Australia*

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

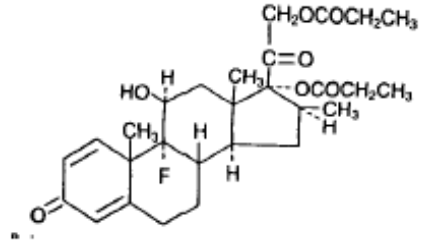
In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Betamethasone dipropionate is a white or almost white, crystalline powder, practically insoluble in water, freely soluble in acetone and in methylene chloride, sparingly soluble in ethanol (96 per cent).

Chemically betamethasone dipropionate is a synthetic corticosteroid which has the chemical name: 9-fluoro-11β-hydroxy-16β-methyl-3,20-dioxopregna-1,4-diene-17,21-diyl dipropanoate. The empirical formula is $C_{28}H_{37}FO_7$. Molecular Weight = 504.6

Chemical structure



CAS number

5593-20-4

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Only Medicine (Schedule 4)

8 SPONSOR

Organon Pharma Pty Limited
Building A, 26 Talavera Road
Macquarie Park NSW 2113

9 DATE OF FIRST APPROVAL

DIPROSONE OV Cream AUST R 18825: 8 October 1991
DIPROSONE OV Ointment AUST R 18823: 8 October 1991

10 DATE OF REVISION

23 March 2022

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.6	Update to pregnancy category from B1 to B3

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