DATA SHEET

1. DIPROSONE OV

DIPROSONE OV (0.05% w/w) cream
DIPROSONE OV (0.05% w/w) ointment

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Betamethasone dipropionate equivalent to betamethasone 0.5 mg/g (0.05% w/w).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

DIPROSONE OV Cream is a white cream in an optimised vehicle.
DIPROSONE OV Ointment is a white ointment in an optimised vehicle.

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 once or twice daily to cover completely the affected area.

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 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, 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 components in DIPROSONE OV. Like other topical corticosteroids, DIPROSONE OV is contraindicated in viral infections of the skin, such as vaccinia, varicella and Herpes simplex, also tuberculosis, acne rosacea, fungal skin infections (moniliasis), perioral dermatitis and ulcerative conditions.

4.4 Special warnings and precautions for use

DIPROSONE OV should not be used in or near the eyes, as there is a potential risk of developing glaucoma and cataract.

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.

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.

DIPROSONE OV Cream has been shown to suppress the HPA axis with repeated application of 7g/day. In patients with psoriasis, application of 14g 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 14g 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 7g per day (applied as 3.5g twice daily), DIPROSONE OV Ointment was shown to cause minimal inhibition of the HPA axis when applied for two to three weeks in normal patients and in patients with psoriasis and eczematous disorders. With 6 to 7g 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.

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

Routine steroid precautions must be observed if the patient is stressed, e.g. as in surgery.

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

Prolonged use on flexures and intertriginous areas is undesirable.

Application to the face is undesirable except in special conditions such as discoid lupus erythematosus.

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 dermatological 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.

Patients who are to use the pulse dose 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.

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.

Use in Children

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. Babies and children up to four years should not be treated with topical steroids for longer than three weeks. The use of potent topical corticosteroids should be avoided in children, unless strictly necessary and then only for short periods.

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.

4.5 Interaction with other medicines and other forms of interaction

No data available.

4.6 Fertility, pregnancy and lactation

Use in Pregnancy

Since safety of topical corticosteroid use in pregnant women has not been established, drugs of this class should be used during pregnancy only if potential benefit justifies the potential risk to the fetus. Topical corticosteroids should not be used extensively in large amounts or for prolonged periods of time in pregnant patients.

Use in Lactation

Since it is not known whether topical administration of corticosteroids can result in sufficient systemic absorption to produce detectable quantities in breast milk, a decision should be made to discontinue breastfeeding or to discontinue the drug, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

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

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

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, telangiectasia, acneiform papules and hyperaesthesia.

Adverse reactions reported with the use of the DIPROSONE OV Ointment pulse dose regimen were mild intermittent hypertension and paraesthesia.

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

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 professionals are asked to report any suspected adverse reactions:
https://nzphvc.otago.ac.nz/reporting/

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 advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACEUTICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: betamethasone: ATC code: D07AC01

DIPROSONE OV is a potent topically active corticosteroid, producing prompt, marked and prolonged anti-inflammatory, anti-pruritic and vasoconstrictive effects. The optimised vehicle

with the propylene glycol component increases penetration and enhances the local effectiveness of the betamethasone dipropionate.

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 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 hypothalamic-pituitary adrenal (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.

5.2 Pharmacokinetic properties

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 dermatological disease processes may increase percutaneous absorption. Occlusive dressings also substantially increase percutaneous absorption.

After dermal absorption, topical corticosteroids enter pharmacokinetic pathways similar to those of systemically administered corticosteroids. In varying degrees, corticosteroids are bound to plasma proteins. They are metabolised primarily in the liver and excreted by the kidneys. Some topical corticosteroids and their metabolites undergo biliary excretion.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the Data Sheet.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

DIPROSONE OV Cream:

- propylene glycol
- carbomer 980
- titanium dioxide
- sodium hydroxide
- purified water

DIPROSONE OV Ointment:

- propylene glycol
- soft white paraffin
- white beeswax
- propylene glycol monostearate

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

6.2 Incompatabilities

None known.

6.3 Shelf life

Cream: 18 months from date of manufacture
Ointment: 24 months from date of manufacture

6.4 Special precautions for storage

Store below 25°C

6.5 Nature and contents of container

Cream: 30g tube, HDPE cap
Ointment: 30g tube, HDPE cap

6.6 Special precautions for disposal

Not applicable.

7. MEDICINE SCHEDULE

Prescription medicine

8. SPONSOR

Organon New Zealand Limited
P O Box 99 851
Newmarket
Auckland 1149

Tel: 0800 111 700

9. DATE OF FIRST APPROVAL

DIPROSONE OV Cream: 15 January 1991
DIPROSONE OV Ointment: 28 July 1981

10. DATE OF REVISION OF THE TEXT

1 December 2020

SUMMARY TABLE OF CHANGES

Date	Change
01-December-2020	Section 8: Amend sponsor details due to transfer of sponsorship