PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

DIPROSONE®

betamethasone dipropionate cream, Organon Standard,
0.05% W/W betamethasone (as dipropionate)

betamethasone dipropionate ointment, Organon Standard,
0.05% W/W betamethasone (as dipropionate)

betamethasone dipropionate lotion, USP,
0.05% W/W betamethasone (as dipropionate)

Topical Corticosteroid

Organon Canada Inc.
16766 route Transcanadienne
Kirkland, Qc Canada H9H 4M7
www.organon.ca

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

DIPROSONE® (betamethasone dipropionate) is indicated for:

- the topical management of corticosteroid-responsive dermatoses. Such disorder include: psoriasis, contact dermatitis (dermatitis venenata), atopic dermatitis (allergic dermatitis), neurodermatitis (lichen simplex chronicus, lichen planus, eczema, eczematous dermatitis), intertrigo, dyshidroses (pompholyx), seborrheic dermatitis, exfoliative dermatitis, solar dermatitis, stasis dermatitis, anogenital and senile pruritus.

The lotion is formulated to spread easily without adherence to hairy areas to facilitate treatment of dermatoses, such as psoriasis, and seborrheic dermatitis of the scalp.

1.1 Pediatrics

Pediatrics: Based on the available data, the safety and efficacy of DIPROSONE® in pediatric patients have not been established.

1.2 Geriatrics

Geriatrics: There is no known evidence to suggest that use in the geriatric population is associated with differences in safety or effectiveness.

2 CONTRAINDICATIONS

DIPROSONE® (betamethasone dipropionate) is contraindicated in:

- patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see Dosage Forms, Strengths, Composition and Packaging.
- untreated bacterial, tubercular and fungal infections involving the skin, and in certain viral diseases such as herpes simplex, chicken pox, and vaccinia.
- hypersensitivity to any of the components.

3 DOSAGE AND ADMINISTRATION

3.1 Dosing Considerations

- For some patients adequate maintenance therapy may be achieved with less frequent application.

3.2 Administration

A thin film of DIPROSONE® should be applied to completely cover the affected area. The preparation should be massaged gently and thoroughly into the skin. The usual frequency of application is twice daily.

4 MISSED DOSE

If a dose is missed, the patient can resume treatment with the next scheduled application.

5 OVERDOSAGE

Symptoms: Excessive or 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 usually reversible. Treat electrolyte imbalance, if necessary. In case of chronic toxicity, slow withdrawal of corticosteroids is advised.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1 – Dosage Forms, Strengths, Composition and Packaging.

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Topical	Cream/0.5 mg betamethasone (as dipropionate) in a water miscible base	cetostearyl alcohol, chlorocresol, liquid paraffin, macrogol cetostearyl ether, phosphoric acid, phosphate dihydrate, sodium dihydrogen, sodium hydroxide, water and white soft paraffin
Topical	Ointment/0.5 mg betamethasone (as dipropionate) in a lanolin free base	liquid paraffin, white soft paraffin
Topical	Lotion/0.5 mg betamethasone (as dipropionate)	carbomer 934P, isopropyl alcohol, sodium hydroxide to adjust pH and water

7 WARNINGS AND PRECAUTIONS

General
If a symptomatic response is not noted within a few days to a week, the local applications of DIPROSONE® should be discontinued until the infection is brought under control.

Significant systemic absorption may occur when steroids are applied over large areas of the body, especially under occlusive dressings. To minimize this possibility, when long term therapy is anticipated, interrupt treatment periodically or treat one area of the body at a time.

Patients should be advised to inform subsequent physicians of the prior use of corticosteroids.

Occlusive dressings should not be applied if there is an elevation of body temperature.

Driving and Operating Machinery
Due caution should be exercised when driving or operating a vehicle or potentially dangerous machinery.

Immune
In cases of bacterial or fungal infections of the skin, appropriate antimicrobial agents should be used as primary therapy. If it is considered necessary, DIPROSONE® may be used as an adjunct to control inflammation, erythema, and itching.

Ophthalmologic
DIPROSONE® is not for ophthalmic use. Do not use in or near the eyes.

Topical corticosteroids should be used with caution on lesions close to the eye.

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.

Sensitivity/Resistance
Although hypersensitivity reactions have been rare with topically applied steroids, the drug should be discontinued, and appropriate therapy initiated if there are signs of sensitivity or irritation.

Skin
The lotion contains isopropyl alcohol and may cause stinging upon application to abraded or sun-burned skin.

7.1 Special Populations

7.1.1 Pregnant Women

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

7.1.2 Breast-feeding

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 nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

7.1.3 Pediatrics

The safety and efficacy of DIPROSONE® in pediatric patients have not been established. 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.

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, particularly in infants and children. Pediatric patients may demonstrate greater susceptibility than mature patients to topical corticosteroid-induced HPA axis suppression and to exogenous corticosteroid effects because of greater absorption due to a larger skin surface area to body weight ratio. Use of topical corticosteroids in children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with growth and development of children.

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 papilledema.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The following local adverse skin reactions have been reported rarely with the use of topical steroids: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis. The following may occur more

frequently with occlusive dressing: maceration of the skin, secondary infection, skin atrophy, striae, miliaria.

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

9 ACTION AND CLINICAL PHARMACOLOGY

Many clinical studies have established the efficacy and relative safety of DIPROSONE® (betamethasone dipropionate) in a variety of steroid responsive dermatological conditions.

In the course of clinical investigations, special emphasis was placed on the more troublesome conditions such as psoriasis and/or atopic dermatitis.

9.1 Mechanism of Action

DIPROSONE® (betamethasone dipropionate) cream and/or ointment provides anti-inflammatory, antipruritic and anti-allergic activity in the topical management of corticosteroid-responsive dermatoses.

10 STORAGE, STABILITY AND DISPOSAL

Store between 15°C and 30°C.

PART II: SCIENTIFIC INFORMATION

11 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Betamethasone-17, 21-dipropionate USP

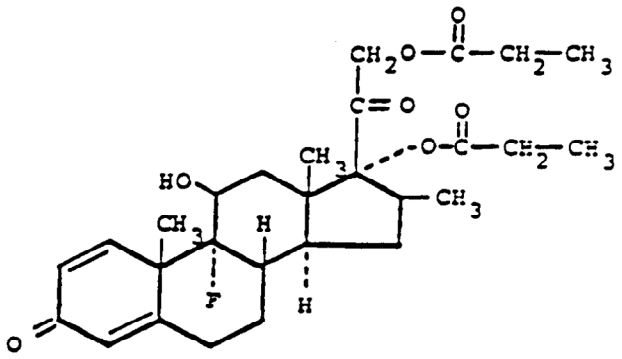
Chemical name:

Pregna-1,4-diene-3,20-dione,9-fluoro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-,(11β,16β)
or
9-Fluoro-11β,17,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione17,21-dipropionate

Molecular formula: $C_{28}H_{37}FO_7$

Molecular mass: 504.59

Structural formula:



Physicochemical properties: White to cream-coloured powder, free from foreign matter with melting point $\pm 3^0$, between 170^0 and 179^0 with decomposition.

12 CLINICAL TRIALS

The McKenzie-Stoughton vasoconstrictor test was conducted to compare betamethasone dipropionate to a number of other leading fluorinated topical corticosteroids. In this test betamethasone dipropionate was demonstrated to be significantly more active ($p<0.05$) than fluocinolone acetonide, fluocortolone caproate plus fluocortolone, flumethasone pivalate, and betamethasone valerate. While the direct applicability of this vasoconstrictor test to clinical situations has not been conclusively demonstrated, the results showed betamethasone

dipropionate to be active in a concentration of 0.000016%, the lowest concentration tested which showed activity.

Early in the clinical pharmacological investigation, a human tolerance and effectiveness study was carried out on four hospitalized psoriasis patients. Each was treated with 15 grams of cream b.i.d. for 10 days. No changes attributable to the treatment were noted in vital signs, weight, blood chemistry, CBC or urinalysis. Three of the four showed decreases in the urinary 17-KS and 17-OHCS levels, however, none showed any significant decrease in serum cortisol levels. There was no evidence of any loss of adrenal responsiveness after the period of treatment.

Clinical trials have shown that betamethasone dipropionate 0.05% is significantly more effective in the treatment of atopic dermatitis than either the vehicle or fluocinolone acetonide cream 0.025%. The same results were obtained in similar comparative trials involving psoriasis.

There was little significant difference when comparative trials were carried out between betamethasone dipropionate 0.05% and fluocinolone acetonide 0.025% in contact dermatitis; both were found effective.

Limited comparative trials with fluocinolone acetonide 0.05% in steroid responsive dermatosis did not show any significant differences between the two.

A study was carried out with the lotion to determine the potential for contact sensitization, assessed by means of the modified Draize test. No cases of sensitization were reported to have the capability of producing photodermatitis.

13 NON-CLINICAL TOXICOLOGY

Acute (betamethasone dipropionate) single administration

Form	Mouse	Rat	Rabbit	Guinea pig
Oral (or.)	>15,000	>15,000	C	C
Oral (oint.)	>2,000	>1,000	C	>2,000
Oral* (lot.)	>5.0	>5.0	C	C
Dermal (Cr.)	C	>3,330	>3,330	C
Dermal*(lot.)	C	>3.3	>3.3	C
I.M. (inj.)	74	>100	2.5-5.5	C

*Deaths attributable to isopropyl alcohol in the lotion.

Subacute

A four-week oral toxicity study in dogs with betamethasone dipropionate did not cause any toxic effects. Changes in some hematological, biochemical and physiological systems as well as changes seen in some organs were reversible and were considered to be caused by the pharmacological action of the corticosteroid. Subacute dermal toxicity studies were carried out in mice, rats and rabbits. Up to one gram of cream per rat per day for six days per week for eight weeks showed the cream to be well tolerated and no lesions attributable to the betamethasone dipropionate cream were found. Results were similar with the ointment formulation.

Dermal toxicity studies of the lotion showed that there were no adverse skin changes in rats or guinea pigs. In rats created for 15 days there was minimal systemic activity (reduced thymus and adrenal weights). Guinea pigs treated dermally with up to 2 ml/kg of the lotion for 15 treatment days showed no evidence of dermal irritation or of percutaneous absorption of the corticosteroid.

In other chronic intramuscular toxicity studies in rats, it was shown that betamethasone dipropionate administered in doses of 0.1, 0.5 and 1 mg/kg once a week for 13 weeks was well tolerated.

Carcinogenicity

Chronic one-year intramuscular toxicity studies in rats showed no indication of carcinogenic activity of betamethasone dipropionate; dosage ranged from 0.5 mg/kg to 3.5 mg/kg.

Reproduction and teratology

Standard reproduction and teratology studies carried out in rabbits showed that betamethasone dipropionate caused the teratogenic effects typical of many other corticosteroids.

Other effects

The effect of the lotion on the ECG of rats was studied and no alterations occurred. As well as effect of the lotion on the blood pressure of rats and cats was studied and no significant immediate or delayed changes in the blood pressure of rats or cats or the respiratory values of cats were seen.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

DIPROSONE®
betamethasone dipropionate cream
betamethasone dipropionate ointment
betamethasone dipropionate lotion USP

Read this carefully before you start taking **DIPROSONE®** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **DIPROSONE®**.

What is DIPROSONE® used for?
DIPROSONE® is used on the skin for the relief of redness, swelling, heat, pain and itching, caused by eczema, psoriasis and other skin problems.

How does DIPROSONE® work?
DIPROSONE® reduces inflammation and makes the blood vessels constrict to help relieve swelling, redness, heat, pain and itching.

What are the ingredients in DIPROSONE®?
Medicinal ingredient: betamethasone dipropionate
Non-medicinal ingredients:

Cream: cetostearyl alcohol, chlorocresol, liquid paraffin, macrogol cetostearyl ether, phosphoric acid, phosphate dihydrate, sodium dihydrogen, sodium hydroxide, water and white soft paraffin

Ointment: liquid paraffin, white soft paraffin

Lotion: carbomer 934P, isopropyl alcohol, sodium hydroxide to adjust pH and water

DIPROSONE® comes in the following dosage forms:
Cream: 0.05% W/W
Lotion: 0.05% W/W
Ointment: 0.05% W/W

Do not use DIPROSONE® if you:
- are allergic to betamethasone dipropionate or any of the other ingredients of **DIPROSONE®**.
- are allergic to a similar medication (corticosteroid).
- have any viral infections of the skin like chicken pox, cold sores or genital herpes, bacterial or fungal infections of the skin or tuberculosis of the skin.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take DIPROSONE®. Talk about any health conditions or problems you may have, including if you:

- already use a similar medication (corticosteroid).
- are pregnant or planning on becoming pregnant. It is not known if **DIPROSONE®** can harm your unborn baby. Your healthcare professional will decide whether giving you **DIPROSONE®** outweighs the potential risk to the unborn baby.
- are breastfeeding or planning to breastfeed. It is not known whether **DIPROSONE®** can pass into your breastmilk. Your healthcare professional will decide whether you should stop breastfeeding or stop using **DIPROSONE®.**
- have any infections.
- have increased pressure in your eyes (glaucoma).

Other warnings you should know about:

Do not use **DIPROSONE®** in or near your eyes.

Do not use **DIPROSONE®** under an air and water tight (occlusive) dressing if you have a high body temperature.

DIPROSONE® lotion contains alcohol and may cause stinging when applied to broken or sun burned skin.

Driving and Using Machinery: Use caution when driving or operating a vehicle or potentially dangerous machinery while using **DIPROSONE®**.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

How to take DIPROSONE®:
Usual dose: Apply a thin film of **DIPROSONE®** to completely cover the affected area twice a day. The cream/ointment/lotion should be massaged gently and thoroughly into the skin.

Overdose:

If you think you have taken too much **DIPROSONE®**, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed dose:
If you missed a dose of this medication, skip the missed dose and continue with your next scheduled dose. Then go back to your regular dosing schedule. Do not take two doses at the same time.

What are possible side effects from using DIPROSONE®?

These are not all the possible side effects you may feel when taking **DIPROSONE®**. If you experience any side effects not listed here, contact your healthcare professional.

Side effects may include:

- Burning, stinging
- Itching
- Irritation
- Dryness
- Swelling of the hair follicles
- Excessive hair growth
- Acne, rosacea
- Change in skin pigmentation
- Skin rash around the mouth
- Red, itchy rash caused by allergy to or contact with a substance (allergic contact dermatitis)
- Blurred vision
- Softening and breaking down of skin due to moisture
- Infection after treatment (secondary infection)
- Thinning of the skin
- Stretch marks
- Heat rash

Using **DIPROSONE®** can affect how your adrenal glands work. This can cause symptoms such as a round appearance of the face (moon face) and stretch marks. If you develop either of these symptoms, contact your healthcare professional.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:
Store between 15°C and 30°C.

Keep out of the reach and sight of children.

If you want more information about DIPROSONE®:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada.html); the manufacturer's website www.organon.ca, or by calling 1-844-820-5468.

This leaflet was prepared by Organon Canada Inc.

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