NEW ZEALAND DATA SHEET

BETNOVATE™-C CREAM and OINTMENT

Name of each active ingredient
Betamethasone valerate 0.1% w/w and clioquinol 3% w/w

Presentations

BETNOVATE-C Cream is a smooth, straw-coloured water-miscible cream.
BETNOVATE-C Ointment is a white or pale straw-coloured paraffin-based ointment.

Indications

BETNOVATE-C preparations are indicated for the treatment of the following conditions where secondary bacterial and/or fungal infection is present, suspected or likely to occur:-

- Eczema including atopic and discoid eczemas.
- Prurigo nodularis.
- Psoriasis (excluding widespread plaque psoriasis).
- Neurodermatoses including lichen simplex, lichen planus.
- Seborrhoeic dermatitis.
- Contact sensitivity reactions.
- Insect bite reactions.
- Prickly heat.
- Anal and genital intertrigo.
- Otitis externa.

Dosage and Administration

BETNOVATE-C cream is often appropriate for moist or weeping surfaces, and BETNOVATE-C ointment for dry, lichenified or scaly lesions, but this is not invariably so.

Adults and Adolescents

Apply thinly and gently rub in using only enough to cover the entire affected area once or twice daily for up to four weeks until improvement occurs, then reduce the frequency of application or change the treatment to a less potent preparation. Allow adequate time for absorption after each application before applying an emollient.

In the more resistant lesions, such as the thickened plaques of psoriasis on elbows and knees, the effect of BETNOVATE-C can be enhanced, if necessary, by occluding the treatment area with polythene film. Overnight occlusion only is usually adequate to bring
about a satisfactory response in such lesions, thereafter improvement can usually be maintained by regular application without occlusion.

If the condition worsens or does not improve within two to four weeks, treatment and diagnosis should be re-evaluated.

**Atopic dermatitis (eczema)**

Therapy with BETNOVATE-C should be gradually discontinued once control is achieved and an emollient continued as maintenance therapy.

Rebound of pre-existing dermatoses can occur with abrupt discontinuation of BETNOVATE-C.

**Recalcitrant dermatosis**

**Patients who frequently relapse**

Once an acute episode has been treated effectively with a continuous course of topical corticosteroid, intermittent dosing (once daily, twice weekly, without occlusion) may be considered. This has been shown to be helpful in reducing the frequency of relapse.

Application should be continued to all previously affected sites or to known sites of potential relapse. This regime should be combined with routine daily use of emollients. The condition and the benefits and risks of continued treatment must be re-evaluated on a regular basis.

**Children aged 1 year and over**

BETNOVATE-C is suitable for use in children and infants (1 year and over) at the same dose as adults. A possibility of increased absorption exists in very young children, thus BETNOVATE-C is contraindicated in neonates and infants under 1 year of age (see Contraindications).

Children are more likely to develop local and systemic side effects of topical corticosteroids and, in general, require shorter courses and less potent agents than adults.

Care should be taken when using BETNOVATE-C to ensure the amount applied is the minimum that provides therapeutic benefit.

**Elderly**

BETNOVATE-C is suitable for use in the elderly. Clinical studies have not identified differences in responses between the elderly and younger patients. The greater frequency of decreased hepatic or renal function in the elderly may delay elimination if systemic absorption occurs. Therefore the minimum quantity should be used for the shortest duration to achieve the desired clinical benefit.

**Renal/Hepatic impairment**

In case of systemic absorption (when application is over a large surface area for a prolonged period), metabolism and elimination may be delayed therefore increasing the risk of systemic toxicity. Therefore the minimum quantity should be used for the shortest duration to achieve the desired clinical benefit.
Contraindications

BETNOVATE-C is contraindicated in children under 1 year of age.

BETNOVATE-C is contraindicated where there is coexisting infection, otherwise concurrent antimicrobial therapy required.

The following conditions should not be treated with BETNOVATE-C:

- Rosacea.
- Acne vulgaris.
- Peri-oral dermatitis.
- Pruritus without inflammation.
- Perianal or genital pruritus.
- Primary cutaneous viral infections (e.g., herpes simplex, chickenpox).
- Hypersensitivity to any component of the preparation or to iodine.
- Primary infected skin lesions caused by infection with fungi or bacteria.
- Primary or secondary infections due to yeasts.

The use of dermal corticosteroids in the eye is contraindicated.

Warnings and Precautions

Hypersensitivity

BETNOVATE-C should not be used in patients with a history of hypersensitivity to betamethasone, clioquinol or to any of the excipients in the preparation, or to iodine. Local hypersensitivity reactions (see Adverse Effects) may resemble symptoms of the condition under treatment. Local hypersensitivity reactions (see Adverse Effects) may resemble symptoms of the condition under treatment.

Reversible hypothalamic-pituitary-adrenal (HPA) axis suppression

Manifestations of hypercortisolism (Cushing’s syndrome) and reversible hypothalamic-pituitary-adrenal (HPA) axis suppression can occur in some individuals as a result of increased systemic absorption of topical corticosteroids. If either of the above are observed, withdraw the drug gradually by reducing the frequency of application, or by substituting a less potent corticosteroid. Abrupt withdrawal of treatment may result in glucocorticosteroid insufficiency (see Adverse Effects).

Risk factors for increased corticosteroidal systemic effects are:

- Potency and formulation of topical corticosteroid
- Duration of exposure
- Application to a large surface area
- Use on occluded areas of skin e.g. on intertriginous areas or under occlusive dressings (nappies may act as an occlusive dressing)
- Increasing hydration of the stratum corneum
- Use on thin skin areas such as the face
• Use on broken skin or other conditions where the skin barrier may be impaired.

**Use in children**

In comparison with adults, children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic adverse effects. This is because children have an immature skin barrier and a greater surface area to body weight ratio compared with adults.

In children under 12 years of age, long-term continuous topical corticosteroid therapy should be avoided where possible, as adrenal suppression can occur.

**Application to the face**

Prolonged application to the face is undesirable as this area is more susceptible to atrophic changes.

**Application to the eyelids**

If applied to the eyelids, care is needed to ensure that the preparation does not enter the eye, as cataract and glaucoma might result from repeated exposure.

**Use in psoriasis**

Topical corticosteroids should be used with caution in psoriasis as rebound relapses, development of tolerance, risk of generalised pustular psoriasis and development of local or systemic toxicity due to impaired barrier function of the skin have been reported in some cases (see Adverse Effects). If used in psoriasis careful patient supervision is important.

**Infection**

Extension of infection may occur due to the masking effect of the steroid. Any spread of infection requires withdrawal of topical corticosteroid therapy and administration of appropriate systemic antimicrobial therapy.

**Infection risk with occlusion**

Bacterial infection is encouraged by the warm, moist conditions within skinfolds or caused by occlusive dressings. When using occlusive dressings, the skin should be cleansed before a fresh dressing is applied.

**Chronic leg ulcers**

Topical corticosteroids are sometimes used to treat the dermatitis around chronic leg ulcers. However, this use may be associated with a higher occurrence of local hypersensitivity reactions and an increased risk of local infection.

**Staining**

BETNOVATE-C may stain hair, skin or fabric, and the application should be covered with a dressing to protect clothing.

**Dilution**

Products which contain antimicrobial agents should not be diluted.
Neurotoxicity

There is a theoretical risk of neurotoxicity from the topical application of clioquinol particularly when BETNOVATE-C is used for prolonged periods or under occlusion.

Fertility

There are no data in humans to evaluate the effect of topical BETNOVATE-C on fertility.

Use in pregnancy

There are limited data from the use of BETNOVATE-C in pregnant women.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, administration of BETNOVATE-C during pregnancy should only be considered if the expected benefit to the mother outweighs the risk to the foetus. The minimum quantity should be used for the minimum duration.

Use in lactation

The safe use of betamethasone valerate-clioquinol during lactation has not been established.

It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable amounts in breast milk.

Administration of BETNOVATE-C during lactation should only be considered if the expected benefit to the mother outweighs the risk to the infant.

If used during lactation, BETNOVATE-C should not be applied to the breasts to avoid accidental ingestion by the infant.

Effects on ability to drive and use machines

There have been no studies to investigate the effect of BETNOVATE-C on driving performance or the ability to operate machinery. A detrimental effect on such activities would not be anticipated from the adverse reaction profile of topical BETNOVATE-C.

Adverse Effects

Clinical Trial and Post-marketing Data

Adverse drug reactions (ADRs) are listed below by system organ class and frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 and <1/10), uncommon (≥1/1000 and <1/100), rare (≥1/10,000 and <1/1000) and very rare (<1/10,000) including isolated reports.

Infections and infestations

Very rare: Opportunistic infection.

Immune system disorders
Very rare:  Local hypersensitivity.

**Endocrine disorders**

Very rare:  Hypothalamic-pituitary-adrenal (HPA) axis suppression: (see also Skin and Subcutaneous Tissue Disorders) Cushingoid features (e.g. moon face, central obesity), delayed weight gain/growth retardation in children, osteoporosis, glaucoma, hyperglycaemia/glucosuria, cataract, hypertension, increased weight/obesity, decreased endogenous cortisol levels.

**Vascular disorders**

Very rare:  Dilatation of the superficial blood vessels.

**Skin and subcutaneous tissue disorders**

Common:  Pruritis, local skin burning/pain of skin.

Very rare:  Allergic contact dermatitis/dermatitis, erythema, rash, urticaria, pustular psoriasis (see Warnings and Precautions), skin thinning*/skin atrophy*, skin wrinkling*, skin dryness*, striae*, telangiectasias*, pigmentation changes*, hypertrichosis, exacerbation of underlying symptoms, alopecia*, trichorrhexis*, hair discoloration.

**General disorders and administration site conditions**

Very rare:  Application site irritation/pain

In very rare instances, treatment of psoriasis with corticosteroid (or its withdrawal) is thought to have provoked the pustular form of the disease.

*Skin features of HPA axis suppression

**Interactions**

Co-administered drugs that can inhibit CYP3A4 (e.g. ritonavir, itraconazole) have been shown to inhibit the metabolism of corticosteroids leading to increased systemic exposure. The extent to which this interaction is clinically relevant depends on the dose and route of administration of the corticosteroids and the potency of the CYP3A4 inhibitor.

Theoretical concerns exist that oculotoxic effects of vigabatrin may be additive with clioquinol. Vigabatrin should not be used with clioquinol.

**Overdose**

**Symptoms and signs**

Topically applied betamethasone valerate-clioquinol may be absorbed in sufficient amounts to produce systemic effects. Acute overdosage is very unlikely to occur, however, in the case of chronic overdosage or misuse, the features of hypercortisolism may occur (see Adverse Effects).
**Treatment**

In the event of chronic overdose or misuse, topical corticosteroids should be withdrawn gradually by reducing the frequency of application, or by substituting a less potent corticosteroid, because of the risk of glucocorticosteroid insufficiency.

Further management should be as clinically indicated or as recommended by the National Poisons Centre (0800 764 766).

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**Further Information**

**Actions**

Betamethasone valerate is an active topical corticosteroid which produces a rapid response in those inflammatory dermatoses that are normally responsive to topical corticosteroid therapy, and is often effective in the less responsive conditions such as psoriasis.

Clioquinol is an anti-infective agent which has both antibacterial and anticandidal activity.

**Pharmacokinetics**

The following data apply to BETNOVATE-C skin preparations.

As with other topical corticosteroids, sufficient betamethasone valerate may be absorbed to give systemic effects if applied under an occlusive dressing or when the skin is broken.

**Other**

**Chemical Structure**

Betamethasone valerate

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\text{Betamethasone valerate}
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Clioquinol

\[
\text{Clioquinol}
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List of excipients

BETNOVATE-C Cream:

- Chlorocresol
- Cetomacrogol 1000
- Cetostearyl Alcohol
- White Soft Paraffin
- Liquid Paraffin
- Sodium Dihydrogen Phosphate Dihydrate
- Phosphoric Acid
- Sodium Hydroxide
- Purified Water

BETNOVATE-C Ointment:

- Liquid paraffin
- White soft paraffin

Pharmaceutical Precautions

Instructions for Handling

Do not dilute.

Incompatibilities

No incompatibilities have been identified.

Special Precautions for Storage

BETNOVATE-C Cream: Store below 30°C.
BETNOVATE-C Ointment: Store below 25°C.

Package Quantities

BETNOVATE-C Cream and Ointment are supplied in collapsible aluminium tubes, internally coated with an epoxy resin based lacquer and closed with a wadless polypropylene cap.

BETNOVATE-C Cream and Ointment are supplied in 15 g tubes.

Medicine Schedule

Prescription Only Medicine

Sponsor Details
Date of Preparation

11 December 2012

Version 2.0

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