

BETNOVATE

Betamethasone 17-valerate

Betamethasone valerate is referred to as '*BETNOVATE*' throughout this information.

PRESENTATION

***BETNOVATE* Cream (non-greasy base)**

0.1% betamethasone as 17-valerate in a water-miscible cream base

CLINICAL INFORMATION

Indications

- Eczema including atopic, infantile, and discoid eczemas
- Prurigo nodularis
- Psoriasis (excluding widespread plaque psoriasis)
- Neurodermatoses including lichen simplex, lichen planus
- Seborrhoeic dermatitis
- Contact sensitivity reactions
- Discoid lupus erythematosus
- An adjunct to systemic steroid therapy in generalised erythroderma
- Insect bite reactions
- Prickly heat

Dosage and Administration

A small quantity should be applied to the affected area two or three times daily until improvement occurs. It may then be possible to maintain improvement by applying once a day, or even less often.

BETNOVATE creams are especially appropriate for moist or weeping surfaces and *BETNOVATE* ointments for dry, lichenified or scaly lesions, but this is not invariably so.

In the more resistant lesions, such as the thickened plaques of psoriasis on elbows and knees, the effect of *BETNOVATE* 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.

Children

BETNOVATE is contraindicated in children under one year of age.

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* to ensure the amount applied is the minimum that provides therapeutic benefit.

Elderly

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

The following conditions should not be treated with *BETNOVATE*:

- Rosacea
- Acne vulgaris
- Perioral dermatitis
- Perianal and genital pruritus
- Pruritus without inflammation
- Primary cutaneous viral infections (e.g. herpes simplex, chickenpox)
- Hypersensitivity to any ingredient of the preparation

The use of *BETNOVATE* skin preparations is not indicated in the treatment of primarily infected skin lesions caused by infection with fungi or bacteria. *BETNOVATE* is contraindicated in dermatoses in infants under one year of age, including dermatitis.

Warnings and Precautions

Local hypersensitivity reactions (*see Adverse Reactions*) may resemble symptoms of the condition under treatment.

Manifestations of hypercortisolism (Cushing's syndrome) and reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, leading to glucocorticosteroid insufficiency, can occur in some individuals as a result of increased systemic absorption of topical steroids. 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 Reactions*).

Risk factors for increased systemic effects are:

- Potency and formulation of topical steroid
- Duration of exposure
- Application to a large surface area

- Use on occluded areas of skin e.g. on intertriginous areas or under occlusive dressings (in infants the nappy 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
- 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.

Visual disturbance has been reported by patients using systemic and / or topical corticosteroids. If a patient has blurred vision or other visual disturbances, consider evaluation of possible causes which may include cataract, glaucoma or central serous chorioretinopathy.

Children

Long-term continuous topical therapy should be avoided where possible, particularly in infants and children, as adrenal suppression can occur even without occlusion.

Infection risk with occlusion

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

Use in psoriasis

Topical corticosteroids should be used with caution in psoriasis as rebound relapses, development of tolerances, 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. If used in psoriasis, careful patient supervision is important.

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.

Concomitant infection

Appropriate antimicrobial therapy should be used whenever treating inflammatory lesions which have become infected. Any spread of infection requires withdrawal of topical corticosteroid therapy and administration of appropriate antimicrobial therapy.

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.

Flammability risk

Product contains paraffin. Instruct patients not to smoke or go near naked flames due to the risk of severe burns. Fabric (clothing, bedding, dressings etc.) that has been in contact with this product burns more easily and is a serious fire hazard. Washing clothing and bedding may reduce product build-up but not totally remove it.

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.

Pregnancy and Lactation

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

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development (*see Non-Clinical Information*).

The relevance of this finding to human beings has not been established; however, administration of *BETNOVATE* 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.

The safe use of topical corticosteroids 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* during lactation should only be considered if the expected benefit to the mother outweighs the risk to the infant.

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

There are no data in humans to evaluate the effect of topical corticosteroids on fertility.

Effects on Ability to Drive and Use Machines

There have been no studies to investigate the effect of *BETNOVATE* 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*.

Adverse Reactions

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

Post-marketing Data

Infections and Infestations

Very rare Opportunistic infection

Immune System Disorders

Very rare Local hypersensitivity

Local hypersensitivity reactions may resemble symptoms of the condition under treatment. If signs of hypersensitivity appear, the drug should be stopped immediately.

Endocrine Disorders

Very rare Hypothalamic-pituitary-adrenal (HPA) axis suppression
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,
alopecia, trichorrhexis

Skin and Subcutaneous Tissue Disorders

Common Pruritus, local skin burning/skin pain

Very rare Allergic contact dermatitis/dermatitis, erythema, rash, urticaria,
pustular psoriasis, skin thinning*/skin atrophy*, skin wrinkling*,
skin dryness*, striae*, telangiectasias*, pigmentation changes*,
hypertrichosis, exacerbation of underlying symptoms

General Disorders and Administration Site Conditions

Very rare Application site irritation/pain

*Skin features secondary to local and/or systemic effects of hypothalamic-pituitary-adrenal (HPA) axis suppression.

Overdose

Symptoms and signs

Topically applied betamethasone valerate 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 Reactions*).

Treatment

In the event of overdose, *BETNOVATE* 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, where available.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamics

ATC code

D07AC01 Corticosteroids, potent (group III)

Mechanism of action

Topical corticosteroids act as anti-inflammatory agents via multiple mechanisms to inhibit late phase allergic reactions including decreasing the density of mast cells, decreasing chemotaxis and activation of eosinophils, decreasing cytokine production by lymphocytes, monocytes, mast cells and eosinophils, and inhibiting the metabolism of arachidonic acid.

Pharmacodynamic effects

Topical corticosteroids have anti-inflammatory, antipruritic, and vasoconstrictive properties.

Pharmacokinetics

Absorption

Topical corticosteroids can be systemically absorbed from intact healthy skin. The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including the vehicle and the integrity of the epidermal barrier. Occlusion, inflammation and/or other disease processes in the skin may also increase percutaneous absorption.

Distribution

The use of pharmacodynamic endpoints for assessing the systemic exposure of topical corticosteroids is necessary because circulating levels are well below the level of detection.

Metabolism

Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. They are metabolised, primarily in the liver.

Elimination

Topical corticosteroids are excreted by the kidneys. In addition, some corticosteroids and their metabolites are also excreted in the bile.

Non-Clinical Information

Carcinogenesis / Mutagenesis

Carcinogenesis

Long-term animal studies have not been performed to evaluate the carcinogenic potential of betamethasone valerate.

Genotoxicity

No specific studies have been conducted to investigate the genotoxic potential of betamethasone valerate.

Fertility

The effect on fertility of betamethasone valerate has not been evaluated in animals.

Pregnancy

Subcutaneous administration of betamethasone valerate to mice or rats at doses ≥ 0.1 mg/kg/day or rabbits at doses ≥ 12 micrograms/kg/day during pregnancy produced foetal abnormalities including cleft palate and intrauterine growth retardation.

PHARMACEUTICAL INFORMATION

List of Excipients

Chlorocresol
Macrogol cetostearyl ether
Cetostearyl alcohol
White soft paraffin
Liquid paraffin
Sodium acid phosphate
Phosphoric acid
Sodium hydroxide
Purified water

For important information about some of these excipients see Warnings and Precautions.

Shelf-Life

The expiry date is indicated on the packaging.

Storage

The storage conditions are detailed on the packaging.

Incompatibilities

No incompatibilities have been identified.

Pack size

5g, 15g and 100g

Not all presentations may be available locally.

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