TITLE

Betamethasone 17-valerate

SCOPE

Tradenames

The tradenames for this product include

BETNOVATE

Formulations and Strengths

Scalp Application

Contains 0.122% w/w betamethasone 17-valerate.

Excipients

Scalp Application

Carbomer
Isopropyl alcohol
Sodium hydroxide
Purified water

CLINICAL INFORMATION

Indications

Scalp Application, Foam

Steroid responsive dermatoses of the scalp such as psoriasis, seborrhoea capitis, inflammation associated with severe dandruff.

Dosage and Administration

Adults, Elderly and Children over 1 year

A small quantity of betamethasone valerate should be applied to the scalp night and morning until improvement is noticeable. It may then be possible to sustain improvement by applyingonce a day, or less frequently.

Due to the flammable nature of betamethasone valerate <scalp application><foam> patients should avoid smoking or being near an open flame during application and immediately after use.

Children

Betamethasone valerate 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 betamethasone valerate to ensure the amount applied is the minimum that provides therapeuticbenefit.

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

- Infections of the scalp

Betamethasone valerate is contraindicated in dermatoses in infants under one year of age, including dermatitis.

Warnings and Precautions

Betamethasone valerate should be used with caution in patients with a history of local hypersensitivity to corticosteroids or to any of the excipients in the preparation. 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
In infants and children under 12 years of age, long-term continuous topical corticosteroid therapy should be avoided where possible, as adrenal suppression can occur.

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.

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

Fertility

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

Pregnancy

There are limited data from the use of betamethasone valerate in pregnant women.

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

The relevance of this finding to humans has not been established; however, administration of betamethasone valerate 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.

Lactation

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 betamethasone valerate during lactation should only be considered if the expected benefit to the mother outweighs the risk to the infant.

If used during lactation betamethasone valerate should not be applied to the breasts to avoid accidental ingestion by theinfant.

Ability to perform tasks that require judgement, motor or cognitive skills

There have been no studies to investigate the effect of betamethasone valerate 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 betamethasone valerate.

Adverse Reactions

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

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, urticarial, 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

Overdosage

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, betamethasone valerate 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.

Clinical Pharmacology

Pharmacodynamics

ATC code

D07AC 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.

Clinical studies

Foam

The safety and efficacy of betamethasone valerate foam has been demonstrated in a four-week trial in 190 patients with moderate to severe scalp psoriasis. Patients were treated twice daily for four weeks with betamethasone valerate foam, placebo foam, a commercially available betamethasone valerate lotion 0.12% (formerly expressed as 0.1% betamethasone), or placebo lotion. At four weeks of treatment, study results of 159 patients demonstrated that the efficacy of betamethasone valerate foam in treating scalp psoriasis is superior to that of placebo foam, and is comparable to that of a currently marketed betamethasone valerate lotion (see table below).

Subjects with Target Lesion Parameter Clear at Endpoint	Betamethasone valerate foam n (%)	Betamethasone valerate lotion n (%)	Placebo foam n (%)
Scaling	30 (47%)	22 (35%)	2 (6%)
Erythema	26 (41%)	16 (25%)	2 (6%)
Plaque Thickness	42 (66%)	25 (40%)	5 (16%)

Investigator's Global: Subjects Completely Clear or Almost Clear at Endpoint	43 (67%)	29 (46%)	6 (19%)

NON-CLINICAL INFORMATION

Carcinogenesis / Mutagenesis

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

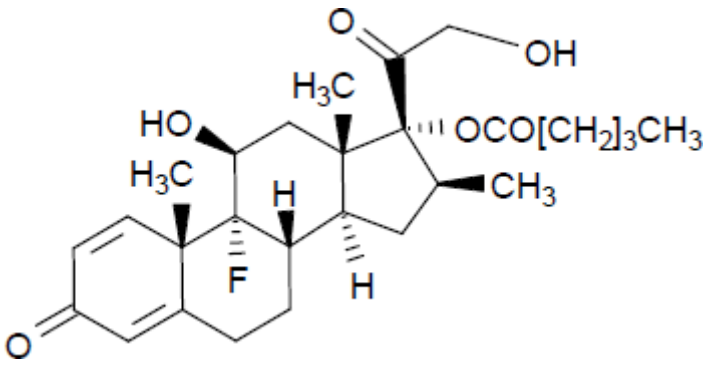
Genotoxicity
No specific studies have been conducted to investigate the genotoxic potential of betamethasone valerate.

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

Chemical structure



Betamethasone 17-valerate

Shelf-life

21 months

Storage

Do not store above 30°C. Keep container tightly closed when not in use. Contents are flammable. Keep away from fire, flame or heat. Do not leave betamethasone valerate scalp application in direct sunlight.

Nature and contents of container

Polyethylene squeeze bottle with a polyethylene nozzle and a polystyrene or polyethylene cap

Or

White High Density Polyethylene (HDPE) Hostalen GF4750 and Remafin White CEG020 container with a polyethylene nozzle and a polystyrene or polyethylene cap.

Incompatibilities

No incompatibilities have been identified.

Use and handling

There are no special requirements for use or handling of this product.

GLOBAL PATIENT LEAFLET

Scalp Application Only

Betnovate 0.122%w/w scalp application

Read all of this leaflet carefully before you start using this medicine.

Keep this leaflet. You may need to read it again. If you have any questions, ask your doctor or pharmacist.

This medicine has been prescribed for you personally. Do not pass it on to other people - it may harm them even if their symptoms seem to be the same as yours.

In this leaflet

1. What Betnovate Scalp Application is and what it is used for

The name of your medicine is Betnovate Scalp Application. Betnovate Scalp Application contains betamethasone valerate which belongs to a group of medicines called steroids. Steroids help to reduce redness, swelling and irritation of the skin.

Scalp Application

Betnovate Scalp Application is used to reduce the redness and itchiness of certain scalp problems, such as psoriasis (thickened patches of inflamed, red skin, often covered by silvery scales) and an inflamed scalp due to severe dandruff.

For children over the age of one year Betnovate Scalp Application is used for dermatitis that has not responded to milder steroid creams or ointments.

2. Before you use Betnovate Scalp Application

Don't use Betnovate Scalp Application

- if you have a skin infection on your scalp
- on children under 1 year.

➔ If you think any of these apply to you**, don't use Betnovate Scalp Application** until you have checked with your doctor or pharmacist.

Take special care with Betnovate Scalp Application

- Tell your doctor if you are allergic (hypersensitive) to Betnovate Scalp Application or any of the ingredients (listed in Section 6).
- Only use Betnovate Scalp Application for as long as your doctor recommends. If your condition does not improve after 2-4 weeks of treatment, speak to your doctor.
- If you experience blurred vision or other visual disturbances, speak to your doctor.
- The treated scalp area should not be bandaged or otherwise covered or wrapped unless directed by your doctor, since it is easier for the active ingredient to pass through the skin and increases the risk of infection.

➔ **Contact your doctor** if an infection develops (*See Section 4 Possible Side Effects*).

Other medicines and Betnovate Scalp Application

Some medicines may affect how Betnovate Scalp Application works or make it more likely that you'll have side effects. Examples of these medicines include:

- ritonavir and itraconazole

➔**Tell your doctor or pharmacist** if you are taking any of these. There are other medicines which may have a similar effect. It's therefore very important to **tell your doctor or pharmacist** if you're taking any other medicines, if you've taken any recently, or if you start taking a new one. This includes medicines bought without a prescription.

Pregnancy and breast-feeding

If you are **pregnant,** or **think you could be,** or if you are **planning to become pregnant, don't use** Betnovate Scalp Application without talking to your doctor first.

If you are breast-feeding, you must check with your doctor before you use Betnovate Scalp Application.

- If you do use Betnovate Scalp Application when breast-feeding, **don't use Betnovate Scalp Application on your breast area** to ensure that the **baby does not accidentally get Betnovate Scalp Application in their mouth.**

3. How to use Betnovate Scalp Application

Always use Betnovate Scalp Application exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

How much to use

a. Use Betnovate Scalp Application once or twice a day. The number of times you use your medicine may be reduced as your skin gets better or your doctor may prescribe a weaker steroid for you to use instead.

How to use

If you wash or shampoo your hair it should be dried before applying the liquid.

Due to the flammable nature of Betnovate Scalp Application Scalp Application, you should avoid smoking or being near an open flame while you're applying Betnovate Scalp Application Scalp Application, and immediately after you've used it.

Unscrew the bottle cap and place the nozzle on the scalp that needs treating. Gently squeeze the bottle to cover the area with a thin and even layer of liquid. You can rub this liquid in, but you don't have to. Your scalp will feel cool until the liquid has dried.

If you forget to use Betnovate Scalp Application

b. If you forget to use Betnovate Scalp Application apply it as soon as you remember then continue as before.

c. Do not apply extra Betnovate Scalp Application to make up for missed doses.

Don't stop using Betnovate Scalp Application without advice

d. **If you use** Betnovate Scalp Application regularly make sure you talk to your doctor before you stop using it.

If you use too much Betnovate Scalp Application

e. If you apply a large amount of Betnovate Scalp Application or accidentally swallow a lot of

Betnovate Scalp Application, it could make you ill. If you do swallow a large amount of Betnovate Scalp Application, rinse your mouth out with plenty of water and contact your doctor or pharmacist for advice.

4. Possible side effects

Like all medicines Betnovate Scalp Application can have side effects although not everybody gets them.

Side effects will affect your skin and may affect other parts of your body if a sufficient quantity of medicine is absorbed through the skin and enters your blood stream.

If your skin condition gets worse or your skin becomes swollen during treatment, you may be allergic to the medicine, have an infection or need other treatment.

➔ **Stop using Betnovate Scalp Application and tell your doctor as soon as possible**

Common side effects

These may affect up to **1 in 10 people**

a. itchy skin
b. local skin burning or pain

Very rare side effects

These may affect up to **1 in 10,000 people**

Use of Betnovate Scalp Application for a long period of time, or use under an airtight dressing, may cause the following symptoms:

c. increased weight
d. moon face / rounding of the face
e. obesity
f. skin thinning, this may cause stretch marks
g. skin wrinkling
h. skin dryness
i. the appearance of blood vessels under the surface of your skin
j. changes to the colour of your skin
k. increased body hair
l. hair loss / lack of hair growth / damaged looking hair

Other very rare skin reactions that may occur are:

m. allergic reaction at the site of application
n. worsening of condition
o. application site irritation
p. redness
q. rash or hives
r. If you have psoriasis you may get raised bumps with pus under the skin. This can happen very rarely during or after treatment and is known as pustular psoriasis.
s. skin infection.

In children also look out for the following symptoms:

t. delayed weight gain
u. slow growth.

Very rare side effects that may show up in blood tests or when your doctor gives you a medical examination.

v. a decrease in the level of the hormone cortisol in your blood
w. increased levels of sugar in your blood or urine
x. high blood pressure
y. cloudy lens in the eye (cataract)
z. increased pressure in the eye (glaucoma)
aa. weakening of the bones through gradual loss of mineral (osteoporosis) additional tests may be needed after your medical examination to confirm if you have this condition.

If you get side effects

➔ **Tell your doctor or pharmacist** if any of the side effects listed becomes **severe or troublesome,** or if you notice any side effects not listed in this leaflet.

5. How to store Betnovate Scalp Application

a. Keep out of the sight and reach of children.
b. Don't use Betnovate Scalp Application after the expiry date on the tube or carton (Exp).
c. Don't dispose of medicines in wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. This will help protect the environment.
d. Do not store Betnovate Scalp Application scalp application above 30°C. Keep the container tightly closed when not in use. Contents are flammable. Keep Betnovate Scalp Application away from all sources of fire, flame and heat. Do not leave Betnovate Scalp Application in direct sunlight.

6. Further information

What Betnovate Scalp Application contains

The active ingredient is betamethasone valerate. Each 1 g contains 1.22 mg of betamethasone valerate (0.122% w/w).

The other ingredients are

Carbomer
Isopropyl alcohol
Sodium hydroxide
Purified water

What Betnovate Scalp Application looks like and contents of the pack

Betnovate Scalp Application is a colourless, hazy, slightly viscous liquid. The product is packaged in polyethylene bottles fitted with polyethylene droppers and screw caps/dropper seals.