Betamethasone (as valerate)

Betnovate®

1 mg/mL Solution for Scalp Application

PRODUCT DESCRIPTION

Each mL of solution contains 1 mg Betamethasone (as valerate) *(Betnovate®)*.

PHARMACOLOGIC PROPERTIES

Pharmacodynamics

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 *(Betnovate®)*.

Genotoxicity

No specific studies have been conducted to investigate the genotoxic potential of Betamethasone valerate *(Betnovate®)*.

Fertility

The effect on fertility of Betamethasone valerate *(Betnovate®)* has not been evaluated in animals.

Pregnancy

Subcutaneous administration of Betamethasone valerate *(Betnovate®)* 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.

INDICATIONS

Betamethasone (as valerate) *(Betnovate®)* Solution for Scalp Application is used for the treatment of 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 (as valerate) *(Betnovate®)* Solution for Scalp Application should be applied to the scalp night and morning until improvement is noticeable. It may then be possible to sustain improvement by applying once a day, or less frequently.

Due to the flammable nature of Betamethasone (as valerate) (Betnovate®) Solution for Scalp Application, patients should avoid smoking or being near an open flame during application and immediately after use.

Children

Betamethasone (as valerate) *(Betnovate®)* Solution for Scalp Application 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 (as valerate) *(Betnovate®)* Solution for Scalp Application to ensure the amount applied is the minimum that provides therapeutic benefit.

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 (as valerate) *(Betnovate®)* Solution for Scalp Application is contraindicated in dermatoses in infants under one year of age, including dermatitis.

WARNINGS AND PRECAUTIONS

Betamethasone (as valerate) *(Betnovate®)* Solution for Scalp Application 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 Effects)* 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 Effects).*
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.

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

- There have been no studies to investigate the effect of Betamethasone (as valerate) *(Betnovate®)* Solution for Scalp Application 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 (as valerate) *(Betnovate®)* Solution for Scalp Application.

DRUG 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 (as valerate) *(Betnovate®)* Solution for Scalp Application 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 humans has not been established; however, administration of Betamethasone (as valerate) *(Betnovate®)* Solution for Scalp Application 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 (as valerate) *(Betnovate®)* Solution for Scalp Application during lactation should only be considered if the expected benefit to the mother outweighs the risk to the infant.

If used during lactation Betamethasone (as valerate) *(Betnovate®)* Solution for Scalp Application should not be applied to the breasts to avoid accidental ingestion by the infant.

ADVERSE EFFECTS

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, 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.*

OVERDOSAGE AND TREATMENT

Symptoms and signs

Topically applied Betamethasone valerate *(Betnovate®)* 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 overdose, Betamethasone valerate *(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.

STORAGE CONDITIONS

Store below 25°C. Keep container tightly closed when not in use. Contents are flammable. Keep away from fire, flame or heat. Do not leave Betamethasone (as valerate) *(Betnovate®)* Solution for Scalp Application in direct sunlight.

AVAILABILITY

Packaging of 30mL in plastic bottle (Box of 1's)

CAUTION

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.
Keep all medicines out of reach of children.

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