For the use only of Registered Medical Practitioners or a Hospital or a Laboratory

BETNOVATE - S

1. GENERIC NAME

Betamethasone Valerate and Salicylic Acid Skin Ointment

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains:
Betamethasone Valerate I.P. equivalent to Betamethasone 0.10 % w/w
Salicylic Acid I.P. 3.0 % w/w
in a greasy base

3. DOSAGE FORM AND STRENGTH

Ointment

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

BETNOVATE – S ointment is indicated for the treatment of subacute and chronic hyperkeratotic and dry skin diseases which respond to external topical steroid therapy.

These conditions include:

- Psoriasis (excluding widespread plaque psoriasis).
- Keratosis palmaris et plantaris (keratinisation of the palm of the hand and the sole of the foot).
- Chronic eczema or allergic skin diseases (including industrial eczema).
- Endogenous eczema/ Atopic dermatitis.
- Seborrhoeic eczema.
- Dyshidrosis lemellosa sicca (itching, dry, squamous vesicles on palms of the hand, sides of fingers or foot-soles).
- Lichen planus and lichen simplex.
- Ichthyosis.

4.2 Posology and Method of Administration

Adults, Elderly and Children over 1 year

Ointments are especially appropriate for dry, lichenified or scaly lesions.

Apply thinly and gently rub in using only enough to cover the entire affected area once or twice daily for up to 4 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.

If the condition worsens or does not improve within 2-4 weeks, treatment and diagnosis should be re-evaluated.

Atopic dermatitis (eczema)

Therapy with *BETNOVATE-S* 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- S.*

Recalcitrant dermatoses

Patients who frequently relapse

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

Application of a topical corticosteroid (without salicylic acid) 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

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

Elderly

Clinical studies of betamethasone 17-valerate 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.

4.3 Contraindications

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

- Untreated cutaneous infections.
- Rosacea.
- Acne vulgaris.
- Prutitis without inflammation.
- Perianal and genital pruritis.
- Perioral dermatitis.
- Primary cutaneous viral infections (e.g. herpes simplex, chicken pox).
- Hypersensitivity to any of the ingredients of the preparation.
- The use of *BETNOVATE – S* ointment is not indicated in the treatment of primary infected skin lesions caused by infection with fungi or bacteria; ulcerated skin lesions; dermatoses in children under one year of age, including dermatitis and napkin eruptions.

4.4 Special Warnings and Precautions for Use

BETNOVATE-S 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 4.8 Undesirable 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 4.8 Undesirable 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.

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.

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 conjunctival irritation, 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.

Percutaneous absorption of salicylic acid due to extensive use may lead to salicylism.

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.

4.5 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.

4.6 Use in Special Population (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

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 6 *Nonclinical properties*).

The relevance of this finding to human beings has not been established; however, administration of *BETNOVATE – S* ointment 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 *BETNOVATE – S* ointment during lactation should only be considered if the expected benefit to the mother outweighs the risk to the infant.

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

Fertility

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

4.7 Effects on Ability to Drive and Use Machines

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.

4.8 Undesirable Effects

Betamethasone Valerate

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, cataract, hyperglycaemia/ glucosuria, 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.

Salicylic acid

Salicylic acid may enhance absorption of steroid. Other possible effects due to salicylic acid content include dryness of the skin, skin irritation and undesired scaling.

Betamethasone valerate - Salicylic acid ointment

Betamethasone 17-valerate – salicylic acid ointment is usually well-tolerated, but if signs of hypersensitivity appear, application should stop immediately. Exacerbation of symptoms may occur.

4.9 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 4.8 Undesirable Effects*).

Treatment

In the event of overdose, *BETNOVATE-S* 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of action

Betamethasone Valerate

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.

5.2 Pharmacodynamic Properties

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

5.3 Pharmacokinetic Properties

Betamethasone Valerate

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.

6. NONCLINICAL PROPERTIES

Betamethasone Valerate

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.

7. DESCRIPTION

Ointment

Contains:
Betamethasone Valerate I.P. equivalent to Betamethasone 0.10 % w/w
Salicylic Acid I.P. 3.0 % w/w
in a greasy base

8. PHARMACEUTICAL PARTICULARS

List of Excipients

Paraffin Liquid; Paraffin White Soft.

8.1 Incompatibilities

No incompatibilities have been identified.

8.2 Shelf Life

The expiry date is indicated on the label and packaging.

8.3 Packaging Information

Aluminium tube in a carton.

8.4 Storage and Handling Instructions

Store protected from light at temperature not exceeding 25°C.
Do not freeze.

Keep out of reach of children.

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

For external use only.

9. PATIENT COUNSELLING INFORMATION

Registered Medical Practitioners may counsel their patients (and/or patient's caregiver as applicable) about the special warnings and precautions for use, drug interactions, undesirable effects, and any relevant contra-indications of *BETNOVATE-S* Patients (and/or patient's caregiver) may also be informed about posology, method of administration and storage/handling information as applicable.

10. DETAILS OF MANUFACTURER

The Manufacturing Site details are mentioned on the label and packaging.

For further information please contact:

GlaxoSmithKline Pharmaceuticals Limited,
Registered Office:
Dr. Annie Besant Road, Worli
Mumbai 400030, India.

11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE

Manufacturing License number is indicated on the label and packaging.

12. DATE OF REVISION

11-Nov-2020

Trade marks are owned by or licensed to the GSK group of companies.

Version: BEVS/PI/IN/2020/01

Prepared from: Betamethasone 17-Valerate GDS 09 / IPI 04 dated 03 April 2018 and Betamethasone 17-Valerate - Salicylic Acid GDS 09 dated 03 April 2018

Current version is Updated based on - Betamethasone 17-Valerate GDS 10 / IPI 05 dated 11 Jun 2020