1. Name of the medicinal product

a) Proprietary name of a medicine

Mediven Cream

b) Approved generic name(s)

Betamethasone Valerate BP

2 Qualitative and quantitative composition

Betamethasone Valerate 0.1% w/w

For Excipients 6.1

3 Pharmaceutical form Dosage form

Cream

4 Clinical particulars

4.1 Therapeutic indication(s)

Indicated for inflammatory dermatoses that are normally responsive to topical corticosteroid therapy and is often effective in the less responsive conditions such as psoriasis.

Indicated specially for eczema, psoriasis, lichen simplex, lichen planus, seborrhoeic dermatitis, contact sensitivity reactions and may be used as an adjunct to systemic steroid therapy in generalized erythroderma.

4.2 Posology and method of administration

Topical

Directions for use:

If no improvement is seen after two to four weeks, the diagnosis should be reconsidered and specialist referral may be necessary.
This regimen should be combined with routine daily use of emollients.
Adults, adolescents and the elderly
A small quantity of Mediven should be applied to the affected area one to three times daily or as directed by physician until improvement occurs. It may then be possible to maintain improvement by applying once a day, or even less often, or by using the appropriate ready diluted (1 in 4) preparation, Mediven Cream.
In the more resistant lesions, such as the thickened plaques of psoriasis on elbows and knees, the effect of Mediven 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.
Paediatric population
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; Courses should be limited to

five days. Occlusion should not be used.
Care should be taken when using betamethasone valerate 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.

4.3 Contra-indications

Rosacea, acne vulgaris, pruritus without inflammation, perioral dermatitis and use in widespread plaque psoriasis. Primary cutaneous viral infections (e.g. herpes simplex, chickenpox).
Hypersensitivity to any component of the preparation.
The use of Mediven skin preparations is not indicated in the treatment of primarily infected skin lesions caused by infections with fungi (e.g. candidiasis, tinea); or bacteria (e.g. impetigo); primary or secondary infections due to yeast; peri-anal and genital pruritus; dermatoses in children under 1 year of age, including dermatitis and napkin eruptions.

4.4 Special warnings and precautions for use

Long-term continuous topical therapy should be avoided where possible, particularly in infants and children, as adrenal suppression, with or without clinical features of Cushing's syndrome and reversible hypothalamic-pituitary-adrenal (HPA) axis, can occur even without occlusion. In this situation, topical steroids should be discontinued gradually under medical supervision by reducing the frequency of application, or by substituting a less potent corticosteroid because of the risk of adrenal insufficiency (see section 4.8 Undesirable Effects and Section 4.9 Overdose).
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.

The face, more than other areas of the body, may exhibit atrophic changes after prolonged treatment with potent topical corticosteroids. This must be borne in mind when treating such conditions as psoriasis, discoid lupus erythematous and severe eczema. Therefore, treatment courses should be limited to five days and occlusion should not be used. If applied to the eyelids, care is needed to ensure that the preparation does not enter the eye, as glaucoma and cataract

might result from repeated exposure.
If used in childhood, or on the face, courses should be limited to five days and occlusion should not be used.
Topical corticosteroids may be hazardous in psoriasis for a number of reasons including rebound relapses, development of tolerance, risk of generalized pustular psoriasis and development of local or systemic toxicity due to impaired barrier function of the skin. If used in psoriasis careful patient supervision is important.
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 systemic administration of antimicrobial agents. Bacterial infection is encouraged by the warm, moist conditions within skin folds or caused by induced by occlusive dressings, and so the skin should be cleansed before a fresh dressing is applied.
In rare instances, treatment of psoriasis with corticosteroids (or its withdrawal) is thought to have provoked the pustular form of the disease. Betamethasone valerate should be used with caution in patients with a history of local hypersensitivity to other corticosteroids. Mediven is usually well tolerated but if signs of hypersensitivity appear, application should stop immediately. Local hypersensitivity reactions (*see section 4.8)* may resemble symptoms of the condition under treatment. Exacerbation of symptoms may occur.
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.

4.5 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 Pregnancy and lactation

Avoid extensive use in pregnancy. There is inadequate evidence of safety. Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development including cleft palate and intrauterine growth retardation. There might therefore be a very small risk of such effects in the human fetus. 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.
This product should not be used during pregnancy or lactation unless considered essential by the physician
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 the infant.

Effects on the ability to drive and operate machinery

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.

4.6 Undesirable effects:

Local skin burning/skin pain and pruritus.

4.7 Overdose

Not applicable.

5 Pharmacological properties

5.1 Pharmacodynamic properties

ATC Code: D07 AC01 (Corticosteroid, potent,(group III))

5.2 Pharmacokinetic properties

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 metabolized, 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

5.4 Preclinical safety data

Subcutaneous administration of betamethasone valerate to mice or rats at doses ≥0.1mg/kg/day or rabbits at doses ≥12 micrograms/kg/day during pregnancy produced fetal abnormalities including cleft palate and intrauterine growth retardation.
The effect on fertility of betamethasone valerate has not been evaluated in animals.

6 Pharmaceutical particulars

6.1 List of excipients

Chlorocresol

Cetomacrogol

Emulsifying wax

Liquid Paraffin

Propylene Glycol

Polysorbate 80 (Tween-80)

Citric Acid Anhydrous

Disodium Hydrogen Phosphate Dodecahydrate

White Soft Paraffin

6.2 Incompatibilities - None known.

6.3Shelf-life -

- **In the original unopened container;** 36 months
- **After reconstitution (where appropriate)** NA
- **Shelf-life after first opening:** Not applicable

Special precautions for storage:

Mediven should be stored below 25°C, in a dry and dark place.

Keep out of the reach of children

6.4 **Nature and composition of containers**

Pack Size: 15g. Mediven Cream aluminum Tubes, Mediven Cream Leaflets, Mediven Cream unit cartons,

Instruction for use/handling

For external use only

Wash hands before and after use.

Restriction on sale / distribution:

Prescription only medicine (POM)

7 Administrative data

i. **Name and address of holder of a registration.**

Regal Pharmaceuticals Limited

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8.i Registration number. - H88/266

ii. Date of first registration- 23/09/1988