SUMMARY OF PRODUCT CHARACTERISTICS.

I. **Name of the medicinal product**

Dawavate Cream

2. Qualitative and quantitative composition

Contains: Betamethasone Valerate BP 0.1%w/w

3.0 Pharmaceutical form: Cream for External Use only

White coloured and non-gritty cream free from any visible evidence of contamination.

4.0 Clinical particulars

4.1 Therapeutic indications

Betamethasone valerate is indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

Treatment beyond 2 consecutive weeks is not recommended, and the total dosage should not exceed 50 g per week because of the potential for the drug to suppress the hypothalamic-pituitary-adrenal (HPA) axis.

In the treatment of moderate to severe plaque-type psoriasis, Betamethasone valerate applied to 5-10% of body surface area can be used up to 4 consecutive weeks. The total dosage should not exceed 50 g per week. When dosing for more than 2 weeks, any additional benefits of extending treatment

should be weighed against the risk of HPA suppression. Treatment beyond 4 consecutive weeks is not recommended.

Some guidelines for the correct use of topical corticosteroids recommend that the starting of treatment should be with a more potent preparation, treatment may then be continued with a less potent preparation and with less frequent application, once control is obtained. The most potent topical corticosteroids are generally reserved for recalcitrant dermatoses. Once the skin has healed, treatment should be tailed off. Particular care is necessary in the use of topical corticosteroids in children, and the more potent preparations like Betamethasone valerate are contra-indicated in infants under 1 year of age, although potent preparations may be needed briefly in older children. It has been suggested that a 'steroid holiday' of at least 2 weeks be considered in children after each 2 or 3 weeks of daily topical therapy to allow thinned epidermis to restore itself and maintain its barrier function.

Care is also necessary in applying corticosteroids to certain anatomical sites such as the face and flexures; some advocate using only hydrocortisone 0.5 or 1% on the face. Advice should be given that topical corticosteroids should be applied sparingly in thin layers, by smoothing gently into the skin preferably after a bath, and that no benefit is gained from more frequent than twice daily application or by vigorous rubbing.

4.2 Posology and method of administration: Cream For External application only

The preparation should be applied twice daily on the affected areas.

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4.3 Contraindications

The preparation is contraindicated in those patients with a history of hypersensitivity to corticosteroids

4.4Special warnings and precautions for u s e

Betamethasone valerate should be used with caution in patients with a history of local hypersensitivity to other corticosteroids. Local hypersensitivity 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 .

Risk factors for increased systemic effects are:

o Potency and formulation of topical steroid
o Duration of exposure
o Application to a large surface area
o 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)
o Increasing hydration of the stratum corneum
o Use on thin skin areas such as the face
o Use on broken skin or other conditions where the skin barrier may be impaired
o 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.

Paediatric population

In infants and children under 12 years of age, treatment courses should be limited to five days and occlusion should not be used; 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.

Application to the face

Prolonged application to the face is undesirable as this area is more susceptible to atrophic changes; therefore, treatment courses should be limited to five days and occlusion should not be used.

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.

Visual disturbance

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

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.

Healthcare professionals should be aware that if this product comes into contact with dressings, clothing and bedding, the fabric can be easily ignited with a naked flame. Patients should be warned of this risk and advised to keep away from fire when using this product.

4.4 Interaction with other medicinal products and other forms of interaction

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, fertility 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.

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 onl 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.

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

When applied topically, particularly to large areas, when the skin is broken, or under occlusive dressings, or when given intranasally, corticosteroids may be absorbed in sufficient amounts to cause systemic effects. Prolonged application to the eye of preparations containing corticosteroids has caused raised intra-ocular pressure and reduced visual function.

The following additional local adverse reactions are reported infrequently with topical corticosteroids, but may occur more frequently with high potency corticosteroids such as Betamethasone valerate cream. These reactions are listed in an approximately decreasing order of occurrence: dryness, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, striae, and miliaria.

4.9 Overdose.

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 .

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.

5. 0 Pharmacological properties

5.1 Pharmacodynamic properties.

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.

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 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.

5.2 Preclinical safety data

Reproductive toxicity

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.

6. Pharmaceutical particulars

6.1 List of excipients

Liquid paraffin

White soft paraffin

Cetostearyl Alcohol

Cetomacrogol 1000

Propylene glycol

Benzyl Alcohol

Sodium Acid

Phosphate

Purified water

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months from the date of manufacture. (3 years)

6.4 Special precautions for storage

Store in a dry place, below 30°C. Protected from light.Keep all medicines out of reach of childeren

6.5 Nature and contents of container

15 gms of Collapsable Aluminium tube packed in a unit box along with a literature insert.

6.6 Special precautions for disposal and other handling

None applicable.

7. Marketing authorization holder/Registrant.

Dawa limited

Plot No.7879/8, Baba Dogo Road, Ruaraka,

P.O Box 16633-00620, Nairobi-Kenya

8. Manufacturer

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9. Legal category: Pharmacy Only

10. Kenya Licence number: H2009/20349/697

11. Date of revision of the text:

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