SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Audavate RD 0.025% w/w Ointment

Betamethasone Valerate RD 0.025% w/w Ointment

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One gram of ointment contains 0.25 mg of betamethasone (0.025% w/w) as valerate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Ointment

Opaque ointment.

4.1 Therapeutic indications

Betamethasone valerate ready diluted preparations are indicated for maintenance treatment once an acute episode has been treated effectively with a continuous course of betamethasone valerate.

Betamethasone valerate is a potent topical corticosteroid indicated for adults, elderly and children over 1 year for the relief of the inflammatory and pruritic manifestations of steroid responsive dermatoses. These include the following:

Atopic dermatitis (including infantile atopic dermatitis)
Nummular dermatitis (discoid eczema)
Prurigo nodularis
Psoriasis (excluding widespread plaque psoriasis)
Lichen simplex chronicus (neurodermatitis) and lichen planus
Seborrhoeic dermatitis
Irritant or allergic contact dermatitis
Discoid lupus erythematosus
Adjunct to systemic steroid therapy in generalised erythroderma
Insect bite reactions.

4.2 Posology and method of administration

Posology

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

Once an acute episode has been treated effectively with a continuous course of betamethasone valerate, improvement may be maintained with a small amount of ready diluted betamethasone valerate applied once or twice a day.

This regimen 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.

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; therefore, courses should be limited to five days and 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.

Method of administration

Cutaneous

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

The following conditions should not be treated with betamethasone valerate:

- Untreated cutaneous infections

- Rosacea
- Acne vulgaris
- Pruritus without inflammation
- Perianal and genital pruritus
- Perioral dermatitis.

Betamethasone valerate skin preparations are contraindicated in dermatoses in infants under one year of age, including dermatitis.

4.4 Special warnings and precautions for use

Betamethasone valerate should be used with caution in patients with a history of local hypersensitivity to other corticosteroids. Local hypersensitivity reactions *(see section 4.8)* 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 section 4.8)*. 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.

<u>Paediatric population</u>
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.

<u>Infection risk with occlusion</u>
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.

<u>Use in psoriasis</u>

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.

Atopic dermatitis (eczema)
Therapy with betamethasone valerate 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 betamethasone valerate.

Topical steroid withdrawal syndrome

Long term use of topical steroids can result in the development of rebound flares after stopping treatment (topical steroid withdrawal syndrome). A severe form of rebound flare can develop which takes the form of a dermatitis with intense redness, stinging and burning that can spread beyond the initial treatment area. It is more likely to occur when delicate skin sites such as the face and flexures are treated. Should there be a reoccurrence of the condition within days to weeks after successful treatment a withdrawal reaction should be suspected. Reapplication should be with caution and specialist advise is recommended in these cases or other treatment options should be considered.

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.

Flammability risk
Product contains paraffin. Instruct patients not to smoke or go near naked flames - 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.

The label will state strong steroid.

4.5 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 Fertility, pregnancy and lactation

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 section 5.3)*.

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.

Breast-feeding

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.

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

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 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000) and not known (cannot be estimated from the available data).

Post-marketing data

Infections and infestations
Very rare: Opportunistic infection.

Immune system disorders
Very rare: Hypersensitivity, generalised rash.

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.

Not known: Withdrawal reactions - redness of the skin which may extend to areas beyond the initial affected area, burning or stinging sensation, itch, skin peeling, oozing pustules (see section 4.4).

General disorders and administration site conditions
Very rare Application site irritation/pain.

Eye disorders
Not known: Vision, blurred (see also section 4.4).

**Skin features secondary to local and/or systemic effects of hypothalamic-pituitary adrenal (HPA) axis suppression.*

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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 section 4.8).*

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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: D07 AC01 (Corticosteroid, 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.

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 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.

5.3 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.

The effect on fertility of betamethasone valerate has not been evaluated in animals.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
White soft paraffin

Liquid paraffin

6.2 Incompatibilities
None known

6.3 Shelf life
3 years.

In-use shelf life: 3 months

6.4 Special precautions for storage
Do not store above 30 °C.

6.5 Nature and contents of container

Collapsible aluminium tubes internally coated with an epoxy resin based lacquer and closed with a polypropylene cap.

Pack sizes: 100g.

6.6 Special precautions for disposal

No special instructions.

7 MARKETING AUTHORISATION HOLDER

Accord-UK Ltd
(Trading style: Accord)
Whiddon Valley
Barnstaple
Devon
EX32 8NS

8 MARKETING AUTHORISATION NUMBER(S)

PL 0142/1199

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18th September 2012

10 DATE OF REVISION OF THE TEXT

30/04/2024