SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

ARISOL CREAM (Clobetasol Propionate Cream USP 0.05% w/w).

2. Qualitative and quantitative composition

Contains:

Clobetasol Propionate USP 0.05%

Cream Base q.s.

3. Pharmaceutical form

Cream

White soft mass filled in lami tubes

4. Clinical particulars

4.1 Therapeutic indications

Clobetasol propionate is a highly active topical corticosteroid indicated adults, elderly and children over one year of the short term treatment only of more resistant inflammatory and pruritic manifestation of steroid responsive dermatoses unresponsive to less potent corticosteroids. These include the following:

Psoriasis (including widespread plaque psoriasis)

Recalcitrant dermatoses

Lichen planus

Discoid lupus erythematosus

Other skin conditions which do not respond satisfactorily to less potent steroids.

4.2 Posology and method of administration

Clobetasol propionate belongs to the most potent class of topical corticosteroids (Group IV) and prolonged use may result in serious undesirable effects (see section 4.4). If treatment with a local corticosteroid is clinically justified beyond 4 weeks, a less potent corticosteroid preparation should be considered. Repeated but short courses of clobetasol propionate may be used to control exacerbations (see details below).

Posology:

Adults and elderly and children over 1 year

Apply thinly and gently rub in using only enough to cover the entire affected area once or twice a day until improvement occurs (in the more responsive conditions this may within a few days). As with other highly active topical steroid preparations therapy should be discontinued when control is achieved.

In very resistant lesions, especially where there is hyperkeratosis, the anti-inflammatory effects of Clobetasol Cream can be enhanced, if necessary, by occluding the treatment area with polythene. Overnight occlusion only is usually adequate to bring about a satisfactory response, thereafter improvement can be usually maintained by application without occlusion.

Treatment should not be continued for more than 7 days without medical supervision. If a longer course is necessary, it is recommended that treatment should not be continued for more than 4 weeks without the patient's condition being reviewed.
Repeat short courses of Clobetasol Cream may be used to control exacerbations. If continuous steroid treatment is necessary, a less potent preparation should be used.
The maximum weekly dose should not exceed 50 g/week.
Dosage in Renal Impairment
Dosage should be reduced in patients with reduced renal function (see section 4.4).
Elderly
Clobetasol/neomycin/nystatin Cream is suitable for use in the elderly. Caution should be exercised in cases where a decrease in renal function exists and significant systemic absorption of neomycin sulfate may occur (see section 4.4). The minimum quantity should be used for the shortest duration to achieve the desired clinical benefit.
Paediatric population
Dermovate is contraindicated in children under one year of age. Children are more likely to develop local and systemic side effect of topical corticosteroids and in general, require short shorter courses and less potent agents than adults.

4.3 Contraindications

Clobetasol propionate is contraindicated in dermatoses in children under one year of age, including dermatitis and nappy eruptions. Hypersensitivity to the active substances (clobetasol propionate) or any of the excipients in section 6.1.
The following condition should not be treated with ARISOL:

Untreated cutaneous infections

Rosacea

Acne vulgaris

Pruritus without inflammation

Perianal and genital pruritus

Perioral dermatitis

4.4 Special warnings and precautions for use

Cases of osteonecrosis serious infections (including necrotizing fasciitis) and systemic immunosuppression (sometime resulting in reversible kaposis sarcoma lesions) have been reported with long term use of clobetasol propionate beyond the recommended doses (see section 4.2).

Manifestations of hypercortisolism (Cushing's syndrome) and reversible hypothalamic-pituitary-adrenal (HPA) axis suppression can occur in some individuals as a result of increased systemic absorption of topical corticosteroids.

If either the above is 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 corticosteroid systemic effects are:

• Potency and formulation of topical corticosteroid

• Duration of exposure

• Application to a large surface area

• Use on occluded areas of skin e.g. on intertriginous areas or under occlusive dressings (nappies 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

Local hypersensitivity

Local hypersensitivity reactions may resemble symptoms of the condition under treatment (see section 4.8). If signs of hypersensitivity appear, application should be stopped immediately.

Paediatric population

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 bodyweight ratio compared with adults.

Long term continuous topical therapy should be avoided where possible, particularly in infants and children, as adrenal suppression can occur readily even without occlusion.

If used in childhood, or on the face, courses should be limited to 5 days and occlusion should not be used. It should be noted that the child's napkin may act as an occlusive dressing.

Application to the face

Application to the face is undesirable as, more than other areas of the body, this area may exhibit atrophic changes after prolonged treatment with potent topical corticosteroids. If used on the face, treatment should be limited to only a few days. This must be borne in mind when treating such conditions as psoriasis and severe eczema.

Topical steroid withdrawal syndrome

Long term continuous or inappropriate 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 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 (see section 4.8). If the cream does enter the eye, it should be bathed in copious amounts of water.

Use in Psoriasis

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.

Osteonecrosis, serious infections and immunosuppression

Cases of osteonecrosis serious infections (including necrotizing fasciitis) and systemic immunosuppression (sometimes resulting in reversible Kaposi's sarcoma lesions) have been reported with long-term use of clobetasol propionate beyond the recommended doses (see section 4.2). In some cases patients used concomitantly other potent oral/topical corticosteroids or immunosuppressors (e.g. methotrexate, mycophenolate mofetil). If treatment with local corticosteroids is clinically justified beyond 4 weeks, a less potent corticosteroid preparation should be considered.

4.5 Interaction with other medicinal products and other forms of interaction

CYP3A4 inhibitors

Co-administered drugs that can inhibit CYP3A4 (e.g. ritonavir and 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.

Systemic aminoglycoside therapy

Possibility of cumulative toxicity should be considered when neomycin sulfate is applied topically in combination with systemic aminoglycoside therapy.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited data from the use of clobetasol propionate in pregnant women.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development (see section 5.3). The relevance of this finding to humans has not been established.

Breast-feeding

The safe use of clobetasol propionate during breast- feeding has not been established. It is not known whether the topical administration of corticosteroids could result in sufficient systemic absorption to product detectable amounts in breast milk. Thus, the use of clobetasol propionate is not recommended in lactation.

Fertility

There are no data in humans to evaluate the effect of topical clobetasol propionate on fertility. Clobetasol propionate administered subcutaneously to rats had no effect upon mating performance; however, fertility was decreased at the highest dose (see section 5.3). The relevant of this finding to humans has not been established.

4.7 Effects on ability to drive and use machines

Clobetasol Cream has no or negligible influence on the ability to drive and use machines.

4.8Undesirable effects

Adverse drug reaction (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 (≥1/1000 and <1/100), rare (≥1/10000 and <1/1000) and very rare (<1/10000) including isolated reports.

4.9 Overdose

Symptoms and signs

Topically applied clobetasol propionate 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 appear (see section 4.4 and 4.8).

Treatment

In the event of chronic overdosage or misuse topical steroids should be withdrawn gradually under medical supervision by reducing the frequency of application or by substituting a less potent corticosteroid because of the risk of adrenal insufficiency.

5. Pharmacological properties

5.1 Pharmacodynamic properties

ATC code: D07AD

Mechanism of action

Topical corticosteroids act as anti-inflammatory agents via multiple mechanisms to inhibit the late phase allergic reaction including decreasing the density of mast cells, decreasing chemotaxis and activation of eosinophils, decreasing cytokines production by lymphocyte, monocytes, mast cell and eosinophils, and inhibiting the metabolism of arachidonic acid.

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

5.2 Pharmacokinetic properties

Absorption

Percutaneous penetration of clobetasol propionate varies among individuals and can be increased by the use of occlusive dressings, or when the skin is inflamed or diseased.

Distribution

Mean peak plasma clobetasol propionate concentrations of 0.63ng/ml occurred in one study 8 hours after the second application (13 hours after an initial application) of 30g clobetasol propionate 0.05% ointment to normal individuals with healthy skin. Following the application of a second dose of 30g of clobetasol propionate cream 0.05% mean peak plasma concentrations were slightly higher than the ointment and occurred 10 hours after application.

Biotransformation

In a separate study, mean peak plasma concentrations of approximately 2.3ng/ml and 4.6ng/ml occurred respectively in patients with psoriasis and eczema 3 hours after a single application of 25g clobetasol propionate 0.05% ointment. However, systemic metabolism of clobetasol has never been fully characterized or quantified. Following percutaneous

ABSORPTION

absorption of clobetasol propionate the drug probably follows the metabolic pathway of systemically administered corticosteroids, i.e. metabolized primarily by the liver and then excreted by the kidneys.

5.3 Preclinical safety data

Carcinogenesis

Long term animal studies have not been performed to evaluate the carcinogenic potential of clobetasol propionate.

Reproductive toxicology

Fertility

In fertility studies, subcutaneous administration of clobetasol propionate to rats at doses of

6.25 to 50 micrograms/kg/day produced no effects on mating, and fertility was only decreased at 50 micrograms/kg/day.

Genotoxicity

Clobetasol propionate was not mutagenic in a range of in vitro bacterial cell assays.

Reproductive toxicology

Fertility

pregnancy

Subcutaneous administration of clobetasol propionate to mice (≥100 micrograms/kg/day), rats (400 micrograms/kg/day) or rabbits (1 to 10 micrograms/kg/day) during pregnancy produced foetal abnormalities including cleft palate.

In the rat study, where some animals were allowed to litter, developmental delay was observed in the F1 generation at ≥100 micrograms/kg/day and survival was reduced at 400 micrograms/kg/day. No treatment-related effects were observed in F1 reproductive performance or in the F2 generation.

6. Pharmaceutical particulars

6.1 List of excipients

Purified Water

Sodium Dihydrogen Phosphate Dihydrate

Propylene Glycol

White Soft Paraffin

Light Liquid Paraffin

Cetostearyl Alcohol

Emulsifying wax

6.2 Incompatibilities

Not applicable

.**6.3 Shelf life**

24 Months

6.4 Special precautions for storage

Do not store above 25°C. Keep out of reach of children

6.5 Nature and contents of container

Cream

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

Ointment

Collapsible, aluminium tubes, coated internally with an epoxy resin based lacquer or unlacquered and closed with a cap

6.6 Special precautions for disposal and other handling

Patients should be advised to wash their hands after applying ARISOL cream unless it is the hands that are being treated.

7. Marketing authorization holder

MERIT ORGANICS LIMITED

PLOT N0. 2104/2/1, G.I.D.C, SARIGAM, DIST. - VALSAD, GUJARAT, INDIA.

NAFDAC REG.NO:

Manufactured By:

MERIT ORGANICS LIMITED

PLOT N0. 2104/2/1, G.I.D.C, SARIGAM, DIST. - VALSAD, GUJARAT, INDIA.