CLOBETASOL CREAM

(Clobetasol Cream USP 0.05%W/W)

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. Name of the medicinal product

CLOBETASOL CREAM

(Clobetasol Cream USP 0.05%W/W)

2. Qualitative and quantitative composition

Composition: Each Gram Contains:
Clobetasol Propionate USP 0.05 % w/w
Cream base……q.s.

BatchSize:1000kg

UNITFORMULA

INGREDIENTS	LABEL CLAIM	OVERAGES	QTY/BATCH(Kg)	REFERENCE
Clobetasol Propionate	0.05% w/w	2%	0.1581	USP
Chlorocresol	0.1%	--	0.310	BP
Light Liquid Paraffin	10%	--	31.00	BP
Hard Paraffin Wax	2%	--	6.200	BP
Microcrystalline Wax	1.5%	--	18.600	BP
BHT	0.05%	--	0.155	BP
CetoSteryl Alcohol	7%	-	21.700	BP
Cetomacrogol-1000	2%	--	6.200	BP
Methyl Paraben	0.16%	--	0.496	BP
Propyl Paraben	0.040%		0.124	BP
Disodium EDTA	0.1%	--	0.310	BP
Col.Erythrocin (Supra)	--	--	2.480	BP
Col Panceau 4 R (Supra)	--	--	1.240	BP
Glycerine	1%		3.00	BP
Propylene Glycol	1.612%		5.00	BP
Perfume Ponds	0.12%		0.372	BP
Purified Water	--	--	QS to 310 Kg	BP

3. Pharmaceutical form

Cream. A pink Coloured Perfumated cream

CLOBETASOL CREAM

(Clobetasol Cream USP 0.05%W/W)

4. Clinical particulars

4.1 Therapeutic indications

Clobetasol is a very potent topical corticosteroid indicated for adults, elderly and children over 1 year for the short term treatment only of more resistant inflammatory and pruritic manifestations of steroid responsive dermatoses unresponsive to less potent corticosteroids. These include the following:

- Psoriasis (excluding 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

Posology

Creams are especially appropriate for moist or weeping surfaces.

Adults, 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 be within a few days), 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.

Repeated short courses of clobetasol propionate may be used to control exacerbations.

In more resistant lesions, especially where there is hyperkeratosis, the effect of clobetasol 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. Thereafter improvement can usually be maintained by application without occlusion.

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

Treatment should not be continued for more than 4 weeks. If continuous treatment is necessary, a less potent preparation should be used.

The maximum weekly dose should not exceed 50 gms/week.

Therapy with clobetasol 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 clobetasol.

Recalcitrant dermatoses: Patients who frequently relapse

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

Application should be continued to all previously affected sites or to known sites of potential relapse. 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

Clobetasol Cream 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 clobetasol propionate to ensure the amount applied is the minimum that provides therapeutic benefit.

Duration of treatment for children and infants

Courses should be limited if possible to five days and reviewed weekly. Occlusion should not be used.

Application to the face

Courses should be limited to five days if possible and occlusion should not be used.

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 Contraindications

Hypersensitivity to the active substance or any of the excipients listed.

The following conditions should not be treated with Clobetasol Cream:

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

Clobetasol is contraindicated in dermatoses in children under one year of age, including dermatitis and nappy eruptions.

4.4 Special warnings and precautions for use

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. 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.

Clobetasol should be used with caution in patients with a history of local hypersensitivity to other corticosteroids or to any of the excipients in the preparation. 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.

Clobetasol Cream contains:

- Propylene glycol may cause skin irritation.
- Cetostearyl alcohol which may cause local skin reactions (e.g. contact dermatitis).
- chlorocresol which may cause allergic reactions.

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 comeum
- 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 and infants 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, long-term continuous topical corticosteroid therapy should be avoided where possible, as adrenal suppression can occur

Children are more susceptible to develop atrophic changes with the use of topical corticosteroids.

Duration of treatment for children and infants

Courses should be limited if possible to five days and reviewed weekly. Occlusion should not be used.

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.

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.

Application to the face

Application to the face is undesirable as this area is more susceptible to atrophic changes.

If used on the face, treatment should be limited to 5 days.

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. If clobetasol does enter the eye, the affected eye should be bathed in copious amounts of water.

Visual disturbance

Visual disturbance has been 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.

Clobetasol cream 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 bums more easily and is a serious fire hazard. Washing clothing and bedding may reduce product build-up but not totally remove it.

4.5 Interaction with other medicinal products and other forms of interaction

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

4.6 Pregnancy and lactation

Pregnancy

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development

The relevance of this finding to humans has not been established. Administration of clobetasol 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 the topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable amounts in breast milk. Administration of clobetasol during lactation should only be considered if the expected benefit to the mother outweighs the risk to the infant.

If used during lactation clobetasol 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 clobetasol 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 clobetasol.

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 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 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, hyperglycaemia/glucosuria, hypertension, increased weight/obesity, decreased endogenous cortisol levels, alopecia, trichorrhexis

Skin and Subcutaneous Tissue Disorders

Common Pruritus, local skin burning /skin pain

Uncommon Skin atrophy*, striae*, telangiectasias*

Very rare Skin thinning*, skin wrinkling*, skin dryness*, pigmentation changes*, hypertrichosis, exacerbation of underlying symptoms, allergic contact dermatitis/dermatitis, pustular psoriasis, erythema, rash, urticaria, acne

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

General Disorders and Administration Site Conditions

Very rare Application site irritation/pain

Eye disorders

Very rare Cataract, central serous chorioretinopathy, glaucoma

Not known (cannot be estimated from available data): Vision, blurred

4.9 Overdose

Symptoms

Topically applied clobetasol 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.

Management

In the event of overdose, clobetasol 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

Pharmacotherapeutic group: Corticosteroids, very potent (group IV)

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.

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

In a separate study, mean peak plasma concentrations of approximately 2.3 ng/ml and 4.6 ng/ml occurred respectively in patients with psoriasis and eczema three hours after a single application of 25 g clobetasol propionate 0.05% ointment.

Distribution

The use of pharmacodynamic endpoints for assessing the systemic exposure of topical corticosteroids is necessary due to the fact that circulating levels are well below the level of detection.

Biotransformation

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

Carcinogenesis / Mutagenesis

Carcinogenesis

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

Genotoxicity

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

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.

Pregnancy

Subcutaneous administration of clobetaol 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 and intrauterine growth retardation.

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

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6. Pharmaceutical particulars

6.1 List of excipients

Clobetasol Propionate ,Chlorocresol ,Light Liquid Paraffin ,Hard Paraffin Wax ,Microcrystalline Wax ,BHT ,CetoSteryl Alcohol ,Cetomacrogol-1000 ,Methyl Paraben ,Propyl Paraben ,Disodium EDTA ,Col.Erythrocin (Supra) ,Col Panceau 4 R (Supra) ,Glycerine Propylene Glycol ,Perfume Ponds
Purified Water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Keep below 30°C & dry place. Protect from light.

6.5 Nature and contents of container

30 g tube in a inner carton. such 10 inner cartons placed in outer carton

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorisation holder

NAFRO PHARMA NIGERIA LTD
Suite B16, Amori shopping Plaza,
113, Idimu Road, Orelope Egbeda Lagos,Nigeria

Manufacturer Name

Astamed Healthcare (I) Pvt. Ltd.

Plot No. 2 & 3, Phase-II, Genesis Ind. Complex,

Kolgaon, Palghar-401404, Maharashtra, India

8. Marketing authorisation number(s)

9. Date of first authorisation/renewal of the authorisation

10. Date of revision of the text