PRIYA PHARMACEUTICAL NIG. LIMITED

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

PRIYA CLOBETASOL CREAM BP (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 which is of particular value when used in short courses for the treatment of recalcitrant eczemas, neurodermatoses, and other conditions which do not respond satisfactorily to less active steroids.

Clobetasol/neomycin/nystatin Cream is indicated in more resistant dermatoses such as recalcitrant eczemas and psoriasis (excluding widespread plaque psoriasis) where secondary bacterial or candidal infection is present, suspected or likely to occur, as when using occlusive dressings.

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 adolescents

Apply sparingly to the affected area once or twice daily until improvement occurs. As with other highly active topical steroid preparations therapy should be discontinued when control is achieved. In the more responsive conditions this may be within a few days.

In very resistant lesions, especially where there is hyperkeratosis, the anti-inflammatory effects of Clobetasol/neomycin/nystatin 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/neomycin/nystatin 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

Clobetasol/neomycin/nystatin Cream is suitable for use in children (2 years and over) at the same dose as adults. A course of treatment for a child 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. A possibility of increased absorption exists in very young children; thus, this cream is not recommended for use in neonates and infants (younger than 2 years) (see sections 4.3 and 4.4).

Care should be taken when using clobetasol propionate with neomycin sulfate and nystatin to ensure the amount applied is the minimum that provides therapeutic benefit.

Method of administration:

For cutaneous use.

4.3 Contraindications

Clobetasol propionate with neomycin sulfate and nystatin is contraindicated in patients who have demonstrated hypersensitivity to the active substances (clobetasol propionate, neomycin sulfate and nystatin), to arachis oil (peanut oil) or any of the excipients listed in section 6.1 (see sections 4.4 and 4.8).

Rosacea, acne vulgaris and perioral dermatitis.

Primary cutaneous viral infections (e.g. herpes simplex, chickenpox).

Pruritus without inflammation.

Use of Clobetasol/neomycin/nystatin skin preparations is not indicated in the treatment of primary infected skin lesions caused by infection with fungi (e.g. candidiasis, tinea), bacteria (e.g. impetigo), or yeast; secondary infections due to Pseudomonas or Proteus species; perianal and genital pruritus, dermatoses in children under 2 years of age, including dermatitis and napkin eruptions.

Preparations containing neomycin should not be used for the treatment of otitis externa when the eardrum is perforated, because of the risk of ototoxicity.

Due to the known ototoxic and nephrotoxic potential of neomycin sulfate the use of this medicinal product in large quantities or on large areas for prolonged periods is not recommended in circumstances where significant systemic absorption may occur.

A possibility of increased absorption exists in very young children; therefore Clobetasol/neomycin/nystatin Cream is not recommended for use in neonates and infants (up to 2 years). In neonates and infants, absorption by immature skin may be enhanced, and renal function may be immature.

4.4 Special warnings and precautions for use

Pseudomembranous colitis

Pseudomembranous colitis has been reported with the use of antibiotics and may range in severity from mild to life-threatening. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea during or after antibiotic use. Although this is less likely to occur with topically applied neomycin, if prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further.

Reversible hypothalamic-pituitary-adrenal (HPA) axis suppression

Manifestations of hypercortisolism (Cushing's syndrome) and reversible hypothalamicpituitary-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 corticosteroidal 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.

Infection

Extension of the infection may occur due to the masking effect of the steroid.

If infection persists, systemic chemotherapy is required. Any spread of infection requires withdrawal of topical corticosteroid therapy.

Infection risk with occlusion

Bacterial infection is encouraged by the warm, moist conditions induced by occlusive dressings, and the skin should be cleansed before a fresh dressing is applied.

Ototoxicity and nephrotoxicity

Following significant systemic absorption, aminoglycosides such as neomycin can cause irreversible ototoxicity; and neomycin has nephrotoxic potential (see section 4.3).

Renal impairment

In renal impairment, the plasma clearance of neomycin is reduced (see section 4.2).

Contact sensitisation

Extended or recurrent application may increase the risk of contact sensitization.

Dilution

Products which contain antimicrobial agents should not be diluted.

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.

Fire hazard in contact with dressings, clothing and bedding

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.

Excipients:

Arachis oil: Clobetasol/neomycin/nystatin Cream contains arachis oil (peanut oil) and should not be taken/applied by patients known to be allergic to peanuts. As there is a possible relationship between allergy to peanut and allergy to soya, patients with soya allergy should also avoid this medicinal product.

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.

Neuromuscular blocking agents

Following significant systemic absorption neomycin sulfate can intensify and prolong the respiratory depressant effects of neuromuscular blocking agents. However, if used in accordance with the recommendations systemic exposure to neomycin sulfate is expected to be minimal and drug interactions are unlikely to be significant.

No hazardous interactions have been reported with use of clobetasol propionate or nystatin.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited data from the use of clobetasol propionate with neomycin sulfate and nystatin 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.

Breast-feeding

The safe use of clobetasol propionate with neomycin sulfate and nystatin during breastfeeding 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 with neomycin sulfate and nystatin is not recommended in lactation.

Fertility

There are no data in humans to evaluate the effect of topical clobetasol propionate with neomycin sulfate and nystatin 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/neomycin/nystatin Cream has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The following adverse reactions have been reported with use of clobetasol propionate. The frequency of these adverse events is unknown.

Immune System Disorders - Hypersensitivity: Local hypersensitivity reactions such as erythema, rash, pruritus, urticaria and allergic contact dermatitis may occur at the site of application and may resemble symptoms of the condition under treatment. If signs of hypersensitivity appear, application should be stopped immediately.

Endocrine Disorders - Features of Cushing's Syndrome: As with other topical corticosteroids,

prolonged use especially of large amounts, or treatment of extensive areas can lead to sufficient

systemic absorption to produce the features of Cushing's syndrome. This effect is more likely to

occur in infants and children, and if occlusive dressings are used. In infants, the nappy may act as

an occlusive dressing. Provided the weekly dosage is less than 50 gram in adults, any

suppression of the HPA axis is likely to be transient with a rapid return to normal values once the

short course of steroid therapy has ceased. The same applies to children given proportionate

dosage.

Vascular Disorders - Dilatation of the Superficial Blood Vessels: Prolonged and intensive

treatment with potent corticosteroid preparations may cause dilatation of the superficial blood

vessels, particularly when occlusive dressings are used, or when skin folds are involved.

Skin and Subcutaneous Tissue Disorders: Local skin burning, local atrophy, striae, thinning,

pigmentation changes, hypertrichosis, exacerbation of underlying symptoms, pustular psoriasis.

Prolonged and intensive treatment with potent corticosteroid (clobetasol) preparations may cause

local atrophic changes, such as thinning and striae

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.

Consideration should be given to significant systemic absorption of neomycin sulfate (see section 4.4 and 4.5). If this is suspected, use of the product should be stopped and the patient's general status, hearing acuity, renal and neuromuscular functions should be monitored.

Blood levels of neomycin sulfate should also be determined. Haemodialysis may reduce the serum level of neomycin sulfate.

Further management should be as clinically indicated or as recommended by the National Poisons Centre, where available.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacoterapeutic group: Clobetasol and antibiotics, ATC code: D07CD01

Mechanism of action

Clobetasol propionate is a highly active corticosteroid with topical anti-inflammatory activity. The major effect of clobetasol propionate on skin is a non-specific anti-inflammatory response, partially due to vasoconstriction and decrease in collagen synthesis.

The use of nystatin in the local treatment of candidal infections of the skin and of neomycin as a broad-spectrum antibiotic is well known.

The principle action of the preparation is based on the anti-inflammatory activity of the corticosteroid. The broad spectrum antibacterial and anti-candidal activity provided by the combination of neomycin and nystatin allow this effect to be utilised in the treatment of condition which are likely to become infected.

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 characterised or quantified. Following percutaneous absorption of clobetasol propionate the drug probably follows the metabolic pathway of systemically administered corticosteroids, i.e. metabolised primarily by the liver and then excreted by the kidneys.

5.3 Preclinical safety data

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.

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

Cetostearyl Alcohol

Emulsifying wax

6.2 Incompatibilities

Not applicable

.**6.3 Shelf life**

36Months

6.4 Special precautions for storage

Do not store above 30°C. Keep out of reach of children

6.5 Nature and contents of container

1x30g Tube packed in a unit carton along with pack insert.

6.6 Special precautions for disposal and other handling Do not dilute.

Patients should be advised to wash their hands after applying Clobetasol/neomycin/nystatin Cream unless it is the hands that are being treated.

7. Marketing authorisation holder Priya Pharmaceutical Nig. Ltd

Location (address):

C-1, Airport Road 2F,

Kano, Kano State,

Country: NIGERIA

Telephone: 08120966231

E-Mail: priyapharmaceutical1@gmail.com

Website:

Manufacturer

Gopaldas Visram and Company Limited, PLOT NO. A-327, TTC INDUSTRIAL AREA, MIDC, MAHAPE, NAVI MUMBAI - 400710, INDIA

8. Marketing authorisation number(s)

A4-100198

9. Date of first authorisation/renewal of the authorisation

28th April, 2022

10. Date of revision of the text

April, 2027