1.3 Product Information

1.3.1 Summary of Product Characteristics (SmPC): Enclosed

1. NAME OF THE MEDICINAL PRODUCT:

SAVIXINE (Clobetasol Propionate and Clotrimazole Cream)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Composition:

- Clobetasol Propionate USP (0.05 % W/W)
- Clotrimazole BP (1.00 % W/W)
- Cream Base (- QS)

3. PHARMACEUTICAL FORM: TOPICAL CREAM

A white to off-white smooth perfumed cream.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications:

Clobetasol propionate is a very active topical corticosteroid which is of particular value when used in short courses for the treatment of more resistant dermatoses such as psoriasis (Excluding widespread plaque psoriasis), recalcitrant eczemas, lichen planus, discoid lupus erythematosus, and other skin conditions which do not respond satisfactorily to less active steroids. Clotrimazole is indicated for the topical treatment of candidiasis due to Candida albicans and Tinea versicolor due to Malassezia furfur gel is also indicated for the topical treatment of the following dermal infections: Tinea pedis, Tinea cruris and Tinea corporis due to Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum and Microsporum canis.

4.2 Posology and method of administration

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.

If no improvement is seen within two to four weeks, reassessment of the diagnosis, or referral, may be necessary.

Repeated short courses of Clobetasol Propionate & Clotrimazole Cream may be used to control exacerbations. If continuous steroid treatment is necessary, a less potent preparation should be used.

In very resistant lesions, especially where there is hyperkeratosis, the anti-inflammatory effect of Clobetasol Propionate & Clotrimazole Cream 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.

Gently massage sufficient Clobetasol Propionate & Clotrimazole Cream into the affected and surrounding skin areas twice a day in the morning and evening. Clinical improvement with relief of pruritus usually occurs within the first week of treatment with Clobetasol Propionate & Clotrimazole Cream. If the patient shows no clinical improvement after 4 weeks of treatment with Clobetasol Propionate & Clotrimazole Cream the diagnosis should be reviewed.

Method of Administration: For topical application.

4.3 Contraindications

• Rosacea

• Acne vulgaris

• Perioral dermatitis

• Perianal and genital pruritus

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

• Hypersensitivity to the preparation

• The use of Clobetasol Propionate & Clotrimazole Cream skin preparations is not indicated in the treatment of primary infected skin lesions caused by infection with fungi (e.g. candidiasis, tinea) or bacteria (e.g. impetigo); or dermatoses in children under one year of age, including dermatitis and napkin eruptions.

4.4 Special warnings and precautions for use

Long-term continuous therapy should be avoided where possible, particularly in infants and children, as adrenal suppression can occur even without occlusion. If Clobetasol Propionate & Clotrimazole Cream is required for use in children, it is recommended that the treatment should be reviewed weekly. It should be noted that the infant's napkin may act as an occlusive dressing.

If used in childhood or on the face, courses should be limited if possible to five days and occlusion should not be used.

The face, more than other areas of the body, may exhibit atrophic changes after prolonged treatment with potent topical corticosteroids. This must be borne in mind when treating such conditions as psoriasis, discoid lupus erythematosus and severe eczema.

If applied to the eyelids, care is needed to ensure that the preparation does not enter the eye, as glaucoma might result. If Clobetasol Propionate & Clotrimazole Cream gel does enter the eye, the affected eye should be bathed in copious amounts of water.

Topical steroids 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.

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

There have been a few reports in the literature of the development of cataracts in patients who have been using corticosteroids for prolonged periods of time. Although it is not possible to rule out systemic corticosteroids as a known factor, prescribers should be aware of the possible role of corticosteroids in cataract development.

Clobetasol Propionate & Clotrimazole Cream contains Cetostearyl alcohol which can cause local skin reactions (e.g. contact dermatitis), propylene glycol which may cause skin irritation and chlorocresol which may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

SAVIXINE (Clobetasol Propionate and Clotrimazole Cream) may interact with other corticosteroids (prednisone), respiratory-related medicines (budesonide, formoterol) and drugs that lower the immune system (cyclosporine).

4.6 Fertility, pregnancy and lactation

Fertility: No human studies of the effects of clotrimazole on fertility have been performed; however, animal studies have not demonstrated any effects of the drug on fertility.

Pregnancy: There is a limited amount of data from the use of clotrimazole in pregnant women. Animal studies with clotrimazole have shown reproductive toxicity at high oral doses. At the low systemic exposures of clotrimazole following topical treatment, harmful effects with respect to reproductive toxicity are not predicted. Clotrimazole can be used during pregnancy, but only under the supervision of a physician or midwife.

Lactation: Available Pharmacodynamic / toxicological data in animals have shown excretion of clotrimazole/metabolites in milk after intravenous administration. A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from clotrimazole therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

4.7 Effects on ability to drive and use machines

The medicinal product has no influence on the ability to drive or operate machinery.

4.8 Undesirable effects

The following adverse reactions have been identified during post-approval use of clobetasol propionate. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. The frequency of these adverse events has therefore been classified as “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. As the listed undesirable effects are based on spontaneous reports, assigning an accurate frequency of occurrence for each is not possible. Immune system disorders: allergic reaction (syncope, hypotension, dyspnea, urticaria). Skin and subcutaneous tissue disorders: blisters, discomfort/pain oedema, erythema irritation, peeling/exfoliation, pruritus, rash, stinging/burning.

Endocrine disorders

Features of Cushing's syndrome

As with other topical corticosteroids, prolonged use of large amounts, or treatment of extensive areas can result in 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 50g 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 highly active 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 highly active corticosteroid preparations may cause local atrophic changes, such as thinning and striae.

• Treatment of psoriasis with corticosteroids (or its withdrawal) is thought to have provoked the pustular form of the disease.

4.9 Overdose

Acute overdosage is very unlikely to occur, however, in the case of chronic overdosage or misuse, the features of hypercortisolism may appear and in this situation topical steroids should be reduced or discontinued gradually, under medical supervision.

No risk of acute intoxication is seen as it is unlikely to occur following a single dermal application of an overdose (application over a large area under conditions favourable to absorption) or inadvertent oral ingestion. There is no specific antidote. However, in the event of accidental oral ingestion, gastric lavage is rarely required and should be considered only if a life-threatening amount of Clotrimazole has been ingested within the preceding hour or if clinical symptoms of overdose become apparent (e.g. dizziness, nausea or vomiting). Gastric lavage should be carried out only if the airway can be protected adequately.

5. Pharmacological properties

5.1Pharmacodynamic Properties:

Pharmacotherapeutic group: Corticosteroids combinations with antibiotics

ATC code: D07CD01

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.

Clotrimazole acts against fungi by inhibiting ergosterol synthesis. Inhibition of ergosterol synthesis leads to structural and functional impairment of the fungal cytoplasmic membrane. Clotrimazole has a broad antimycotic spectrum of action in vitro and in-vivo, which includes dermatophytes, yeasts, moulds, etc. Under appropriate test conditions, the MIC values for these types of fungi are in the region of less than 0.062-8.0 µg/ml substrate. The mode of action of clotrimazole is primarily fungistatic or fungicidal depending on the concentration of clotrimazole at the site of infection. In vitro activity is limited to proliferating fungal elements; fungal spores are only slightly sensitive. In addition to its antimycotic action, clotrimazole also acts on gram-positive microorganisms (Streptococci/ Staphylococci/

Gardnerella vaginalis), and gram-negative microorganisms (Bacteroides). In vitro clotrimazole inhibits the multiplication of Corynebacteria and gram-positive cocci – with the exception of Enterococci - in concentrations of 0.5-10 µg/ml substrate. Primarily resistant variants of sensitive fungal species are very rare; the development of secondary resistance by sensitive fungi has so far only been observed in very isolated cases under therapeutic conditions.

5.2 Pharmacokinetic properties:

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.

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.

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. However, systemic metabolism of clobetasol has never been fully characterised or quantified.

Pharmacokinetic investigations after dermal application have shown that clotrimazole is minimally absorbed from the intact or inflamed skin into the human blood circulation. The resulting peak serum concentrations of clotrimazole were below the detection limit of 0.001 mcg/ml, suggesting that clotrimazole applied topically is unlikely to lead to measurable systemic effects or side effects.

5.3 Preclinical safety data

Not applicable.

6. Pharmaceutical particulars

6.1 List of excipients

Cetomacrogol 1000 INH

Cetostearyl alcohol BP

White Soft Paraffin BP

Methyl Paraben BP

Propyl Paraben BP

Sodium Acid Phosphate BP

Disodium Acid Phosphate BP

Propylene Glycol BP

Light Liquid Paraffin BP

Isopropyl Myristate BP

Perfume INH

Dimethicone 100 BP

Purified water BP

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at temperature not exceeding 30°C; do not freeze.

6.5 Nature and contents of container

30gm lami tube is packed in printed inner carton along with leaflet.

6.6 Special precautions for disposal and other handling

Not Applicable

ADMINISTRATIVE DATA:

7. Marketing authorization holder

Kremoint Pharma Private Limited

B-8 Additional MIDC, Ambernath

Ambernath (E). Thane 421506.

Applicant
Saivilo Pharmaceutical Ltd
Nigeria.

8. Marketing authorization number(s):

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9. Date of first authorization/renewal of the authorization

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10. Date of revision of the text:
