SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

a) TRADE NAME : SIXNOCID CREAM

b) GENERIC NAME : Clobetasol Propionate & Clotrimazole

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

COMPOSITION:

Clobetasol Propionate USP	0.05 % w/w
Clotrimazole BP	1.00 % w/w
Cream Base	Q.S.

3. PHARMACEUTICAL FORM

CREAM (TOPICAL)

4. Clinical particulars

4.1 Therapeutic indications

SIXNOCID CREAM is indicated for the local treatment of oropharyngeal candidiasis, eczema and psoriasis and vaginal yeast infections, also used in fungal infections of the skin such as ringworm, athlete's foot, and jock itch. It is also highly effective for contact dermatitis caused by exposure to poison ivy/oak.

4.2 Posology and method of administration

Apply SIXNOCID CREAM in sufficient quantity covering the affected zone and massage till complete absorption of the product. Apply SIXNOCID CREAM once or twice a day, in small quantities till there is an improvement like with other very active corticoids, the treatment will be stopped as soon as the lesions are under control. In infections which respond well to the treatment, stoppage can take place after a few days. If a long-term treatment is necessary it is advisable not to extend it beyond 2 weeks without medical supervision.

4.3 Contraindications

SIXNOCID CREAM is contraindicated in Children <12 years. Long-term treatment of ulcerative conditions, rosacea, pruritus; presence of acute infections Hypersensitivity.

4.4 Special warnings and precautions for use

General: Clotrimazole should be used cautiously during pregnancy. It should be used with caution in patients with medical history or allergies. Topical application of clotrimazole is contraindicated in the children under the age of 2, unless recommended by the physician. **Clobetasol propionate** is a highly potent topical corticosteroid that has been shown to suppress the HPA axis at doses as low as 2 g per day. Systemic absorption of topical corticosteroids has resulted in reversible HPA axis suppression, manifestations of Cushing' syndrome, hyperglycaemia, and glucosuria in some patients.

Conditions that augment systemic absorption include the application of the more potent corticosteroids, use over large surface areas, prolonged use, and the addition of occlusive dressings. Therefore, patients receiving a large dose of a potent topical steroid applied to a large surface area should be evaluated periodically for evidence of HPA axis suppression by using the urinary free cortisol and ACTH stimulation tests. If HPA axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid.
Recovery of HPA axis function is generally prompt and complete upon discontinuation of the drug. Infrequently, signs and symptoms of steroid withdrawal may occur, requiring supplemental systemic corticosteroids.
Children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity.
If irritation develops, topical corticosteroids should be discontinued and appropriate therapy instituted.
In the presence of dermatologic infections, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favourable response does not occur promptly, the corticosteroid should be discontinued until the infection has been adequately controlled.
Certain areas of the body, such as the face, groin, and axillae, are more prone to atrophic changes than other areas of the body following treatment with corticosteroids. Frequent observation of the patient is important if these areas are to be treated.
As with other potent topical corticosteroids, Clobetasol Propionate Cream should not be used in the treatment of rosacea and perioral dermatitis. Topical corticosteroids in general should not be used in the treatment of acne or as sole therapy in widespread plaque psoriasis.

Information for Patients: Patients using Clobetasol Propionate Cream should receive the following information and instructions:
This medication is to be used as directed by the physician and should not be used longer than the prescribed time period. It is for external use only. Avoid contact with the eyes.
This medication should not be used for any disorder other than that for which it was prescribed.
The treated skin area should not be bandaged or otherwise covered or wrapped so as to be occlusive.
Patients should report any signs of local adverse reactions to the physician.

4.5 Interaction with other medicinal products and other forms of interaction
None have been reported on local application. Avoid using other topical medications, harsh or abrasive soaps, or cosmetics on the affected area.

4.6 Fertility, pregnancy and lactation

Pregnancy: Teratogenic Effects: Pregnancy Category C: The more potent corticosteroids have been shown to be teratogenic in animals after dermal application. Clobetasol propionate has not been tested for teratogenicity by this route; however, it is absorbed percutaneously, and when administered subcutaneously it was a significant teratogen in both the rabbit and the mouse. Clobetasol propionate has greater teratogenic potential than steroids that are less potent.

There are no adequate and well-controlled studies of the teratogenic effects of topically applied corticosteroids, including clobetasol, in pregnant women. Therefore, clobetasol and other topical corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus, and they should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.

Nursing Mothers: It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. Systemically administered corticosteroids are secreted into breast milk in quantities not likely to have a deleterious effect on the infant. Nevertheless, caution should be exercised when topical corticosteroids are prescribed for a nursing woman.

Paediatric Use: Use of this Cream in children under 12 years of age is not recommended. Paediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced HPA axis suppression and Cushing' syndrome than mature patients because of a larger skin surface area to body weight ratio.

HPA axis suppression, Cushing' syndrome, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include linear growth retardation, delayed weight gain, low plasma cortisol levels, and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelle, headaches, and bilateral papilledema.

Clotrimazole has not been associated with teratogenic effects but following oral administration of high doses to rats, there was evidence of Foetotoxicity. The relevance of this effect to topical application in humans is not known. However, clotrimazole has been used in pregnant patients for over a decade without attributable effects. It is therefore recommended that clotrimazole should be used in pregnancy only when considered necessary by the clinician.

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

SIXNOCID CREAM is generally well tolerated when used for two-week treatment periods. Burning sensation, stinging sensation, Erythema, stinging, irritation; hypersensitivity reactions; contact dermatitis, and itching of skin may occur on applied portion which disappear shortly after application.

Use of large amounts of SIXNOCID CREAM over prolonged periods can lead to sufficient systemic levels, which produces adrenal suppression, Cushing’s syndrome.

4.9 Overdose

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

5. Pharmacological properties

5.1 Pharmacodynamic properties

Mechanism of Action:

1. Clobetasol propionate

Like other topical corticosteroids, has anti-inflammatory, antipruritic, and vasoconstrictive properties. The mechanism of the anti-inflammatory activity of the topical steroids, in general, is unclear. However, corticosteroids are thought to act by the induction of phospholipase A2 inhibitory proteins, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2.

2. Clotrimazole

Clotrimazole alters the permeability of the fungal cell wall and inhibits the activity of enzymes within the cell. It specifically inhibits the biosynthesis of ergosterol and other sterols required for cell membrane production. Clotrimazole may also inhibit endogenous respiration, interact with membrane phospholipids, inhibit the transformation of yeasts to mycelia forms and the uptake of purine, impair triglyceride and/or phospholipid biosynthesis, and inhibit the movement of calcium and potassium ions across the cell membrane by blocking the ion transport pathway known as the Gardos channel.

5.2 Pharmacokinetic properties

1. Clobetasol propionate:

The extent of percutaneous absorption of topical corticosteroids, including clobetasol propionate, is determined by many factors, including the vehicle, the integrity of the epidermal barrier, and the use of occlusive dressings.

As with all topical corticosteroids, clobetasol propionate can be absorbed from normal skin. Inflammation and/or other disease processes in the skin may increase percutaneous absorption. Occlusive dressings substantially increase the percutaneous absorption of topical corticosteroids. Once absorbed through the skin, topical corticosteroids enter pharmacokinetic pathways similarly to systemically administered corticosteroids. Corticosteroids are bound to plasma proteins in varying degrees. Corticosteroids are metabolized primarily in the liver and are then excreted by the kidneys. Some of the topical corticosteroids, including clobetasol propionate and its metabolites, are also excreted into the bile.

This Cream has been shown to depress the plasma levels of adrenal cortical hormones following repeated nonocclusive application to diseased skin in patients with psoriasis and eczematous dermatitis. These effects have been shown to be transient and reversible upon completion of a two-week course of treatment.

2. Clotrimazole

Pharmacokinetic investigations after dermal application have shown that clotrimazole is practically not absorbed from intact or inflamed skin into the human blood circulation. The resulting peak serum concentrations of clotrimazole were below the detection limit of 0.01

microg/ ml, reflecting that clotrimazole applied topically does not lead to measurable systemic effects or side effects.

5.3 Preclinical safety data
Not applicable.

6. Pharmaceutical particulars

6.1 List of excipients
Cetamacrogal 1000
Cetostearyl Alcohol
White Soft Paraffin
Methyl Paraben
Propyl Paraben
Sodium Acid Phosphate
Disodium Hydrogen Phosphate
Propylene Glycol
Light Liquid Paraffin
Iso-Propyl Myristate
Dimethicone 100 cps
Purified Water

6.2 Incompatibilities
None known.
6.3 Shelf life
36 months

6.4 Special precautions for storage
Store at a temperature not exceeding 30°C, Protect from light, Do not refrigerated.
Keep out of the reach of children.

6.5 Nature and contents of container
The cream is filled into Lami tubes with white colour caps and enclosed in an outer carton.
Pack sizes- 30g.

6.6 Special precautions for disposal and other handling
Not Applicable

7. Marketing authorisation holder
FIRSTSOURCE® (PHARMACHEM) LTD.
71B Adebayo Mokuolu Street, Anthony Village, Lagos, Nigeria.

8. Marketing authorisation number(s)
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9. Date of first authorisation/renewal of the authorisation

Date of first authorisation:

Date of first renewal:

10. Date of revision of the text

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11. REGISTRANT/OPERATOR:

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12. MANUFACTURER

Cotec Healthcare Pvt. Ltd.

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