[Instructions in this font/colour are from the World Health Organisation Public Assessment Report WHOPAR guidelines.]

[Additional instructions and examples]

{<example text>}

1. NAME OF THE MEDICINAL PRODUCT

KREMBAZOL CREAM (CLOTRIMAZOLE & CLOBETASOL PROPIONATE CREAM)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition:
Clobetasol Propionate B.P.....0.05% w/w
Clotrimazole B.P.....1.0% w/w
Cream base.....q.s.

3. PHARMACEUTICAL FORM

Topical cream , White coloured, soft cream.

4. Clinical particulars

4.1 Indication

It is indicated in resistant dermatoses where secondary bacterial infection and/or fungal infection is present, suspected, or likely to occur.

e.g., psoriasis (excluding widespread plaque psoriasis), recalcitrant eczemas

4.2 Posology and Administration

Adults and adolescents

Apply thinly and gently rub in using only enough to cover the entire affected area twice daily until improvement occurs.

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

4.3 Contraindications

Hypersensitivity to the cephalosporin or to any of the excipients.

4.4 Special warnings and precautions for use

No special warning.

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**

The minimum quantity should be used for the minimum duration.

4.7 **Effects on ability to drive and use machines**
Not applicable.

4.8 **Undesirable effects**

None known

4.9 **Overdose**

Not applicable

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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.

Clotrimazole acts against fungi by inhibiting ergosterol synthesis. Inhibition of ergosterol synthesis leads to structural and functional impairment of the cytoplasmic membrane.

5.2 **Pharmacokinetic properties**
CLOBETASOL
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 0.63 ng/ml occurred in one study 8 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 3 hours after a single application of 25 g clobetasol propionate 0.05 % ointment.
Clobetasol propionate is extensively bound to plasma proteins (> 90 %) and has a small volume of distribution.
Metabolism
Following percutaneous absorption of clobetasol propionate the drug probably follows the metabolic pathway of systemically administered corticosteroids. They are metabolized primarily in the liver. However, systemic metabolism of clobetasol propionate has never been fully characterised or quantified.
Elimination
Topical corticosteroids are excreted by the kidneys. In addition, some corticosteroids and their metabolites are also excreted in the bile.

CLOTRIMAZOLE
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**

None Stated

6. PHARMACEUTICAL PARTICULARS

6.1 **List of excipients**

Not Applicable

6.2 **Incompatibilities**

Not applicable

6.3 **Shelf life**

24 months from the date of manufacture

6.4 **Special precautions for storage**

Store below 30°C. Protect from light.

6.5 **Nature and contents of container <and special equipment for use, administration or implantation>**

30 gm tube in a carton along with insert.

6.6 **Special precautions for disposal <and other handling**

No special requirement

7. <APPLICANT/MANUFACTURER>

APPLICANT :

ROOTSTOCK PHARMACEUTICAL LTD.

272, Ziks Avenue, Awka Anambra State, Nigeria.

MANUFACTURER :

FLOURISH PHARMA

24 E , GOA IDC, DAMAN INDUSTRIAL AREA,

DAMAN, INDIA.