SUMMARY OF PRODUCT CHARACTERISTICS (SmPC) FOR DRUG PRODUCTS IN NIGERIA

1. **NAME OF THE DRUG PRODUCT**
   Brand Name: ZUKOREN CREAM
   Generic Name: Clotrimazole, Betamethasone & Neomycin Sulfate Cream

   Strength:
   Betamethasone Dipropionate USP
   Eq. to Betamethasone…….0.05%w/w
   Neomycin Sulfate USP……...0.05%w/w
   Clotrimazole USP……...1.0% w/w
   Preservative: Chlorocresol USP…….0.1%w/w
   Cream base…….q.s.

   Dosage form: Semi-solid Dosage form (Cream)

   Rout of administration: Tropical Use

2. **QUALITATIVE AND QUANTITATIVE COMPOSITION**

   Label claim:
   Betamethasone Dipropionate USP
   Eq. to Betamethasone…….0.05%w/w
   Neomycin Sulfate USP……...0.05%w/w
   Clotrimazole USP……...1.0% w/w
   Preservative: Chlorocresol USP…….0.1%w/w
   Cream base…….q.s.

   UNIT FORMULA:

	Name of Ingredient	Specification	Over age (%)	Quantity for 600 kg Without Overage	Quantity for 600 kg With Overage	Function
1.	Betamethasone Dipropionate*	USP	5	0.384	0.403*	Active Ingredient
2.	Clotrimazole *	USP	5	6.00	6.300*	Active Ingredient
3.	Neomycin Sulfate**	USP	10	3.00	3.300**	Active Ingredient
4.	Macrogol Cetostearyl Ether	BP		15.00	15.00	Emulsifier
5.	Cetostearyl alcohol	BP	-	60.00	60.00	Emulsion Stabilizer
6.	Propylene Glycol	BP	--	36.00	36.00	Humectants
7.	Light Liquid Paraffin	BP	--	30.00	30.00	Emollient
8.	Disodium Edetate	BP	--	0.600	0.600	Chelating Agent
9.	Chlorocresol*	USP	5	0.600	0.630*	Preservative
10.	Sodium Metabisulphite	BP	--	0.600	0.600	Antioxidant
11.	Purified Water	BP	2%	q.s.	q.s.	Vehicle

3. PHARMACEUTICAL FORM

Cream

4. CLINICAL PARTICULARS

4.1 Therapeutic indications:

Zukoren Cream is indicated for relief of the inflammatory and pruritic manifestations of corticosteroid responsive dermatoses e.g. Psoriasis, eczema, seborrhoeic dermatitis, contact dermatitis associated with bacterial infections and fungal infections.

4.2 Posology/Dosage and method of administration:

Apply a thin film of Zukoren Cream to the affected skin areas once or twice daily, preferably morning and evening. The treatment should be continued for several days after disappearance of symptoms such as itching and burning, in order to assure complete eradication of the infection. Treatment beyond two consecutive weeks is not recommended.

Method of administration: Tropical

4.3 Contraindication:

This medicine is contraindicated in patients with a history of hypersensitivity to any of the components of the preparation.

Use of Betamethasone+Clotrimazole+Neomycin is considered to be harmful for patients with known allergy to any of the components or excipients of this medicine. Avoid its use in case of any fungal infections (ringworm or athlete's foot), viral infections (herpes or chickenpox) or for treatment of acne or rosacea. Consult your doctor before using it for any condition.

4.4 Special warnings and precautions for use

This medicine is for external use only. Avoid getting this medicine in your eye, mouth or nose. Rinse with water if contact occurs. This medicine should be used with caution in pediatric patients under 12 years of age and pregnant women. The medication should not be used for any disorder other than that for which it is prescribed.

4.5 Interaction with other drug products and other forms of interaction

This medicine is not known to affect other medicines. If you are using other topical medicines or moisturisers on the same area of skin it is recommended that you leave several minutes between applying each product. However, as with all medicines, it is important to tell your doctor what medicines you are using.

4.6 Fertility, pregnancy and lactation

Pregnancy: Safety of using this medicine during pregnancy has not been evaluated. Topical corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing mothers: It is not known whether topical administration of this medicine is absorbed to produce detectable quantities in breast milk. Use with caution in breast-feeding women.

4.7 Effects on ability to drive and use machines

There have been no studies to investigate the effect of Betamethasone+Clotrimazole+Neomycin 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 Betamethasone+Clotrimazole+Neomycin.

4.8 Undesirable effects

Burning, tingling, dry skin, or stinging may occur. If any of these effects persist or worsen, notify your doctor or pharmacist promptly.

Remember that your doctor has prescribed this medication because he or she has judged that the benefit to you is greater than the risk of side effects. Many people using this medication do not have serious side effects.

Rarely, it is possible this medication will be absorbed from the skin into the bloodstream. This can lead to side effects of too much corticosteroid. These side effects are more likely in children, and in people who use this medication for a long time or over large areas of the skin. Tell your doctor right away if any of the following side effects occur: unusual/extreme tiredness, weight loss, headache,

swelling ankles/feet, increased thirst/urination, vision problems.

A very serious allergic reaction to this drug is rare. However, seek immediate medical attention if you notice any of the following symptoms of a serious allergic reaction: rash, itching/swelling (especially of the face/tongue/throat), severe dizziness, trouble breathing

4.9 Overdose

Excessive or prolonged use of this medicine can suppress hypothalamic function, resulting in secondary adrenal insufficiency, hypercorticism including cushings disease. Appropriate symptomatic treatment is indicated. In case of chronic toxicity, slow withdrawal of medicine is advised.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Antifungal for tropical use
ATC Code: D07CC01

Clotrimazole exerts antifungal effects by inhibition of fungal sterol synthesis. It appears to inhibit the enzymatic conversion of 2,4-methylene-dihydrolanosterol to demethylsterol, the precursor to ergosterol which is an essential building block of the cytoplasmic membrane of the fungi. Clotrimazole is a broad spectrum antifungal agent that inhibits the growth of most fungi pathogenic to man, including the Candida and Dermatophytes (Trichophyton, Microsporum, Epidermophyton).

Topical corticosteroids, such as betamethasone dipropionate, are effective in the treatment of corticosteroid-responsive dermatoses primarily because of their anti-inflammatory, antipruritic and vasoconstrictive actions. 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 phospholipaseA2 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.

Neomycin acts both on gram-positive bacteria such as Streptococci, Staphylococci and on gram-negative bacteria such as E. coli and Proteus. This antibiotic is used in wide variety of local infections, including infected dermatoses, burns, wounds and/or ulcers. This is incorporated into topical steroid preparations to control secondary

infections in inflammatory disorders. Applied topically, this drug is well tolerated, relatively non-irritating, and has a low index of sensitivity.

In cases where local action on infecting bacteria and fungi is required, the anti-inflammatory and antipruritic effects accelerate the improvement of clinical symptoms. In cases where a local anti-inflammatory and antipruritic effect is required, any infection by bacteria and fungal is at the same time eliminated or prevented. The base is a cosmetically acceptable, well tolerated cream (Type O/W) which will not stain the skin.

5.2 Pharmacokinetic properties

Small amount of Clotrimazole (<2-3% of the dose) is absorbed following dermal application. The resulting peak plasma concentrations of the active ingredient are <10mglml and do not lead to noticeable systemic effects or side effects.

Betamethasone dipropionate - The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle, the integrity of the epidermal barrier, and the use of occlusive dressings. Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin increase percutaneous absorption. Occlusive dressings substantially increase the percutaneous absorption of topical 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 and their metabolites are also excreted into the bile.

Neomycin sulfate is not absorbed following topical application to intact skin; however, the drug is readily absorbed through denuded or abraded areas of skin or skin that has lost the keratin layer as in wounds, burns, or ulcers. Neomycin is rapidly absorbed from the peritoneum, draining sinuses, wounds, or surgical sites; use of large doses at these sites may result in substantial plasma concentrations of the drug.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of this SmPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients:

Sr. No	Excipients
1	Macrogol Cetostearyl Ether BP
2	Cetostearyl alcohol BP
3	Propylene Glycol BP
4	Light Liquid Paraffin BP
5	Disodium Edetate BP
6	Chlorocresol USP
7	Sodium Metabisulphite BP
8	Purified Water BP

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store below 30^{O} C in dry & dark place, do not freeze.

6.5 Nature and contents of container

Supplied as 30 g tube in monocarton & 12 such monocarton in an outer carton.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements for disposal.

7. APPLICANT/HOLDER OF CERTIFICATE OF PRODUCT REGISTRATION

M/S. AQUATIX PHARMACEUTICALS LIMITED
No.7, Sapara Williams Street,
Industrial Estate, Ikeja, Lagos,
Nigeria

8. DRUG PRODUCT MANUFACTURER

M/S. CURETECH SKINCARE
Plot No, 33-34, phase-IV Bhatoli Kalan,
Baddi. Distt. Solan, (H.P.) 173205
India

9. NAFDAC REGISTRATION NUMBER(S): C4-1146