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

1. NAME OF THE DRUG PRODUCT

Brand Name: --

Generic Name: TRETINOIN CREAM USP

Strength:

Tretinoin USP……..0.05% w/w

Dosage form: Cream

Rout of administration: Topical

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Label claim:

Tretinoin USP……0.05% w/w

Cream Base…….Q.S

3. PHARMACEUTICAL FORM

Cream

Pale yellow to light yellow colour semi solid mass filled in printed lami tube.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications:

Tretinoin cream is indicated for topical application in the treatment of acne vulgaris. The safety and efficacy of the long-term use of this product in the treatment of other disorders have not been established.

4.2 Posology/Dosage and method of administration:

Posology:

Tretinoin Cream should be applied once a day, before retiring, to the skin where acne lesions appear, using enough to cover the entire affected area lightly.

Application may cause a transitory feeling of warmth or slight stinging. In cases where it has been necessary to temporarily discontinue therapy or to reduce the frequency of application, therapy may be resumed or frequency of application increased when the patients become able to tolerate the treatment.

Alteration of vehicle, drug concentration, or dose frequency should be closely monitored by

careful observation of the clinical therapeutic response and skin tolerance. During the early weeks of therapy, an apparent exacerbation of inflammatory lesions may occur. This is due to the action of the medication on deep, previously unseen lesions and should not be considered a reason to discontinue therapy.

Therapeutic results should be noticed after two to three weeks but more than six weeks of therapy may be required before definite beneficial effects are seen.

4.3 Contraindication:

Use of the product should be discontinued if hypersensitivity to any of the ingredients is noted.

4.4 Special warnings and precautions for use

Do not take tretinoin if you are pregnant or breastfeeding as it may cause adverse effects in the baby. If you have depression or any suicidal thoughts while taking tretinoin or after stopping treatment with tretinoin, please consult a doctor. Avoid sun exposure while using tretinoin as it may make the skin more sensitive to sunlight and cause sunburn. Wear protective clothing and use sunscreen while going out to protect your skin from sunburn. Do not undergo any cosmetic procedures while taking tretinoin and for a minimum of 6 months after stopping treatment with tretinoin as it may increase the risk of scarring. lnfonTI your doctor if you have asthma, diabetes, hypervitaminosisA(high levels of vitamin A), liver or heart problems, weak bones, osteoporosis (bone loss), anorexia nervosa (an eating disorder where people eat too little), any mental problems such as psychosis (loss of contact with reality) or depression before taking tretinoin.

4.5 Interaction with other drug products and other forms of interaction

Drug-Drug Interaction: Tretinoin may interact with anticonvulsants (phenytoin), antibiotics (doxycycline, demeclocycline, minocycline, oxytetracycline, tetracycline, eravacycline), vitamins (vitamin A).

Drug-Food Interaction: Do not use tretinoin with St. John's Wort (a herbal supplement used to treat depression) as it may reduce the effectiveness of honTional contraceptive pills, raising the risk of pregnancy.

Drug-Disease Interaction: If you have asthma, diabetes, liver or heart problems, hypervitaminosis A (high levels of vitamin A), weak bones, osteoporosis (bone loss), anorexia nervosa (an eating disorder where people eat too little), any mental problems such as psychosis (loss of contact with reality) or depression before taking tretinoin.

4.6 Fertility, pregnancy and lactation

Tretinoin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when tretinoin is administered to a nursing woman.

4.7 Effects on ability to drive and use machines

Tretinoin Cream is administered topically and is unlikely to have an effect on one's ability to drive or operate machinery.

4.8 Undesirable effects

The skin of certain sensitive individuals may become excessively red, edematous, blistered, or crusted. If these effects occur, the medication should either be discontinued until the integrity of the skin is restored, or the medication should be adjusted to a level the patient can tolerate.

True contact allergy to topical tretinoin is rarely encountered. Temporary hyper- or hypopigmentation has been reported with repeated application of tretinoin. Some individuals have been reported to have heightened susceptibility to sunlight while under treatment with tretinoin. To date, all adverse effects of tretinoin have been reversible upon discontinuance of therapy.

4.9 Overdose

If medication is applied excessively, no more rapid or better results will be obtained and marked redness, peeling, or discomfort may occur. Oral ingestion of the drug may lead to the same side effects as those associated with excessive oral intake of Vitamin A.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Tretinoin (ß-All trans retinoic acid, vitamin A acid) produces profound metabolic changes in keratinizing epithelia.

Tretinoin increases the proliferative activity of epidermal cells in *in vivo* and *in vitro* studies, and cellular differentiation (keratinization and cornification) is also altered.

5.2 Pharmacokinetic properties

Absorption

Tretinoin is an endogenous metabolite of Vitamin A metabolism in man. Upon topical application, tretinoin is minimally absorbed, penetrating both the epidermis and dermis.

Percutaneous absorption of tretinoin, as determined by the cumulative excretion of radiolabeled drug into urine and feces, was assessed in healthy men and women after single and/or repeated daily applications of a 0.05%, 0.1% or 0.5% tretinoin cream formulation or a 0.01% tretinoin gel formulation, at doses of 100, 150 or 500 mg. The mean percutaneous absorption ranged from 1.0 to 4.3%.

Endogenous plasma concentrations of tretinoin and its metabolites, 13-cis-retinoic acid, all-trans-4-oxo-retinoic acid and 13-cis-4-oxo-retinoic acid were essentially unaltered after either single or multiple daily applications relative to baseline levels.

Distribution

Approximately 80% of tretinoin applied remains on the skin surface, whereas its penetration through the stratum corneum and the hair follicle is vehicle-dependent. After the initial diffusion into the stratum corneum that occurs within a few minutes, further diffusion into epidermis and dermis proceeds more slowly.

Metabolism

Topically-applied tretinoin is metabolized by CYP2S1 and CYP26. Metabolites are 13-cis-retinoic acid, all-trans-4-oxo-retinoic acid and 13-cis-4-oxo-retinoic acid.

Elimination

After application of radiolabelled tretinoin emollient cream or cream, urinary excretion occurred mainly in the first 48 hours, whereas radioactivity was eliminated in the faeces throughout the 7 days after dose application. On average 1 – 1.5% of the radioactivity was recovered in urine and less than 1 % was recovered in feces.

Paediatric Population

It is expected that pharmacokinetic behavior of tretinoin topical formulations and drug-drug interactions with Tretinoin topical formulations will be similar to those in adults. In a study in 20 adolescent patients with moderate to severe acne treated for 12 weeks with tretinoin gel, none of the plasma samples obtained at Week 12 of the treatment period contained quantifiable tretinoin levels.

5.3 Preclinical safety data

Topical administration of Tretinoin Cream products produces dose-dependent erythema, peeling and irritation and excessive use of the products should be avoided. Tretinoin Cream 0.1% w/w did not produce an allergic response when tested in 160 subjects by the Draize test. No systemic toxic effects have been reported following topical application of Tretinoin Cream formulations.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients:

Ingredients	Specification
Paraffin Wax	BP
Cetosteryl alcohol	BP
Liquid-Liquid paraffin	BP
Methyl Paraben	USP
Propyl paraben	USP
Sodium Metabisulphite	BP
Citric acid	BP
Polyethylene glycol 400	USP
Sodium citrate	BP
Glyceryl Monostearate	BP
Cetomacrogol 1000	BP
Propylene glycol	BP
Butylated Hydroxy toluene	BP

Micro wax	IHS
Compound HNS	IHS
Purified water	BP

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store below 30 ^{0}C. Protect from light. Do not freeze.

6.5 Nature and contents of container

30g Lami tube packed in a carton along with the pack insert.

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

NIMO PHARMACEUTICALS LIMITED

No. 29 Irone Avenue, Aguda,

Surulere, Lagos, Nigeria

8. DRUG PRODUCT MANUFACTURER

M/S. CURETECH SKINCARE

Plot No. 32, 33 & 34, Phase-IV,

Bhatoli Kalan, Baddi, Distt. Solan,

HP – 173205, India.

9. NAFDAC REGISTRATION NUMBER(S): New Registration