1.3 Product Information

1.3.1 Summary of Product Characteristics (SmPC)

Enclosed.

Module I Administrative Information
Product Name: SKIDON
Generic Name: Ketoconazole, Clobetasol Propionate, Neomycin Sulphate & Vitamin E Cream.

Summary Product Characteristics

1. **Name of the proprietary product: SKIDON**

   Name of the nonproprietary International Product:
   Ketoconazole, Clobetasol Propionate, Neomycin Sulphate & Vitamin E Cream.

   Route of Administration: Topical Cream

2. **Qualitative and Quantitative composition:**

Sr. No.	Ingredients	Specification	Label Claim	Qty/ Gram /in mg	Qty/ tube in gm	Over ages	Reason for inclusion
1.	Clobetasol Propionate	USP	0.025 %	0.25	0.0075	--	Active
2.	Ketoconazole	USP	1%	10.00	0.30	--	Active
3.	Neomycin Sulphate	USP	0.50%	8.40	0.252	--	Active
4	Vitamin E	USP	1%	10.00	0.30		Active
4.	White Soft Paraffin	BP	--	200.00	6.00	--	Emollient
5.	Light Liquid Paraffin	BP	--	35.00	1.05	--	Emollient
6.	Cetosteryl Alcohol	BP	--	72.00	2.16	--	Emollient
7.	Cetamacrogol - 1000	BP	--	20.00	0.60	--	Emulsifier
8.	Propylene Glycol	BP	--	100.00	3.00	--	Solvent
9.	Disodium Hydrogen Orthophosphate	BP	--	0.15	0.0045	--	pH Adjustment
10.	Para Chloro Meta Cresol	BP	--	1.00	0.03	--	Preservative
11.	Sodium Dihydrogen Orthophosphate	BP	--	0.70	0.021	--	pH Adjustment
12.	Perfume Lavender	IH	--	5.0 ml	0.15 lit	--	Fragrant
13.	Purified Water	BP	--	q.s to 1g	q.s to 30 gm	--	Vehicle

Where,
USP: United State Pharmacopoeia, BP: British Pharmacopoeia, IH: In-House q.s: Quantity Sufficient.

3. Pharmaceutical Form: Topical Cream.

4. Clinical Particulars:

4.1 Therapeutic Indications:
Skidon Cream is used in short courses to treat severe inflammatory skin conditions such as eczema, dermatitis or psoriasis that are infected orlikely to become infected.
Ketoconazole is used to treat serious fungal or yeast infections, such as candidiasis (thrush, oral thrush), blastomycosis (Gilchrist's disease) etc. It works by killing the growth of fungus and yeast.
Clobetasol is a topical corticosteroid. It works by reducing skin inflammation (redness, swelling, itching, and irritation).
Neomycin helps in reducing bacterial infection. In addition, it may be used before any surgery to help prevent infection.
Vitamin E -Treatment of vitamin E deficiency which can occur in cystic fibrosis, cholestasis and severe liver disease, abetalipoproteinemia or simply poor diet

4.2 Posology and method of administration:
Gently massage sufficient cream into the affected and surrounding skin areas twice a day, in the morning and evening. OR As directed by Physicians.

4.3 Contraindications
Skidon Cream is contraindicated in individuals sensitive to its components. If have inflammatory skin disorders infected with pseudomonas or proteus species of bacteria; If have viral skin infections such as chickenpox, shingles, cold sores or herpes simplex.

4.4 Special warnings and precautions for use
WARNING: Skidon Cream is not for ophthalmic use. PRECAUTIONS: General: If irritation or sensitivity develops with the use of this cream,treatment should be discontinued, and appropriate therapy instituted.
Information for Patients:
The patient should be advised to:
Do NOT use Skidon Cream if:
If You have inflammatory skin disorders infected with pseudomonas or proteus species of bacteria; If You have viral skin infections such as chickenpox, shingles, cold sores or herpes simplex.
Skidon Cream topical creams are created for cutaneous use only and should not be used in the eye nose, mouth and ear.
1. Use the medication for the full treatment time even though the symptoms may have improved. Notify the physician if there is no improvement after four weeks of treatment.
2. Inform the physician if the area of application shows signs of increased irritation (redness, itching, burning, blistering, swelling, oozing) indicative of possible sensitization.
3. Avoid the use of occlusive wrappings or dressings.
4. Avoid sources of infection or reinfection.

4.5 Interaction with other medicinal products and other forms of interaction

Laboratory tests have suggested that, when used together, this product may cause damage to latex contraceptives. Consequently the effectiveness of such contraceptives may be reduced. Patients should be advised to use alternative precautions for at least five days after using this product.

Synergism or antagonism between nystatin or amphotericin B, or flucytosine against strains of C. albicans has not been reported.

4.6 Pregnancy and Lactation:

Fertility: No human studies of the effects of Skidon Cream 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 Skidon Cream in pregnant women. Animal studies with this cream have shown reproductive toxicity at high oral doses. At the low systemic exposures of Skidon Cream following topical treatment, harmful effects with respectto reproductive toxicity are not predicted.

Skidon Cream 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 Ketoconazole + Clobetasol + Neomycin + Vitamin E /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 cream therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

4.7 Effects on the ability to drive and use machines

Cream has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects:

Common side effects are similar to those from ketoconazole cream and include skin conditions like itching, burning, stinging, dryness, scaly patches and redness.

4.9 Overdose:

Overdosage, application frequency, and treatment duration of Skidon Cream should not be exceeded.

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.

5. Pharmacological Particulars:

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:

Ketoconazole: Anti-fungal

Clobetasol Propionate: Corticosteroid; Anti-Inflammatory

Neomycin Sulphate: Antibiotic

Vitamin E- Antioxidant

ATC code:
Ketoconazole: D01AC08
Clobetasol Propionate: D07AD01
Neomycin Sulphate: D06AX04
Vitamin E - A11HA03

Mechanism of Action

Ketoconazole: Ketoconazole interacts with 14-α demethylase, a cytochrome P-450 enzyme necessary for the conversion of lanosterol to ergosterol. This results in inhibition of ergosterol synthesis and increased fungal cellular permeability. Other mechanisms may involve the inhibition of endogenous respiration, interaction with membrane phospholipids, inhibition of yeast transformation to mycelial forms, inhibition of purine uptake, and impairment of triglyceride and/or phospholipid biosynthesis. Ketoconazole can also inhibit the synthesis of thromboxane and sterols such as aldosterone, cortisol, and testosterone.

Clobetasol Propionate: The precise mechanism of the antiinflammatory activity of topical steroids in the treatment of steroid-responsive dermatoses, in general, is uncertain. 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. Initially, however, clobetasol, like other corticosteroids, bind to the glucocorticoid receptor, which complexes, enteres the cell nucleus and modifies genetic transcription (transrepression/transactivation)

Neomycin Sulphate:

Neomycin is an aminoglycoside antibiotic. Aminoglycosides work by binding to the bacterial 30S ribosomal subunit, causing misreading of t-RNA, leaving the bacterium unable to synthesize proteins vital to its growth. Aminoglycosides like neomycin "irreversibly" bind to specific 30S-subunit proteins and 16S rRNA. Specifically neomycin binds to four nucleotides of 16S rRNA and a single amino acid of protein S12. This interferes with decoding site in the vicinity of nucleotide 1400 in 16S rRNA of 30S subunit. This region interacts with the wobble base in the anticodon of tRNA. This leads to interference with the initiation complex, misreading of mRNA so incorrect amino acids are inserted into the polypeptide leading to nonfunctional or toxic peptides and the breakup of polysomes into nonfunctional monosomes.

Vitamin E - The mechanism of vitamin E (alpha-tocopherol)-mediated low-density lipoprotein lipid peroxidation. It has been found that alpha-tocopherol mainly inhibits the production of new free radicals, while gamma-tocopherol traps and neutralizes the existing free radicals.

5.2 Pharmacokinetic properties

Ketoconazole: Pharmacokinetic investigations after dermal application have shown that Ketoconazole is minimally absorbed from the intact or inflamed skin into the human blood circulation.

Ketoconazole, a synthetic imidazole antifungal, is effective for superficial fungal infections, genital candidosis and chronic mucocutaneous candidosis, and has been used in immunocompromised patients and advanced prostatic carcinoma. Absorption of ketoconazole

is variable after oral administration, with large variability in peak serum concentrations. Antacids reduce, and food or dilute hydrochloric acid increase, absorption. Renal failure and bone marrow transplantation are associated with reduced absorption. Ketoconazole is not absorbed systemically after topical administration, and minimally absorbed from the vagina. Distribution of ketoconazole varies according to the tissue sampled, the underlying disease and the dose and duration of treatment. Ketoconazole does not cross the intact blood-brain barrier, and crosses to only a limited extent in fungal meningitis. Urinary concentrations of ketoconazole are usually low, but vaginal and vaginal tissue concentrations correlate with those in serum. Seminal fluid concentrations are inadequate for treatment of epididymitis. Ketoconazole is 83.7% plasma protein (mainly albumin) bound, and 15.3% is erythrocyte bound, resulting in only 1% of free drug. Animal studies indicate strong binding to the cytochrome P-450 mono-oxygenase complex. Extensive metabolism to inactive metabolites occurs, the products being mainly excreted in the faeces. Saturable hepatic first-pass metabolism is probable. The half-life of ketoconazole is dose-dependent, increases during long term treatment, suggesting auto-inhibition of metabolism. The kinetics after oral administration fit a 2-compartment model. Drug interactions of theoretical, if not practical, significance include warfarin, chlordiazepoxide, methylprednisolone, cyclosporin and drugs known to induce microsomal enzymes. In each case, some dosage adjustment for ketoconazole, or the interacting drug, may be required.

Clobetasol Propionate: Topical corticosteroids can be absorbed from intact healthy skin. The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including the vehicle and the integrity of the epidermal barrier. Occlusion, inflammation and/or other disease processes in the skin may also increase percutaneous absorption.

Metabolized, primarily in the liver, and then excreted by the kidneys.

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.

Neomycin Sulphate: Poorly absorbed from the normal gastrointestinal tract. Although only approximately 3% of neomycin is absorbed through intact intestinal mucosa, significant amounts may be absorbed through ulcerated or denuded mucosa or if inflammation is present. Protein binding studies have shown that the degree of aminoglycoside protein binding is low and, depending upon the methods used for testing, may be between 0% and 30%. Neomycin undergoes negligible biotransformation after parenteral administration.

The small, absorbed fraction is rapidly distributed in the tissues and is excreted by the kidney in keeping with the degree of kidney function.

5.3 Pre-clinical Safety:
Non-clinical data reveal no special hazard for humans based on studies of repeated dose toxicity, genotoxicity and carcinogenicity.

6. Pharmaceutical Particulars:
6.1 List of Excipients:

White Soft Paraffin	BP
Light Liquid Paraffin	BP
Cetosteryl Alcohol	BP
Cetamacrogol -1000	BP
Propylene Glycol	BP
Disodium Hydrogen Orthophosphate	BP
Para Chloro Meta Cresol	BP
Sodium Dihydrogen Orthophosphate	BP
Perfume Lavender	IH
Purified Wather	BP

6.2 Incompatibilities: Nil

6.3 Shelf life: 36 months

6.4 Special Precautions for storage:
Store below 30°C in a dry place. Protect from light.

6.5 Nature and contents of container:
An Lami tube containing 30 gm cream is packed in a primary carton along with the packinsert.

6.6 Special precautions for disposal and other handling
No special requirements.

7. Marketing Authorization Holder:
LESANTO LABORATORIES

8. **Marketing Authorization Number:**
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9. **Date of first Authorization /renewal of the authorization:** Not Applicable

10. **Date of Revision of text:** June-2022

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