1. Name of the Medicinal Product

(a) Product Name : FEXOTOP CREAM
(b) Pharmaceutical Dosage Form : Cream

2. Quality and Quantitative Composition

(a) Qualitative Declaration, the active substance should be declared by its recommended INN. Accompanied by its salt or hydrate form if relevant.

Composition:
Each gm contains:
Betamethasone Dipropionate U.S.P 0.643 mg
Gentamycin Sulphate B.P Eq. to Gentamycin 1.0 mg
Tolnaftate U.S.P 10 mg
Iodochlorhydroxyquin U.S.P 10 mg

(b) Quantitative Declaration, the quantity of the active substance must be expressed per dosage unit

Sr. No.	Name of the Materials	Specification	Label Claim	Quantity	Active/ Inactive
1	Betamethasone Dipropionate	U.S.P.	0.643 mg	0.9645 kg	Active
2	Gentamycin Sulphate Eq. to Gentamycin	B.P.	1 mg	249.90 gm	Active
3	Tolnaftate	U.S.P.	10 mg	1.5000 kg	Active
4	Iodochlorhydroxyquin	U.S.P.	10 mg	1.5000 kg	Active

3. Pharmaceutical Form Visual description of the appearance of the product (colour, markings, etc.) e.g.:

Off white colour cream having characteristic odour filled in printed lemi tube

4. Clinical Particulars

4.1 Therapeutic Indications:

FEXOTOP CREAM is indicated for the relief of the inflammatory manifestations of corticosteroid- responsive dermatoses when complicated by secondary infection caused by organisms sensitive to the components of this dermatologic preparation or when the possibility of such infection is suspected. Such disorders include: inguinal dermatosis, chronic dermatitis of the extremities, erythrasma, balanoposthitis,

herpes zoster, eczematoid dermatitis, contact dermatitis, follicular dermatitis, dyshidrosis, paronychia, anal pruritus, seborrheic eczema, intertrigo, seborrheic dermatitis, pustular acne, impetigo, neurodermatitis, angular stomatitis, photosensitivity dermatitis, lichenified inguinal dermatophytosis and tinea infections such as tinea pedis, tinea cruris and tinea corporis.

4.2 Posology and method of administration:
A thin film of FEXOTOP CREAM should be applied to cover completely the affected area two or three times daily, or as prescribed by the physician. Frequency of application should be determined according to severity of the condition.

Duration of therapy should be determined by patient response. In cases of tinea pedis, longer therapy (2-4 weeks) may be necessary.

Method of Administration
Topical Use only

4.3 Contraindications:

FEXOTOP CREAM is contraindicated in those patients with a history of sensitivity reactions to any of its components

4.4 Special warning and precautions for use:

Any of the side effects that are reported following systemic use of corticosteroids, including adrenal suppression, may also occur with topical corticosteroids, especially in infants and children.

Systemic absorption of topical corticosteroids will be increased if extensive body surface areas are treated or if the occlusive technique is used. Suitable precautions should be taken under these conditions or when long-term use is anticipated, particularly in infants and children. Systemic absorption of topically applied gentamicin may be increased if extensive body surface areas are treated, especially over prolonged time periods or in the presence of dermal disruption. In these cases, the undesirable effects which occur following systemic use of gentamicin may potentially occur.

Cautious use is recommended under these conditions, particularly in infants and children.
Prolonged use of topical antibiotics occasionally may result in overgrowth of non-susceptible organisms. If this occurs or if irritation, sensitization or superinfection develops, treatment with FEXOTOP CREAM should be discontinued and appropriate therapy instituted. Systemic absorption of Iodochlorhydroxyquin may interfere with thyroid function tests. Therapy should be discontinued one month before these tests are conducted. The ferric chloride test for phenylketonuria can yield a false-positive result if Iodochlorhydroxyquin is present in the urine. Slight staining of linens or clothing due to Iodochlorhydroxyquin may occur. FEXOTOP CREAM is not for ophthalmic use.

Pediatric Use: Pediatric patients may demonstrate greater susceptibility to topical corticosteroid- induced hypothalamic-pituitary-adrenal (HPA) axis suppression and to exogenous corticosteroid effects than mature patients because of greater absorption due to a large skin surface area to body weight ratio.

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

4.5 Interaction with other medicinal products and other forms of interactions:

CYP3A4 inhibitors

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.

Systemic aminoglycoside therapy

Possibility of cumulative toxicity should be considered when gentamicin sulphate is applied topically in combination with systemic aminoglycoside therapy

4.6 Pregnancy and lactation:

Since safety of topical corticosteroid use in pregnant women has not been established, drugs of this class should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Drugs of this class should not be used extensively in large amounts or for prolonged periods of time in pregnant patients.

Since it is not known whether topical administration of corticosteroids can result in sufficient systemic absorption to produce detectable quantities in breast milk, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machine:

There have been no studies to investigate the effect of Betamethasone Dipropionate with gentamicin, Tolnaftate and Iodochlorhydroxyquin 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 FEXOTOP CREAM.

4.8 Undesirable effects:
Local adverse reactions reported with the use of topical corticosteroids, especially under occlusive dressings, include: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae and miliaria. Rash, irritation and hypersensitivity have been reported with the topical usage of gentamicin sulfate, Iodochlorhydroxyquin and rarely with tolnaftate.

4.9 Overdose:
Symptoms
Excessive or prolonged use of topical corticosteroids can suppress pituitary-adrenal function, resulting in secondary adrenal insufficiency, and produce manifestations of hypercorticism, including Cushing's disease.
A single overdose of gentamicin would not be expected to produce symptoms.
Excessive or prolonged use of topical antibiotics may lead to over-growth of lesions by nonsusceptible organisms.
Systemically, tolnaftate is pharmacologically inactive.
Iodochlorhydroxyquin rarely produces iodism.

Treatment
Appropriate symptomatic treatment is indicated. Acute hypercorticoid symptoms are usually reversible. Treat electrolyte imbalance, if necessary. In case of chronic toxicity, slow withdrawal of corticosteroids is advised.
If overgrowth by nonsusceptible organisms occurs, stop treatment with FEXOTOP CREAM and institute appropriate therapy.

5. Pharmacological Properties

5.1 Pharmacodynamic Properties:

FEXOTOP CREAM combines the anti-inflammatory, antipruritic and vasoconstrictive agent beta- methasone valerate, the wide-spectrum antibiotic gentamicin sulfate, the fungicidal agent tolnaftate and Iodochlorhydroxyquin, an antibacterial and antifungal agent.

The corticosteroids are a class of compounds comprising steroid hormones, secreted by the adrenal cortex and their synthetic analogs. In pharmacologic doses corticosteroids are used primarily for their anti-inflammatory and/or immunosuppressive effects.

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. However, while the physiologic, pharmacologic, and clinical effects of the corticosteroids are well known, the exact mechanisms of their actions in each disease are uncertain.
Betamethasone dipropionate, a corticosteroid, has been shown to have topical (dermatologic) and systemic pharmacologic and metabolic effects characteristic of this class of drugs.

Gentamicin sulphate is mixture of antibiotic substances produced by the growth of micromonospora purpurea. It is a bactericidal antibiotic which acts by inhibiting protein synthesis. It has greater antibacterial activity than streptomycin, neomycin or kanamycin. Gentamicin exerts a number of effects on cells of susceptible bacteria. It affects the integrity of the plasma membrane and the metabolism of RNA, but it's most important effect is inhibition of protein synthesis at the level of the 30s ribosomal subunit.

Iodochlorhydroxyquin is a broad spectrum anti-bacterial and anti-fungal agent. Its precise mechanism of action is unknown.

Tolnaftate is a potent fungicidal agent against Trichophyton mentagrophytes, Trichophyton rubrum, Microsporum canis, Epidermophyton floccosum and Malassezia furfur. Clinical studies have shown the excellent fungicidal effect of tolnaftate in a large number of patients with superficial fungal infections.1 Therapy with tolnaftate has been notable for lack of recurrence.

Each component of FEXOTOP CREAM makes a significant contribution to the efficacy of the product in treating infections of mixed etiology.

5.2 Pharmacokinetic Properties:

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.

Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar 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 and their metabolites are also excreted into the bile.

Sixty-three pediatric patients ages 1 to 12 years, with atopic dermatitis, were enrolled in an open-label, hypothalamic-pituitary-adrenal (HPA) axis safety study. Betamethasone dipropionate cream was applied twice daily for 2 to 3 weeks over a mean body surface area of 40% (range 35% to 90%). In 10 of 43 (23%) evaluable patients, adrenal suppression was indicated by either a less than or equal to 5 mcg/dL pre-stimulation cortisol, or a cosyntropin post-stimulation cortisol less than or equal to 18 mcg/dL and/or an increase of less than 7 mcg/dL from the baseline cortisol.

Gentamicin sulphate
Absorption:
Topical application of gentamicin can result in some systemic absorption. Treatment of large areas can result in plasma concentrations of up to 1µg/ml.
Gentamicin is 70-85% bound to plasma albumin following administration.
Effective plasma concentration is 4 - 8ug/ml.
The volume of distribution (VD) is 0.31/kg.
Elimination
> 90% Gentamicin is excreted unchanged in the urine by glomerular filtration.
T½ = 2 -3 hours in individuals with normal kidney function, but can be increased in cases of renal insufficiency.
The elimination rate constant is;
0.02 Hr-1 for anuric patients*
0.30 Hr-1 normal
*Therefore, in those with anuria, care must be exercised.

5.3 Preclinical Safety Data:
There are no preclinical data of relevance to the prescriber which are additional to that in other sections of the SmPC.

6 Pharmaceutical Particulars
6.1 List of excipients:

Excipients	**Reference**
Ceto-stearyl Alcohol	B.P
Cetomacragol-1000	B.P
Chlorocresol	B.P
Methyl paraben sodium	B.P
Propyl paraben sodium	B.P
Di- Sodium Hydrogen ortho-phosphate anhydrous	I.H
Liquid Parafin Heavy	I.H
Propylene Glycol	B.P

6.2 Incompatibilities:
No incompatibilities have been identified

6.3 Shelf life:
36 Months

6.4 Special precautions for storage: Store in cool, dark & dry place.
Store below 30°C in a dry place. Protect from light.

6.5 Nature and contents of container:
A lami tube containing 30 gm cream packed in a Primary Carton along with the Pack Insert.

6.6 Special precaution for disposal
No special requirements.

7. Marketing Authorization Holder

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