1. Name of the Medicinal Product

(a) Product Name : FEXOFYN LOTION
(b) Pharmaceutical Dosage Form : Lotion

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:
Clobetasol Propionate USP 0.05% w/w
Vitamin E USP 1% w/w
Lotion base

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

Sr. No.	Name of the Materials	Specification	Label Claim
1	Clobetasol Propionate	USP	0.05% w/w
2	Vitamin E	USP	1% w/w

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

A white colour lotion having characteristic Odour, filled in white colour (HDPE) plastic bottle properly sealed and labelled.

4. Clinical Particulars

4.1 Therapeutic Indications:

Fexofyn lotion, is a super-high potent topical corticosteroid formulation indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses only in patients 18 years of age or older.
Treatment should be limited to 2 consecutive weeks. For moderate to severe plaque psoriasis, treatment may be extended for an additional 2 weeks for localized lesions (less than 10% body surface area) that have not sufficiently improved after the initial 2-week treatment. Any additional benefits of extending treatment should be weighed against the risk of hypothalamic-pituitary-adrenal (HPA) axis suppression before prescribing for more than 2 weeks. The total dosage should not exceed 50 g (50 mL or 1.75 fl. oz) per week.
Patients should be instructed to use Fexofyn lotion, for the minimum amount of time necessary to achieve the desired results.

Use in patients under 18 years of age is not recommended due to numerically high rates of HPA axis suppression.

4.2 Posology and method of administration:

Fexofyn lotion, is for topical use only, and not for ophthalmic, oral or intravaginal use.

Fexofyn lotion, should be applied to the affected skin areas twice daily and rubbed in gently and completely.

The total dosage should not exceed 50 g (50 mL or 1.75 fl. oz.) per week because of the potential for the drug to suppress the hypothalamic-pituitary-adrenal (HPA) axis.

Clobetasol Propionate Lotion, 0.05% contains a topical corticosteroid; therefore treatment should be limited to 2 consecutive weeks for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses and up to 2 additional weeks in localized lesions (less than 10% body surface area) of moderate to severe plaque psoriasis that have not sufficiently improved after the initial 2 weeks of treatment with Clobetasol Propionate Lotion, 0.05%.

Unless directed by physician, Clobetasol Propionate Lotion, 0.05% should not be used with occlusive dressings.

4.3 Contraindications:

Contraindicated in those patients with a history of hypersensitivity to any of the components of the preparations.

4.4 Special warning and precautions for use:

Effects on the Endocrine system

Clobetasol propionate is a highly potent topical corticosteroid that has been shown to suppress the HPA axis at the lowest doses tested. Systemic absorption of topical corticosteroids has caused reversible adrenal suppression with the potential for clinical glucocorticosteroid insufficiency after withdrawal of treatment. This may occur during treatment or upon withdrawal of the topical corticosteroid.

The effect of Clobetasol Propionate cream, 0.05% on HPA axis function was compared to clobetasol propionate lotion 0.05% (Temovate E Emollient, 0.05%) in adults in two trials, one for psoriasis and one for atopic dermatitis. In total, 8 of 10 evaluable subjects with moderate to severe plaque psoriasis experienced adrenal suppression following 4 weeks of Clobetasol Propionate Lotion, 0.05% therapy (treatment beyond 4 consecutive weeks is not recommended in moderate to severe plaque psoriasis). In follow-up testing, 1 of 2 subjects remained suppressed after 8 days. In this comparative trial, for clobetasol propionate lotion, 0.05% there were 3 of 10 evaluable subjects with HPA axis suppression.
Furthermore, 5 of 9 evaluable subjects with moderate to severe atopic dermatitis experienced adrenal suppression following 2 weeks of Clobetasol Propionate Lotion, 0.05% therapy (treatment beyond 2 consecutive weeks is not recommended in

moderate to severe atopic dermatitis). Of the 3 subjects that had follow-up testing, one subject failed to recover adrenal function 7 days post-treatment. For subjects treated with clobetasol propionate lotion, 0.05%, 4 of 9 evaluable subjects experienced adrenal suppression following 2 weeks of treatment. Of the 2 subjects that had follow-up testing, both recovered adrenal function 7 days post-treatment. The proportion of subjects suppressed may be underestimated because the adrenal glands were stimulated weekly with cosyntropin in these trials.

Because of the potential for systemic absorption, use of topical corticosteroids may require that patients be periodically evaluated for HPA axis suppression. Factors that predispose a patient using a topical corticosteroid to HPA axis suppression include the use of more potent steroids, use over large surface areas, use over prolonged periods, use under occlusion, use on an altered skin barrier, and use in patients with liver failure.

An adrenocorticotropic hormone (ACTH) stimulation test may be helpful in evaluating patients for HPA axis suppression. If HPA axis suppression is documented, an attempt should be made to gradually withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid. Manifestations of adrenal insufficiency may require supplemental systemic corticosteroids. Recovery of HPA axis function is generally prompt and complete upon discontinuation of topical corticosteroids.

Cushing's syndrome, hyperglycemia, and unmasking of latent diabetes mellitus can also result from systemic absorption of topical corticosteroids.

Use of more than one corticosteroid-containing product at the same time may increase the total systemic exposure.

Pediatric patients may be more susceptible to systemic toxicity from use of topical corticosteroids. Use in patients under 18 years of age is not recommended due to numerically high rates of HPA axis suppression.

Local Adverse Reactions with Topical corticosteroids

Local adverse reactions may occur more frequently with the use of occlusive dressings and higher potency corticosteroids, including clobetasol propionate. These reactions are listed in an approximate decreasing order of occurrence: folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, striae, miliaria, skin atrophy and telangiectasia. Some local adverse reactions may be irreversible. Fexofyn lotion is not recommended in patients with acne vulgaris, rosacea or perioral dermatitis.

Allergic contact Dermatitis

Allergic contact dermatitis to any component of topical corticosteroids is usually diagnosed by a failure to heal rather than a clinical exacerbation. Clinical diagnosis of allergic contact dermatitis can be confirmed by patch testing.

Concomitant Skin infections

In the presence of dermatologic infections, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, use of Fexofyn lotion should be discontinued until the infection has been adequately controlled.

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

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:

Pregnancy

There are limited data from the use of FEXOFYN LOTION in pregnant women. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development.

The relevance of this finding to humans has not been established. Administration of FEXOFYN LOTION during pregnancy should only be considered if the expected benefit to the mother outweighs the risk to the foetus. The minimum quantity should be used for the minimum duration.

Lactation

The safe use of topical corticosteroids during lactation has not been established. It is not known whether the topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable amounts in breast milk. Administration of FEXOFYN LOTION during lactation should only be considered if the expected benefit to the mother outweighs the risk to the infant.

If used during lactation FEXOFYN LOTION should not be applied to the breasts to avoid accidental ingestion by the infant.

4.7 Effects on ability to drive and use machine:

There have been no studies to investigate the effect of FEXOFYN LOTION 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 FEXOFYN LOTION.

4.8 Undesirable effects:

Adverse drug reactions (ADRs) are listed below by MedDRA system organ class and by frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 and

<1/10), uncommon (≥1/1,000 and <1/100), rare (≥1/10,000 and <1/1,000) and very rare (<1/10,000), including isolated reports.

Post-marketing data

Infections and Infestations

Very rare	Opportunistic infection

Immune System Disorders

Very rare	Local Hypersensitivity

Endocrine Disorders

Very rare	Hypothalamic-pituitary adrenal (HPA) axis suppression: Cushingoid features: (e.g. moon face, central obesity), delayed weight gain/growth retardation in children, osteoporosis, hyperglycaemia/glucosuria, hypertension, increased weight/obesity, decreased endogenous cortisol levels, alopecia, trichorrhexis

Eye disorders

Very rare	Cataract, central serous chorioretinopathy, glaucoma

Skin and Subcutaneous Tissue Disorders

Common	Pruritus, local skin burning /skin pain
Uncommon	Skin atrophy*, striae*, telangiectasias*****
Very rare	Skin thinning*, skin wrinkling*, skin dryness*, Pigmentation changes*, hypertrichosis, exacerbation of underlying symptoms, allergic contact dermatitis/dermatitis, Pustular psoriasis, erythema, rash, urticaria, acne

General Disorders and Administration site conditions

Very rate	Application site irritation/pain

*Skin features secondary to local and/or systemic effects of hypothalamic-pituitary adrenal (HPA) axis suppression.

4.9 Overdose:

Topically applied FEXOFYN LOTION may be absorbed in sufficient amounts to produce systemic effects. Acute overdosage is very unlikely to occur, however, in the case of chronic overdosage or misuse the features of hypercortisolism may occur.

Treatment

In the event of overdose, FEXOFYN LOTION should be withdrawn gradually by reducing the frequency of application or by substituting a less potent corticosteroid because of the risk of glucocorticosteroid insufficiency.

Further management should be as clinically indicated or as recommended by the national poisons center, where available.

5. Pharmacological Properties

5.1 Pharmacodynamic Properties:

Vasoconstrictor Assay

Fexofyn lotion is in the super-high range of potency as demonstrated in vasoconstrictor studies in healthy subjects when compared with other topical corticosteroids. However, similar blanching scores do not necessarily imply therapeutic equivalence.

Hypothalamic-Pituitary-Adrenal (HPA) Axis Suppression

In studies evaluating the potential for hypothalamic-pituitary-adrenal (HPA) axis suppression, Clobetasol Propionate Lotion, 0.05% demonstrated rates of suppression that were numerically higher than those of a clobetasol propionate 0.05% lotion (T emovate E Emollient, 0.05%), [see Warnings and Precautions (5.1) and Use in Specific Population (8.4)

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 occlusion.

Topical corticosteroids can be absorbed from normal intact skin. Inflammation and other disease processes in the skin may increase percutaneous absorption.

There are no human data regarding the distribution of corticosteroids to body organs following topical application. Nevertheless, once absorbed through the skin, topical corticosteroids are handled through metabolic pathways similar to systemically administered corticosteroids. They are metabolized, primarily in the liver, and are then excreted by the kidneys. In addition, some corticosteroids and their metabolites are also excreted in the bile.

5.3 Preclinical Safety Data:

Carcinogenesis / Mutagenesis

Carcinogenesis
Long-term animal studies have not been performed to evaluate the carcinogenic potential of clobetasol propionate.

Genotoxicity
Clobetasol propionate was not mutagenic in a range of in vitro bacterial cell assays.

Fertility
In fertility studies, subcutaneous administration of clobetasol propionate to rats at doses of 6.25 to 50 micrograms/kg/day produced no effects on mating, and fertility was only decreased at 50 micrograms/kg/day.

Pregnancy
Subcutaneous administration of clobetasol propionate to mice (≥100 micrograms/kg/day), rats (400 micrograms/kg/day) or rabbits (1 to 10 micrograms/kg/day) during pregnancy produced foetal abnormalities including cleft palate. In the rat study, where some animals were allowed to litter, developmental delay was observed in the F1 generation at ≥100 micrograms/kg/day and survival was reduced at 400 micrograms/kg/day. No treatment-related effects were observed in F1 reproductive performance or in the F2 generation.

6 Pharmaceutical Particulars
6.1 List of excipients:

Sr. No.	Excipients
1.	Ceto-Stearyl Alcohol
2.	Cetomacragol-1000
3.	Liquid Paraffin Heavy
4.	Methyl Paraben Sodium
5.	Propyl Paraben Sodium
6.	Chlorocresol
7.	Carbopol-934
8.	Cresmer-RH-40
9.	Ess Rose White
10.	PEG-400
11.	Glycerin Refined
12.	Citric Acid Monohydrate
13.	Emulsifying Wax Non-Ionic

6.2 Incompatibilities:
No incompatibilities have been identified

6.3 Shelf life:
36 Months

6.4 Special precautions for storage:
Store Protected from light & moisture, below 30°C. Do not freeze. Non greasy. Wash Hands after each use. Keep medicine out of reach of children.

6.5 Nature and contents of container:
60 ml lotion packed in a HDPE plastic bottle. Such 1 plastic bottle is packed in printed carton along with pack insert.

6.6 Special precaution for disposal
No special requirements.

7. Marketing Authorization Holder

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