

For the use only of Registered Medical Practitioners or a Hospital or a Laboratory

TENOVATE

1. GENERIC NAME

Clobetasol Cream IP/Clobetasol Ointment IP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

TENOVATE Cream contains:

Clobetasol Propionate IP 0.05 % w/w

Chlorocresol IP (as preservative) 0.1 % w/w

in a non -greasy base.

TENOVATE Ointment contains:

Clobetasol Propionate IP 0.05 % w/w

3. DOSAGE FORM AND STRENGTH

Cream and Ointment.

TENOVATE Cream contains:

Clobetasol Propionate IP 0.05 % w/w

Chlorocresol IP (as preservative) 0.1 % w/w

in a non - greasy base.

TENOVATE Ointment contains:

Clobetasol Propionate IP 0.05 % w/w

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication

TENOVATE is a very potent topical corticosteroid indicated for adults, elderly and children over 1 year for the relief of the inflammatory and pruritic manifestations of steroid responsive dermatoses.

These include the following:

- Psoriasis (excluding widespread plaque psoriasis),
- Recalcitrant dermatoses,
- Lichen planus,
- Discoid lupus erythematosus,
- Other skin conditions which do not respond satisfactorily to less potent steroids.

4.2 Posology and Method of Administration

Pharmaceutical form: Cream and Ointment

Ointment

Ointments are especially appropriate for dry, lichenified or scaly lesions.

Cream

Creams are especially appropriate for moist or weeping surfaces.

Adults, Elderly and Children over 1 year

Apply thinly and gently rub in using only enough to cover the entire affected area once or twice a day for up to 4 weeks until improvement occurs, then reduce the frequency of application or change the treatment to a less potent preparation. Allow adequate time for absorption after each application before applying an emollient.

Repeated short courses of *TENOVATE* may be used to control exacerbations.

In more resistant lesions, especially where there is hyperkeratosis, the effect of *TENOVATE* can be enhanced, if necessary, by occluding the treatment area with polythene film.

Overnight occlusion only is usually adequate to bring about a satisfactory response. Thereafter, improvement can usually be maintained by application without occlusion.

If the condition worsens or does not improve within 2-4 weeks, treatment and diagnosis should be re-evaluated.

Treatment should not be continued for more than 4 weeks. If continuous treatment is necessary, a less potent preparation should be used.

The maximum weekly dose should not exceed 50gms/week.

Atopic dermatitis (eczema)

Therapy with *TENOVATE* cream and ointment should be gradually discontinued once control is achieved and an emollient continued as maintenance therapy.

Rebound of pre-existing dermatoses can occur with abrupt discontinuation of *TENOVATE*.

Recalcitrant dermatoses

Patients who frequently relapse

Once an acute episode has been treated effectively with a continuous course of topical corticosteroid, intermittent dosing (once daily, twice weekly, without occlusion) may be considered. This has been shown to be helpful in reducing the frequency of relapse.

Application should be continued to all previously affected sites or to known sites of potential relapse. This regime should be combined with routine daily use of emollients. The condition and the benefits and risks of continued treatment must be re-evaluated on a regular basis.

Children

TENOVATE is contraindicated in children under one year of age.

Children are more likely to develop local and systemic side effects of topical corticosteroids and, in general, require shorter courses and less potent agents than adults.

Care should be taken when using *TENOVATE* to ensure the amount applied is the minimum that provides therapeutic benefit.

Elderly

Clinical studies have not identified differences in responses between the elderly and younger patients. The greater frequency of decreased hepatic or renal function in the elderly may delay elimination if systemic absorption occurs. Therefore, the minimum quantity should be used for the shortest duration to achieve the desired clinical benefit.

Renal/Hepatic Impairment

In case of systemic absorption (when application is over a large surface area for a prolonged period) metabolism and elimination may be delayed therefore increasing the risk of systemic toxicity. Therefore, the minimum quantity should be used for the shortest duration to achieve the desired clinical benefit.

4.3 Contraindications

The following conditions should not be treated with *TENOVATE*:

- Untreated cutaneous infections,
- Rosacea,
- Acne vulgaris,
- Pruritus without inflammation,
- Perianal and genital pruritus,
- Perioral dermatitis.

TENOVATE is contraindicated in dermatoses in children under one year of age, including dermatitis.

4.4 Special Warnings and Precautions for Use

TENOVATE should be used with caution in patients with a history of local hypersensitivity to corticosteroids or to any of the excipients in the preparation. Local hypersensitivity reactions (*See Section 4.8 Undesirable Effects*) may resemble symptoms of the condition under treatment.

Manifestations of hypercortisolism (Cushing's syndrome) and reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, leading to glucocorticosteroid insufficiency, can occur in some individuals as a result of increased systemic absorption of topical steroids. If either of the above are observed, withdraw the drug gradually by reducing the frequency of application, or by substituting a less potent corticosteroid. Abrupt withdrawal of treatment may result in glucocorticosteroid insufficiency (*See Section 4.8 Undesirable Effects*).

Risk factors for increased systemic effects are:

- Potency and formulation of topical steroid,
- Duration of exposure,
- Application to a large surface area,
- Use on occluded areas of skin e.g. on intertriginous areas or under occlusive dressings (in infants the nappy may act as an occlusive dressing),

- Increasing hydration of the stratum corneum,
- Use on thin skin areas such as the face,
- Use on broken skin or other conditions where the skin barrier may be impaired,
- In comparison with adults, children and infants may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic adverse effects. This is because children have an immature skin barrier and a greater surface area to body weight ratio compared with adults.

Visual disturbances

Visual disturbance has been reported by patients using systemic and/or topical corticosteroids. If a patient has blurred vision or other visual disturbances, consider evaluation of possible causes which may include cataract, glaucoma or central serous chorioretinopathy.

Children

In infants and children under 12 years of age, long-term continuous topical corticosteroid therapy should be avoided where possible, as adrenal suppression can occur.

Children are more susceptible to develop atrophic changes with the use of topical corticosteroids. If *TENOVA* is required for use in children, it is recommended that the treatment should be limited to only a few days and reviewed weekly.

Infection risk with occlusion

Bacterial infection is encouraged by the warm, moist conditions within skin folds or caused by occlusive dressings. When using occlusive dressings, the skin should be cleansed before a fresh dressing is applied.

Use in Psoriasis

Topical corticosteroids should be used with caution in psoriasis as rebound relapses, development of tolerances, risk of generalised pustular psoriasis and development of local or systemic toxicity due to impaired barrier function of the skin have been reported in some cases. If used in psoriasis careful patient supervision is important.

Concomitant infection

Appropriate antimicrobial therapy should be used whenever treating inflammatory lesions which have become infected. Any spread of infection requires withdrawal of topical corticosteroid therapy and administration of appropriate antimicrobial therapy.

Chronic leg ulcers

Topical corticosteroids are sometimes used to treat the dermatitis around chronic leg ulcers. However, this use may be associated with a higher occurrence of local hypersensitivity reactions and an increased risk of local infection.

Application to the face

Application to the face is undesirable as this area is more susceptible to atrophic changes. If used on the face, treatment should be limited to only a few days.

Application to the eyelids

If applied to the eyelids, care is needed to ensure that the preparation does not enter the eye, as cataract and glaucoma might result from repeated exposure.

Ointment

TENOVATE Ointment contain paraffin. Instruct patients not to smoke or go near naked flames due to the risk of severe burns. Fabric (clothing, bedding, dressings etc.) that has been in contact with these products burns more easily and is a serious fire hazard. Washing clothing and bedding may reduce product build-up but not totally remove it.

4.5 Drug Interactions

Co-administered drugs that can inhibit CYP3A4 (e.g. ritonavir, 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 Use in Special Populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

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Care should be taken when using TENOVATE to ensure the amount applied is the minimum that provides therapeutic benefit.

Elderly

Clinical studies have not identified differences in responses between the elderly and younger patients. The greater frequency of decreased hepatic or renal function in the elderly may delay elimination if systemic absorption occurs. Therefore, the minimum quantity should be used for the shortest duration to achieve the desired clinical benefit.

Renal/Hepatic Impairment

In case of systemic absorption (when application is over a large surface area for a prolonged period) metabolism and elimination may be delayed therefore increasing the risk of systemic toxicity. Therefore, the minimum quantity should be used for the shortest duration to achieve the desired clinical benefit.

Fertility

There are no data in humans to evaluate the effect of topical corticosteroids on fertility. Clobetasol administered subcutaneously to rats had no effect upon mating performance; however, fertility was decreased at the highest dose (*See Section 6 Nonclinical Properties*).

Pregnancy

There are limited data from the use of *TENOVATE* in pregnant women.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. (*See Section 6 Nonclinical Properties*).

The relevance of this finding to humans has not been established. Administration of *TENOVATE* 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 *TENOVATE* during lactation should only be considered if the expected benefit to the mother outweighs the risk to the infant.

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

4.7 Effects on Ability to Drive and Use Machines

There have been no studies to investigate the effect of *TENOVATE* 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 *TENOVATE*.

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 ($\geq 1/10$), common ($\geq 1/100$ and $< 1/10$), uncommon ($\geq 1/1,000$ and $< 1/100$), rare ($\geq 1/10,000$ and $< 1/1,000$) and very rare ($< 1/10,000$), including isolated reports.

Postmarketing 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, hyperglycemia/gluco-suria, 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 rare: Application site irritation/pain.

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

4.9 Overdose

Symptoms and signs

Topically applied *TENOVATE* 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 (*See Section 4.8 Undesirable Effects*).

Treatment

In the event of overdose, *TENOVATE* 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 centre, where available.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of action

Topical corticosteroids act as anti-inflammatory agents via multiple mechanisms to inhibit late phase allergic reactions including decreasing the density of mast cells, decreasing chemotaxis and activation of eosinophils, decreasing cytokine production by lymphocytes, monocytes, mast cells and eosinophils, and inhibiting the metabolism of arachidonic acid.

5.2 Pharmacodynamic effects

ATC code: D07AD Corticosteroids, very potent (group IV).

Topical corticosteroids, have anti-inflammatory, antipruritic, and vasoconstrictive properties.

5.3 Pharmacokinetic Properties

Absorption

Topical corticosteroids can be systemically 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. Mean peak plasma Clobetasol Propionate concentrations of 0.63 nanograms/ml occurred in one study eight hours after the second application (13 hours after an initial application) of 30 g Clobetasol Propionate 0.05 % ointment to normal individuals with healthy skin. Following the application of a second dose of 30 g Clobetasol Propionate cream 0.05 %, mean peak plasma concentrations were slightly higher than the ointment and occurred 10 hours after application. In a separate study, mean peak plasma concentrations of approximately 2.3 nanograms/ml and 4.6 nanograms/ml occurred respectively in patients with psoriasis and eczema three hours after a single application of 25 g Clobetasol Propionate 0.05 % ointment.

Distribution

The use of pharmacodynamic endpoints for assessing the systemic exposure of topical corticosteroids is necessary due to the fact that circulating levels are well below the level of detection.

Metabolism

Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. They are metabolised, primarily in the liver.

Elimination

Topical corticosteroids are excreted by the kidneys. In addition, some corticosteroids and their metabolites are also excreted in the bile.

6. NONCLINICAL PROPERTIES

Carcinogenesis / Mutagenesis

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.

Reproductive Toxicology

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 and intrauterine growth retardation.

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.

7. DESCRIPTION

TENOVATE Cream contains:

Clobetasol Propionate IP 0.05 % w/w

Chlorocresol IP (as preservative) 0.1 % w/w

in a non - greasy base.

TENOVATE Ointment contains:

Clobetasol Propionate IP 0.05 % w/w

Cream and Ointment.

8. PHARMACEUTICAL PARTICULARS

List of Excipients

TENOVATE Cream

Cetostearyl Alcohol, Arlacel 165, Beeswax White, Propylene Glycol, Chlorocresol, Finester 1240, Citric Acid Monohydrate, Sodium Citrate, and Purified Water.

TENOVATE Ointment

Propylene Glycol, Sorbitan Sesquioleate, and White Soft Paraffin.

For important information about some of these excipients see 4.4 *Special Warnings and Precautions for use*.

8.1 Incompatibilities

No incompatibilities have been identified.

8.2 Shelf Life

The expiry date is indicated on the label and packaging.

8.3 Packaging Information

Tube in a carton.

All presentations may not be marketed in India.

8.4 Storage and Handling Instructions

TENOVATE Cream

Store at a temperature not exceeding 25°C. Do not freeze.

TENOVATE Ointment

Store at a temperature not exceeding 30°C. Do not freeze

Keep out of reach of children.

For external use only.

There are no other special requirements for use or handling of this product.

9. PATIENT COUNSELLING INFORMATION

Registered Medical Practitioners may counsel their patients (and/or patient's caregiver as applicable) about the special warnings and precautions for use, drug interactions, undesirable effects, and any relevant contra-indications of *TENOVATE*. Patients (and/or patient's caregiver) may also be informed about posology, method of administration and storage/handling information as applicable

10. DETAILS OF MANUFACTURER

The Manufacturing Site details are mentioned on the label and packaging.

For further information please contact:

GlaxoSmithKline Pharmaceuticals Limited.,

Registered Office

Dr. Annie Besant Road, Worli,

Mumbai 400 030, India.

11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE

Manufacturing Licence number is indicated on the label and packaging.

12. DATE OF REVISION

05 May 2021

Trade marks are owned by or licensed to the GSK group of companies.

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Adapted from Clobetasol Propionate (topical)] (DERMOVATE) GDS16/IPI09 dated 05 December 2020