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

TENOVATE M

1. GENERIC NAME

Clobetasol Propionate and Miconazole Nitrate Skin Cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains:

Clobetasol Propionate IP	0.05% w/w
Miconazole Nitrate IP	2.0 % w/w
Chlorocresol IP (as Preservative)	0.1% w/w
in a non-greasy base	

List of Excipients
Finester-1240 (GMS-NSE), Cetostearyl Alcohol, Arlacel-165, Beeswax White, Propylene Glycol, Chlorocresol, Citric Acid Monohydrate, Sodium Citrate, Purified Water.

3. DOSAGE FORM AND STRENGTH

Cream.

For information on strength refer *2. Qualitative and Quantitative Composition* above.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication

TENOVATE M is indicated in resistant dermatoses where secondary fungal infection is present, suspected, or likely to occur e.g. psoriasis (excluding widespread plaque psoriasis), recalcitrant dermatoses.

4.2 Posology and Method of Administration

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 twice daily for up to 4 weeks until improvement occurs, then change the treatment to a less potent steroid.

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.

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 clobetasol propionate containing preparations to ensure the amount applied is the minimum that provides therapeutic benefit.

Elderly

Clinical studies have not identified differences in responses to clobetasol propionate between the elderly and younger patients. The greater frequency of decreased hepatic or renal function in the elderly may delay elimination if systemic absorption of clobetasol propionate 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 of clobetasol propionate (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 M*:

- Rosacea.
- Acne vulgaris.
- Perioral dermatitis.
- Pruritus without inflammation.
- Perianal and genital pruritus.

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

TENOVATE M is contraindicated in patients who have demonstrated hypersensitivity to clobetasol propionate, miconazole nitrate (or to other imidazole derivatives) or any components of the formulation.

4.4 Special Warnings and Precautions for Use

Clobetasol 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 *4.8 Undesirable effects*) may resemble symptoms of the condition under treatment.

Severe hypersensitivity reactions, including anaphylaxis and angioedema, have been reported during treatment with miconazole topical formulations. If a reaction suggesting hypersensitivity or irritation should occur, the treatment should be discontinued.

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 corticosteroids. If either of the above is 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 *4.8 Undesirable Effects*).

Risk factors for increased systemic effects of topical corticosteroids are:

- Potency and formulation of topical corticosteroid
- 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 infant nappies 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 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 clobetasol propionate 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 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 tolerance, risk of generalised pustular psoriasis (see *4.8 Undesirable Effects*) 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 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 (see *4.8 Undesirable Effects*).

4.5 Drug 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.

Miconazole administered systemically is known to inhibit CYP3A4/2C9. Due to the limited systemic availability after topical application, clinically relevant interactions are rare. However, in patients on oral anticoagulants, such as warfarin, caution should be exercised and anticoagulant effect should be monitored.

4.6 Use in Special Populations

Fertility

There are no data in humans to evaluate the effect of topical corticosteroids on fertility.

Clobetasol propionate administered subcutaneously to rats had no effect upon mating performance; however, fertility was decreased at the highest dose (see *6. Nonclinical Properties).*

Pregnancy

There are limited data from the use of clobetasol propionate in pregnant women.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development (see *6. Nonclinical Properties)*. The relevance of this finding to human beings has not been established.

In animals, miconazole nitrate has shown no teratogenic effects but is foetotoxic at high oral doses. Only small amounts of miconazole nitrate are absorbed following topical administration.

Administration of *TENOVATE M* 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.

Topically applied miconazole is minimally absorbed into the systemic circulation, and it is not known whether miconazole is excreted in human breast milk.

Administration of *TENOVATE M* during lactation should only be considered if the expected benefit to the mother outweighs the risk to the infant.

If used during lactation *TENOVATE M* 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 M* 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 the active ingredients of *TENOVATE M*.

4.8 Undesirable Effects

In absence of availability of adverse event data on the fixed dose combination of Clobetasol propionate and Miconazole, adverse event data of the individual ingredients is presented below.

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.

Clobetasol propionate

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 rare	Application site irritation/pain

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

Miconazole nitrate

Adverse reactions reported among 426 patients who received miconazole 2% cream base in 21 double-blind clinical trials are presented in Table 1 below.

Based on pooled safety data from these clinical trials, the most commonly reported adverse reaction was Application site irritation (0.7%).

Including the above-mentioned adverse reaction, Table 1 displays adverse reactions that have been reported with the use of topical, non-gynaecological, miconazole nitrate/miconazole from either clinical trial or postmarketing experiences.

The displayed frequency categories use the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); and very rare (< 1/10,000, including isolated reports) and Not Known (cannot be estimated from the available data).

Table 1: Adverse Reactions Reported in Clinical Trials and Post-marketing Experience

System Organ Class	**Adverse Drug Reactions**	
	Frequency Category	
	Uncommon (≥1/1,000 to <1/100)	**Not Known**
Immune System Disorders		Anaphylactic reaction, Hypersensitivity
Skin and Subcutaneous Tissue Disorders	Skin burning sensation Skin inflammation	Angioedema Urticaria Contact dermatitis Rash Erythema Pruritus
General Disorders and Administration Site Conditions	Application site reactions (including application site irritation, burning, pruritus, reaction NOS and warmth)	

4.9 Overdose

Symptoms and Signs

Topically applied clobetasol propionate 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 *4.8 Undesirable Effects*).

Excessive use can result in skin irritation, which usually disappears after discontinuation of therapy. In case of accidental ingestion, stomach irritation may occur.

Treatment

In the event of overdose, *TENOVATE M* should be withdrawn gradually by reducing the frequency of application or by substituting a less potent corticosteroid because of the risk of glucocorticosteroid insufficiency.
TENOVATE M is intended for cutaneous use, not for oral use. If accidental ingestion of large quantities of the product occurs, use appropriate supportive care.
Further management should be as clinically indicated.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of action and Pharmacodynamic Properties

Clobetasol propionate

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

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.

Miconazole Nitrate

Miconazole nitrate is an imidazole antifungal agent and may act by interfering with the permeability of the fungal cell membrane. It possesses a wide antifungal spectrum and has some antibacterial activity.

5.2 Pharmacokinetic Properties

Clobetasol propionate

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 ng/ml occurred in one study 8 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 ng/ml and 4.6 ng/ml occurred respectively in patients with psoriasis and eczema 3 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.

Miconazole nitrate

Absorption

There is little absorption through skin or mucous membranes when miconazole nitrate is applied topically.

Distribution

Absorbed miconazole is bound to plasma proteins (88.2%) and red blood cells (10.6%).

Metabolism and Elimination

The small amount of miconazole that is absorbed is eliminated predominantly in faeces as both unchanged drug and metabolites.

6. NONCLINICAL PROPERTIES

Clobetasol propionate

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.

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.

Miconazole nitrate

Preclinical data reveal no special hazard for humans based on conventional studies of local irritation, single and repeated dose toxicity, genotoxicity and toxicity to reproduction.

7. DESCRIPTION

Contains:

Clobetasol Propionate IP	0.05% w/w
Miconazole Nitrate IP	2.0 % w/w
Chlorocresol IP (as Preservative)	0.1% w/w

in a non-greasy base

List of Excipients

Finester-1240 (GMS-NSE), Cetostearyl Alcohol, Arlacel-165, Beeswax White, Propylene Glycol, Chlorocresol, Citric Acid Monohydrate, Sodium Citrate, Purified Water.

8. PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

No relevant data available.

8.2 Shelf Life

The expiry date is indicated on the label and packaging.

8.3 Packaging Information

Aluminum tube in a carton.

8.4 Storage and Handling Information

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

Keep out of reach of children.

For external use only.

9. PATIENT COUNSELLING INFORMATION

Registered Medical Practitioners may counsel their patients (and/or patients' caregivers as applicable) about the special warnings and precautions for use, drug interactions, undesirable effects, and any relevant contra-indications of *TENOVATE M*. Patients (and/or patients' caregivers) 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 License number is indicated on the label and packaging.

12. DATE OF REVISION

07-MAY-2025

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

Version TEN-M/PI/IN/2025/01

Adapted from:

- *Clobetasol propionate (topical) GDS v17 dated 19 November 2024*
- *Daktarin 2% w/w cream SmPC (last updated on emc: 26 Apr 2023). Available at: https://www.medicines.org.uk/emc/product/14745/smpc*