SUMMARY OF PRODUCT CHARACTERISTICS (SMPC)

1. Name of drug product

ZYCOZOLE CREAM

2. QUALITATIVE & QUANTITATIVE COMPOSITION

Each gm contains:

Miconazole nitrate USP..…….2.0 %w/w

Neomycin Sulfate USP..…….… ...0.5 % w/w

Clobetasol propionate USP……...0.05 % w/w

Chlorocresol USP/NF……..0.1 %w/w

(As Preservative).

Cream Base…….Q.S.

3. PHARMACEUTICAL FORM

CREAM

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ZYCOZOLE CREAM is indicated in resistant dermatoses where secondary bacterial infection and/or fungal infection is present, suspected, or likely to occur.
e.g., psoriasis (excluding widespread plaque psoriasis), recalcitrant eczemas.

4.2 Posology and method of administration

For topical use only.
Creams are especially appropriate for moist or weeping surfaces.

Adults and adolescents
Apply thinly and gently rub in using only enough to cover the entire affected area twice daily until improvement occurs. As with other highly active topical corticosteroid preparations, therapy should be discontinued when control is achieved. In the more responsive conditions this may be within a few days. If the condition worsens or does not improve within seven days, treatment and diagnosis should be re-evaluated. If a longer course is necessary, it is recommended that treatment should not be continued for more than four weeks. However, treatment should not be continued for more than seven days without medical supervision. Repeated short courses of *ZYCOZOLE CREAM*may be used to control exacerbations. If continuous corticosteroid treatment is necessary, a less potent preparation which does not contain neomycin sulphate should be used.
Allow adequate time for absorption after each application before applying an emollient.
Patients should be advised to wash their hands after applying *TENOVATE NM*, unless it is the hands that are being treated.
In very resistant lesions, especially where there is hyperkeratosis, the anti-inflammatory effect of *ZYCOZOLE CREAM* 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

The maximum weekly dose should not exceed 50 g/week.
C***hildren aged 2 years and over***
*ZYCOZOLE CREAM*is suitable for use in children (2 years and over) at the same dose as adults. A possibility of increased absorption exists in very young children, thus *ZYCOZOLE CREAM*is contraindicated in neonates and infants (less than 2 years) (see *Contraindications*).
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 (see *Special Warnings and Special Precautions for Use*).
Care should be taken when using *ZYCOZOLE CREAM*to ensure the amount applied is the minimum that provides therapeutic benefit.

Elderly
ZYCOZOLE CREAMis suitable for use in the elderly. Caution should be exercised in cases where a decrease in renal function exists and significant systemic absorption of neomycin sulphate may occur (see Special Warnings and Special Precautions for Use). The minimum quantity should be used for the shortest duration to achieve the desired clinical benefit .

Renal Impairment
Dosage of ZYCOZOLE CREAMshould be reduced in patients with reduced renal function (see Special Warnings and Special Precautions for Use).

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 NM*:

- Hypersensitivity to any of the ingredients of the preparation.
- Rosacea.
- Acne vulgaris.
- Perioral dermatitis.
- Pruritus without inflammation.
- Perianal and genital pruritus.
- Primary cutaneous viral infections (e.g., herpes simplex, chickenpox).
- Primary infected skin lesions caused by infection with fungi, bacteria or yeast.
- Secondary infections due to *Pseudomonas* or *Proteus* species.
- Otitis externa where the eardrum is perforated because of the risk of ototoxicity.

Due to the known ototoxic and nephrotoxic potential of neomycin sulphate, the use of *ZYCOZOLE CREAM*in large quantities or on large areas for prolonged periods of time is not recommended in circumstances where significant systemic absorption may occur.

A possibility of increased absorption exists in very young children, thus *ZYCOZOLE CREAM*is not recommended for use in neonates and infants (up to 2 years). In neonates and infants, absorption by immature skin may be enhanced and renal function may be immature.

4.4 Special warnings and precautions for use

Miconazole Nitrate

When Miconazole Nitrate is used by patients taking oral anticoagulants, the anticoagulant effect should be carefully monitored.

As with any topical corticosteroid, caution is advised with infants and children when Miconazole Nitrate is to be applied to extensive surface areas or under occlusive dressings including baby napkins; similarly, application to the face should be avoided.

In infants, long term continuous topical corticosteroid therapy should be avoided. Adrenal suppression can occur even without occlusion.

Neomycin Sulfate

For nasal application only. Keep out of the eyes and ears.

Neomycin sulfate contains Arachis oil (peanut oil) and should not be taken/applied by patients known to be allergic to peanut. As there is a possible relationship between allergy to peanut and allergy to Soya, patients with Soya allergy should also avoid Neomycin sulfate.

Clobetasol Propionate

Clobetasol should be used with caution in patients with a history of local hypersensitivity to other corticosteroids or to any of the excipients in the preparation. Local hypersensitivity reactions may resemble symptoms of the condition under treatment.

4.5 Interaction with other medicinal products and other forms of interaction

Miconazole Nitrate

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.

Neomycin Sulfate

None known.

Clobetasol Propionate

Co-administered drugs that can inhibit CYP3A4 (eg 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 Fertility, pregnancy and lactation

Miconazole Nitrate

Pregnancy

Clinical data on the use of miconazole nitrate in pregnancy are limited. In animals, corticosteroids are known to cross the placenta and consequently can affect the foetus. Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of these findings to humans has not been established.

As a precautionary measure, it is preferable to avoid the use of miconazole nitrate during pregnancy. Treatment of large surfaces and the application under occlusive dressing is not recommended.

Breastfeeding

There are no adequate and well-controlled studies on the topical administration of miconazole nitrate during breastfeeding. It is not known whether concomitant topical administration of miconazole nitrate to the skin could result in sufficient systemic absorption to produce detectable quantities of hydrocortisone and miconazole in breast milk in humans

Neomycin Sulfate

Chlorhexidine and neomycin cannot be detected in the blood following application of neomycin sulfate and its use is unlikely to have any effect on the foetus or on breast feeding.

Clobetasol Propionate

Pregnancy

There are limited data from the use of Clobetasol 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 Clobetasol 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.

Breast-feeding

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 Clobetasol propionate during lactation should only be considered if the expected benefit to the mother outweighs the risk to the infant. If used during lactation Clobetasol propionate should not be applied to the breasts to avoid accidental ingestion by the infant.

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.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Safety information from clinical trial data is not available for Zycozole Cream. The following information is available for Zycozole Cream. As the cream and ointment formulations contain the same active ingredients in the same concentrations, the safety data for the cream formulation is considered applicable to the ointment formulation.

The safety of Zycozole Cream was evaluated in 480 patients who participated in 13 clinical trials (six double-blind and seven open-label trials) of Zycozole Cream but not with Zycozole Ointment. These studies examined patients from 1 month to 95 years of age with infections of the skin caused by dermatophytes or Candida species in which inflammatory symptoms were prominent.

All Patients

No adverse reactions were reported by ≥1% of the 480 Zycozole Cream-treated patients (adult and paediatric patients combined).

The 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); very rare (<1/10,000); and not known (cannot be estimated from the available clinical trial data).

Of the three adverse reactions identified from the 13 clinical trials of Zycozole Cream, skin irritation was reported in one clinical trial that included patients aged 17 to 84 years, skin burning sensation in two clinical trials that included patients aged 13 to 84 years, and irritability in one clinical trial of infants aged 1 to 34 months.

Paediatric Population

The safety of Zycozole Cream was evaluated in 63 paediatric patients (1 month to 14 years of age) who were treated with Zycozole Cream in 3 of the 13 clinical trials noted above. One adverse reaction term (irritability) was reported in these 3 trials. The frequency of irritability in Zycozole Cream-treated paediatric patients was common (3.2%).

All events of irritability occurred in one clinical trial of infants (aged 1 to 34 months) with napkin (diaper) dermatitis. The frequency, type, and severity of other adverse reactions in paediatric patients are expected to be similar to those in adults. Adverse reactions were reported by ≥1% of the 480 Zycozole Cream-treated patients (adult and paediatric patients combined).

Adverse Reactions in Adult and Paediatric Patients Treated With Zycozole Cream

	System Organ Class	Adverse reactions	
		Frequency Category	
		Uncommon (≥1/1,000 to <1/100)	Not Known
	Immune System Disorders		Anaphylactic reaction, Hypersensitivity
	Skin and Subcutaneous Tissue Disorders	Skin irritation, Skin burning sensation, Urticaria, Pruritus	Angioedema, Rash, Contact dermatitis, Erythema, Skin inflammation, Skin hypopigmentat Application site reaction
	General Disorders and Administration Site Conditions	Irritability	
	Eye disorders		Vision, blurred

4.9 Overdose

Prolonged and excessive use can result in skin irritation, which usually disappears after discontinuation of therapy. Topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Miconazole Nitrate

Pharmacotherapeutic group: Imidazole and triazole derivatives, combinations, ATC code: D01AC20.

Miconazole nitrate is active against dermatophytes and pathogenic yeasts, and many Gram-positive bacteria.

Neomycin Sulfate

Neomycin is a rapidly bactericidal aminoglycoside antibiotic effective against Gram positive organisms including staphylococci and a wide range of Gram negative organisms. Strains of *Pseudomonas aeruginosa* are resistant to neomycin, as are fungi and viruses.

Clobetasol Propionate

Pharmacotherapeutic group: Corticosteroids, very potent, dermatological preparations (group IV)

ATC code: D07 AD01

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.

Pharmacodynamic effects

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

5.2 Pharmacokinetic properties

Miconazole Nitrate

Miconazole remains in the skin after topical application for up to 4 days. Systemic absorption of miconazole is limited, with a bioavailability of less than 1% following topical application of miconazole. Plasma concentrations of miconazole and/or its metabolites were measurable 24 and 48 hours after application. Approximately 3% of the dose of hydrocortisone is absorbed after application on the skin.

Neomycin Sulfate

Neomycin is either not absorbed or is absorbed only minimally through intact skin. Any neomycin which is absorbed will be rapidly excreted by the kidneys in an unchanged state.

Clobetasol Propionate

Mean peak plasma Clobetasol propionate concentrations of 0.63 ng/ml occurred in one study eight hours after the second application (13 hours after an initial application) of 30 g Clobetasol propionate 500 micrograms/g ointment to normal individuals with healthy skin. Following the application of a second dose of 30 g Clobetasol propionate cream 500 micrograms/g 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 three hours after a single application of 25 g Clobetasol propionate 500 micrograms/g ointment.

5.3 Preclinical safety data

Preclinical data on the drug product (Miconazole nitrate, Neomycin Sulphate & Clobetasole propionate) revealed no special hazard for humans based on conventional studies of ocular irritation, dermal sensitization, single dose oral toxicity, primary dermal irritation toxicity, and 21- day repeat dose dermal toxicity.

Additional preclinical data on the individual active ingredients in this drug product reveal no special hazard for humans based on conventional studies of local irritation, single and repeated dose toxicity, genotoxicity, and for miconazole toxicity to reproduction. Miconazole has shown no teratogenic effects but is fetotoxic at high oral doses. Reproductive effects (fetotoxicty, reduced weight gain) and developmental abnormalities specifically craniofacial effects including cleft palate have been reported with hydrocortisone in various animal models.

6. Pharmaceutical particulars

6.1 List of excipients

White petroleum jelly, Light liquid paraffin,
Cetostearyl Alcohol, Cetomacrogol 1000,
Butyl Hydroxy Toluene, Disodium Edetate,
P-chloro m-cresol, Propylene glycol,
Sodium Dihydrogen orthophosphate & Imidurea.

6.2 Incompatibilities: Not Applicable.

6.3 Shelf life: 36 months.

6.4 Special precautions for storage

Store in cool place at a temperature not exceeding 25°C. Do not or freeze

6.5 Nature and contents of container

15g cream packed in the liquor coated aluminum tube and each tube is packed in the printed mono carton with insert.

6.6 Special precautions for disposal and other handling

No special requirements for disposal. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorisation holder

8. Marketing authorization number(s)

FDA/SD.213-121801

9. Date of first authorization/renewal of the authorization

Dec. 2021

10. Date of revision of the text

08.2025