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

8027817-9093

CORTAZ NC

Clobetasol Propionate, Clotrimazole & Neomycin Sulphate Cream

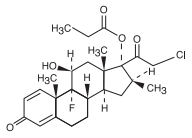
Composition:

Clobetasol Propionate U.S.P.	0.05 % w/w
Clotrimazole I.P.	1.00 % w/w
Neomycin Sulphate I.P.	0.5 % w/w
Added Chlorocresol I.P. as preservative	0.10 % w/w
In cream base	q.s.

DESCRIPTION

Clobetasol propionate:

Clobetasol propionate, a synthetic corticosteroid for topical dermatologic use. Chemically, clobetasol propionate is (11β,16β)-21-chloro-9-fluoro-11-hydroxy-16-methyl-17-(1-oxopropoxy)-pregna-1,4-diene-3,20-dione, and it has the following structural formula:



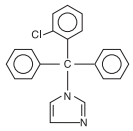
Chemical Formula: $C_{25}H_{32}ClFO_5$

Molecular Weight: 466.97

It is a white to cream-colored crystalline powder insoluble in water.

Clotrimazole:

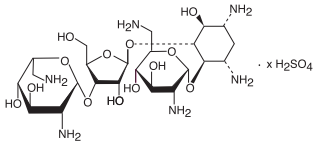
Clotrimazole, a synthetic antifungal agent having the chemical name 1-[(2-chlorophenyl)diphenylmethyl]-1*H*-imidazole, the molecular formula $C_{22}H_{17}ClN_2$; a molecular weight of 344.84; and the structural formula:



Clotrimazole is a white or pale yellow, crystalline powder. It is freely soluble in acetone, in chloroform, in ethanol (95 percent) and in methanol; practically insoluble in water.

Neomycin Sulphate:

It is a mixture of sulphates of substances produced by the growth of certain selected strains of *Streptomyces fradiae,* the main component being the sulphate of 2-deoxy-4-*O*-(2,6-diamino-2,6-dideoxy-α-D-glucopyranosyl)-5-*O*-[3-*O*-(2,6-diamino-2,6-dideoxy-β-L-idopyranosyl)-β-D-ribofuranosyl]-D-streptamine(neomycin B). The chemical formula is $C_{23}H_{46}N_6O_{13}.xH_2SO_4$ and molecular weight is 615 (base) and the structural formula is :



A white or yellowish white odourless hygroscopic powder. It is freely soluble in water; is slightly soluble in ethanol (95 percent); practically insoluble in acetone, in chloroform and in ether.

CLINICAL PHARMACOLOGY

Clobetasol Propionate:

Clobetasol propionate has anti-inflammatory, antipruritic, and vasoconstrictive properties. The mechanism of the anti-inflammatory activity of the topical steroids, in general, is unclear. However, corticosteroids are thought to act by the induction of phospholipase A_2 inhibitory proteins, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A_2.

Pharmacokinetics

The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including the vehicle and the integrity of the epidermal barrier. Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin may increase percutaneous absorption. When applied topically, particularly to large areas, when the skin is broken, or under occlusive dressings, corticosteroids may be absorbed in sufficient amounts to cause systemic effects

Clotrimazole:

Clotrimazole is a broad-spectrum antifungal agent that is used for the treatment of dermal infections caused by various species of pathogenic dermatophytes, yeasts, and Malassezia furfur. The primary action of clotrimazole is against dividing and growing organisms.

In vitro, clotrimazole exhibits fungistatic and fungicidal activity against isolates of *Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum, Microsporum canis* and *Candida* species including *Candida albicans*. In general, the *in vitro* activity of clotrimazole corresponds to that of tolnaftate and griseofulvin against the mycelia of dermatophytes (*Trichophyton, Microsporum,* and *Epidermophyton*), and to that of the polyenes (amphotericin B and nystatin) against budding fungi (*Candida*). Using an in vivo (mouse) and an in vitro (mouse kidney homogenate) testing system, clotrimazole and miconazole were equally effective in preventing the growth of the *pseudomycelia* and *mycelia* of *Candida albicans*.

Strains of fungi having a natural resistance to clotrimazole are rare. Only a single isolate of *Candida guilliermondi* has been reported to have primary resistance to clotrimazole.

No single-step or multiple-step resistance to clotrimazole has developed during successive passages of *Candida albicans* and *Trichophyton mentagrophytes*. No appreciable change in sensitivity was detected after successive passage of isolates of *C. albicans, C.krusei,* or *C. pseudotropicalis* in liquid or solid media containing clotrimazole. Also, resistance could not be developed in chemically induced mutant strains of polyene-resistant isolates of *C. albicans*. Slight, reversible resistance was noted in three isolates of *C. albicans* tested by one investigator. There is a single report that records the clinical emergence of *C. albicans* strain with considerable resistance to flucytosine and miconazole, and with cross-resistance to clotrimazole, the strain remained sensitive to nystatin and amphotericin B.

Pharmacokinetics

When applied topically clotrimazole penetrates the epidermis but there is little if any systemic absorption. Absorption of 3 to 10% of a dose has been reported after vaginal use. Clotrimazole is metabolised in the liver to inactive compounds and excreted in the faeces and urine.

Neomycin Sulphate:

Actively transported across the bacterial cell membrane, binds to a specific receptor protein on the 30S subunit of bacterial ribosomes, and interferes with an initiation complex between mRNA (messenger RNA) and the 30 S subunit, inhibiting protein synthesis. DNA may be misread, thus producing nonfunctional proteins; polyribosomes are split apart and are unable to synthesize protein.

Pharmacokinetics

Although not absorbed through intact skin, topical neomycin is readily absorbed from large denuded, burned, or granulating areas. Greater and more rapid absorption occurs with neomycin cream than with the ointment.

Special Populations

Pregnancy

CORTAZ NC cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

It is not known whether topical administration of CORTAZ NC cream could result in sufficient systemic absorption to produce detectable quantities in human milk. Because many drugs are excreted in human milk, caution should be exercised when either CORTAZ NC cream is administered to a nursing woman.

Pediatric Use

Safety and effectiveness of CORTAZ NC cream in pediatric patients have not been established.

INDICATIONS AND USAGE

CORTAZ NC cream is indicated for the topical treatment of bacterial, fungal skin infections with associated inflammation.

DOSAGE AND ADMINISTRATION

Apply a thin layer of CORTAZ NC cream to the affected skin areas twice daily and rub in gently and completely. The treated skin area should not be bandaged, otherwise covered, or wrapped so as to be occlusive unless directed by the physician.

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

CORTAZ NC cream contains clobetasol propionate systemic absorption of topical corticosteroids can produce reversible HPA axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal from treatment. Manifestations of Cushing's syndrome, hyperglycemia, and glucosuria can also be produced in some patients by systemic absorption of topical corticosteroids while on therapy.

If HPA axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent corticosteroid. Recovery of HPA axis function is generally prompt upon discontinuation of topical corticosteroids. Infrequently, signs and symptoms of glucocorticosteroid insufficiency may occur requiring supplemental systemic corticosteroids. For information on systemic supplementation, see prescribing information for those products. If irritation develops, CORTAZ NC cream should be discontinued and appropriate therapy instituted.

Information for Patients

1. This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes.
2. This medication should not be used for any disorder other than that for which it was prescribed.
3. The treated skin area should not be bandaged, otherwise covered, or wrapped so as to be occlusive unless directed by the physician.
4. Patients should report any signs of local adverse reactions to the physician.
5. Not for ophthalmic use.

DRUG INTERACTIONS

Neomycin Sulphate:

Aminoglycosides, other concurrent topical and systemic use of neomycin or related drugs is not recommended since hypersensitivity reactions may occur more frequently during concurrent use; if significant systemic absorption occurs, hearing loss may also result; this may progress to deafness even after discontinuation of the drug, and may be permanent.

ADVERSE REACTIONS

Clobetasol propionate:

In controlled clinical trials, the most frequent adverse reactions reported for clobetasol cream were burning and stinging sensation in 1% of treated patients. Less frequent adverse reactions were itching, skin atrophy, and cracking and fissuring of the skin. Cushing's syndrome has been reported in infants and adults as a result of prolonged use of topical clobetasol propionate formulations. The following additional local adverse reactions have been reported with topical corticosteroids, and they may occur more frequently with the use of occlusive dressings and higher potency corticosteroids. These reactions are listed in an approximately decreasing order of occurrence: dryness, acneform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, irritation, striae, and miliaria.

Clotrimazole:

The following adverse reactions have been reported in connection with the use of this product: erythema, stinging, blistering, peeling, edema, pruritus, urticaria, burning, and general irritation of the skin.

Neomycin Sulphate:

Contact dermatitis (itching, rash, redness, swelling, or other sign of skin irritation not present before therapy)

Incidence rare: Ototoxicity (any loss of hearing)

OVERDOSAGE

Clobetasol propionate:

Topically applied clobetasol propionate cream can be absorbed in sufficient amounts to produce systemic effects

Clotrimazole:

Acute overdosage with topical application of clotrimazole is unlikely and would not be expected to lead to a life-threatening situation.

EXPIRY DATE

Do not use later than the date of expiry.

STORAGE

Store in a dry place at a temperature not exceeding 25°C, protected from light. Do not freeze. Keep out of reach of children. For external use only. Keep tube tightly closed after use.

PRESENTATION

CORTAZ NC cream is available in 15g Tube

torrent

Marketed by :
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist. Mehsana, INDIA.

Manufactured by :
Aurochem Laboratories (I) Pvt. Ltd.
8, Palghar Taluka Industrial Co-op. Estate Limited.
Palghar- 401 404. Dist. Thane. Maharashtra.