BETASOL GM

CLOBETASOL PROPIONATE, NEOMYCIN & MICONAZOLE NITRATE CREAM

COMPOSITION:

Clobetasol Propionate BP	0.05 % w/w
Neomycin Sulfate BP Eq. to Neomycin	0.5 % w/w
Miconazole Nitrate BP	2.5 % w/w
Cream Base	q.s.

DESCRIPTION:

This cream contains a combination of Clobetasol Propionate BP, Neomycin Sulfate BP & Miconazole Nitrate BP. Clobetasol Propionate, Neomycin Sulfate & Miconazole Nitrate is having anti-inflammatory, antibiotic & antifungal activity respectively.

INDICATIONS:

Clobetasol Propionate, Neomycin & Miconazole Nitrate Cream is used to help reduce the redness and itchiness of certain skin problems. These skin problems include eczema, psoriasis, dermatitis or insect bites, where an infection may be a problem.

PHARMACOKINETICS:

Clobetasol propionate-

Absorption: Topical corticosteroids can be systemically absorbed from intact healthy skin. The extent of topical absorption of corticosteroids is determined by many factors, including the vehicle and the integrity of the epidermal barrier.

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 Clobetasol Propionate cream to normal individuals with healthy skin. Following the application of a second dose of 30 g Clobetasol Propionate cream mean peak plasma concentrations were slightly higher than the ointment and occurred 10 hours after application.

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

Neomycin

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.

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

PHARMACODYNAMICS:

Clobetasol propionate- Clobetasol propionate is a highly active corticosteroid with topical anti-inflammatory activity. The major effect of Clobetasol propionate on skin is a nonspecific anti-inflammatory response, partially due to vasoconstriction and decrease in collagen synthesis.

Neomycin- 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.

Miconazole – 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.

DOSAGE AND ADMINISTRATION:

Method of administration: Topical

Adults and children over 2 years:

Apply sparingly to the affected area once or twice daily until improvement occurs. As with other highly-active topical steroid preparations therapy should be discontinued when control is achieved. In the more responsive conditions this may be within a few days.

In very resistant lesions, especially where there is hyperkeratosis, the anti-inflammatory effects of Clobetasol Propionate, Neomycin & Miconazole Nitrate Cream can be enhanced. Overnight occlusion only is usually adequate to bring about a satisfactory response, thereafter improvement can be usually maintained by application without occlusion.

Treatment should not be continued for more than 7 days without medical supervision. If a longer course is necessary, it is recommended that treatment should not be continued for more than 4 weeks without the patient's condition being reviewed.

Dosage in Renal Impairment:

Dosage should be reduced in patients with reduced renal function.

Elderly:

Clobetasol Propionate, Neomycin & Miconazole Nitrate Cream is 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.

Children:

Clobetasol Propionate, Neomycin & Miconazole Nitrate 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 this ointment is not recommended for use in neonates and infants (younger than 2 years).

CONTRAINDICATION:

Clobetasol Propionate, Neomycin & Miconazole Nitrate Cream is contra-indicated in patients with hypersensitivity to Clobetasol propionate, Neomycin, Miconazole Nitrate or any of the excipients.

SPECIAL WARNING AND PRECAUTION FOR USE:

- Long term continuous topical therapy should be avoided where possible, particularly in infants and children, as adrenal suppression can occur readily even without occlusion.
- If used in childhood, or on the face, courses should be limited to 5 days and occlusion should not be used.
- The face, more than other areas of the body, may exhibit atrophic changes after prolonged treatment with potent topical corticosteroids. This must be borne in mind when treating such conditions as psoriasis and severe eczema.
- If applied to the eyelids, care is needed to ensure that the preparation does not enter the eye, as glaucoma might result. If the cream does enter the eye, the affected eye should be bathed in copious amounts of water.
- Topical corticosteroids may be hazardous in psoriasis for a number of reasons, including rebound relapses, development of tolerance, risk of generalized pustular psoriasis and development of local or systemic toxicity due to impaired barrier function of the skin. If used in psoriasis careful patient supervision is important.
- Extension of the infection may occur due to the masking effect of the steroid. If infection persists, systemic chemotherapy is required. Any spread of infection requires withdrawal of topical corticosteroid therapy.
- Bacterial infection is encouraged by the warm, moist conditions induced by occlusive dressings, and the skin should be cleansed before a fresh dressing is applied.
- Following significant systemic absorption, aminoglycosides such as Neomycin can cause irreversible ototoxicity; and Neomycin has nephrotoxic potential.
- In renal impairment, the plasma clearance of neomycin is reduced.
- Extended or recurrent application may increase the risk of contact sensitization.
- Products which contain antimicrobial agents should not be diluted.

INTERACTION WITH OTHER MEDICINE AND CONCOMITANT USE:

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.

Neomycin- Neomycin Sulphate can intensify and prolong the respiratory depressant effects of neuromuscular blocking agents following systemic absorption.

Miconazole - 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.

PREGNANCY AND LACTATION:

Neomycin present in maternal blood can cross the placenta and may give rise to a theoretical risk of foetal toxicity, thus the use of Clobetasol Propionate, Neomycin & Miconazole Nitrate Cream is not recommended in pregnancy and lactation.

The safe use of clobetasol propionate during lactation has not been established.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:

Clobetasol Propionate, Neomycin & Miconazole Nitrate Cream is not expected to have any effect.

ADVERSE REACTION:

Adverse drug reactions (ADRs) are listed below by Med DRA 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.

Infections and Infestations

Very rare: Opportunistic infection

Immune System Disorders

Very rare: Hypersensitivity, generalised rash

Not known: anaphylaxis, Angioneurotic edema

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, glaucoma, hyperglycaemia/glucosuria, cataract, hypertension, increased weight/obesity, decreased endogenous cortisol levels, alopecia, trichorrhexis

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.

General Disorders and Administration Site Conditions

Uncommon: Application site irritation, Application site burning, Application site pruritus, Application site reaction NOS, Application site warmth

OVERDOSE:

Symptoms and signs

In topically applied Clobetasol Propionate, Neomycin & Miconazole Nitrate Cream, Clobetasol 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. Neomycin is unlikely to have any adverse effects on the patient. Excessive use can result in skin irritation, which usually disappears after discontinuation of therapy.

Treatment

In the event of overdose, treatment 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.

INCOMPATIBILITY:

Not Applicable

SHELF LIFE:

3 Years

PACKAGING:

30 gm laminated tube is packed in a printed carton along with pack insert.

STORAGE CONDITION:

Store in a dry place below 30° C. Protect from light.

Keep out of reach of children.

MANUFACTURED BY:

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MARKETED BY:

Metpharm, Haiti.