1. NAME OF THE MEDICINAL PRODUCT

BG CREAM / CLOBETASOL PROPIONATE, MICONAZOLE NITRATE, GENTAMICIN SULFATE CREAM

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition:

Clobetasol Propionate BP 0.05% w/w

Gentamicin Sulphate BP Eq. to Gentamicin 0.1% w/w

Miconazole Nitrate BP 2% w/w

Chlorocresol (As Presevative) BP 0.10% w/w

Excipients with known effect:
Propylene glycol
Cetosteryl Alcohol
PEG 4000
C.M. 1000
Glycerine
Liquid Paraffin
Disodium EDTA
Di Sodium Hydrogen Phosphate
Steric Acid
Butylated hydroxy Toluene
Chlorocresol
Purified Water

3. PHARMACEUTICAL FORM

Topical Cream

4. Clinical particulars

4.1 Therapeutic indications

Clobetasol propionate is a very active topical corticosteroid which is of particular value when used in short courses for the treatment of more resistant dermatoses such as psoriasis excluding widespread plaque psoriasis), recalcitrant eczemas, lichen planus, discoid lupus erythematosus, and other skin conditions which do not respond satisfactorily to less active steroids. For the topical treatment of inflamed dermatoses where infection by susceptible organisms and inflammation co-exist, eg intertrigo and infected eczema. Moist or dry eczema or dermatitis including atopic eczema primary irritant or contact allergic eczema or seborrhoeic eczema including that associated with acne. Intertriginous eczema or dermatitis including atopic eczema, primary irritant or contact allergic eczema or seborrhoeic eczema including that associated with acne. Intertriginous eczema including inframammary intertrigo, perianal and genital dermatitis. Primary skin infections: impetigo contagiosa, superficial folliculitis, eczema, furunculosis, sycosis barbae, and pyoderma gangrenosum. Secondary skin Infections: infectious ecezematoid dermatitis, pustular acne, pustular psoriasis, infected seborrheic dermatitis, infected contact dermatitis, infected excoriations, and bacterial super-infections of fungal or viral infections. Please Note: Gentamicin sulfate is a bactericiadal

agent that is not effective against viruses or fungi in skin infections.

Method of administration
Topical

4.2 Contraindications
Rosacea, Acne vulgaris, Perioral dermatitis, Perianal and genital pruritus Primary cutaneous viral infections (e.g herpes simplex, chickenpox), Hypersensitivity to the preparation.

4.3 Special warnings and precautions for use
Long-term continuous therapy should be avoided where possible, particularly in infants and children, as adrenal suppression can occur even without occlusion. If required for use in children, it is recommended that the treatment should be reviewed weekly. It should be noted that the infant's napkin may act as an occlusive dressing. Topical steroids 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.

4.4 Interaction with other medicinal products and other forms of interaction
None reported.

4.5 Pregnancy and Lactation
There is inadequate evidence of safety in human pregnancy. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate and intrauterine growth retardation. The relevance of this finding to humans has not been established, therefore, topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods. The safe use of clobetasol propionate during lactation has not been established.

4.6 Effects on ability to drive and use machines
None

4.7 Undesirable effects
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.

Skin and Subcutaneous Tissue Disorders	
Common:	Skin atrophy*, telangiectasis*
Uncommon:	Striae*

Post-marketing data

Infections and Infestations	
Very rare:	Opportunistic infection

Immune System Disorders	
Very rare:	Allergic reactions including anaphylaxis and 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, glaucoma, hyperglycaemia/glucosuria, cataract, hypertension, increased weight/obesity, decreased endogenous cortisol levels

Skin and Subcutaneous Tissue Disorders	
Very rare:	Skin thinning*, skin wrinkling*, skin dryness*, pigmentation changes*, hypertrichosis, exacerbation of underlying symptoms, allergic contact dermatitis/dermatitis, pustular psoriasis (see *Special Warnings and Special Precautions for Use*), erythema, rash, urticaria, alopecia*, trichorrhexis*, pruritus, local skin burning /skin pain, acne

**Skin features related to hypothalamic-pituitary adrenal (HPA) axis suppression.*

General Disorders and Administration Site Conditions	
Very rare:	Application site irritation/pain

Neomycin Sulphate

The incidence of allergic hypersensitivity reactions to neomycin sulphate in the general population is low. There is, however, an increased incidence of hypersensitivity to neomycin in certain selected groups of patients in dermatological practice particularly those with venous stasis eczema and ulceration. Allergic hypersensitivity to neomycin sulphate following topical application may manifest itself as a reddening and scaling of the affected skin, as an eczematous exacerbation of the lesion or as a failure of the lesion to heal.

Miconazole nitrate

Adverse drug reactions reported among 834 patients who received miconazole nitrate 2% cream (n=426) and/or placebo cream base (n=408) in 21 double-blind clinical trials are presented in Table 1 below. Moreover, adverse drug reactions from spontaneous reports during the worldwide post-marketing experience with miconazole nitrate 2% cream that meet threshold criteria are included in Table 1. The adverse drug reactions are ranked by frequency, using the following convention:

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)
Adverse reactions obtained from clinical studies and post-marketing surveillance are presented by frequency category based on incidence in clinical trials or epidemiology studies, when known.
Table 1: Adverse reactions reported in clinical trials and post-marketing experience.

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

4.8 Overdose

Acute overdosage is very unlikely to occur, however, in the case of chronic overdosage or misuse, the features of hypercortisolism may appear and in this situation topical steroids should be reduced or discontinued gradually, under medical supervision.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

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

antifungal and antibacterial agent with marked activity against dermatophytes, pathogenic yeasts (eg Candida spp) and many Gram-positive bacteria including most strains of Streptococcus and Staphylococcus. Gentamycin is antibacterial agent.

5.2 Pharmacokinetic properties

Percutaneous penetration of clobetasol propionate varies among individuals and can be increased by the use of occlusive dressings, or when the skin is inflamed or diseased. 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 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.

Three hours after a single application of 25 g clobetasol propionate 0.05% ointment. Following percutaneous absorption of clobetasol propionate, the drug probably follows the metabolic pathway of systemically administered corticosteroids, i.e. metabolised primarily by the liver and then excreted by the kidneys. However, systemic metabolism of clobetasol has never been fully characterised or quantified. Following topical administration of 100 mg miconazole nitrate cream, plasma concentrations of 0.01 µg/ml were never exceeded. Allowing for a 100 fold increase due to the occlusive effects of the ointment base, if the whole of a 30 g tube (containing 600 mg miconazole) was applied at once, maximum plasma levels would be of the order of 6 µg/ml. This would correspond approximately to an iv dose of 5 mg/kg. Similar plasma levels are achieved in rabbits after an oral dose of 40 mg/kg and in rats and rabbits after an intravenousdose of 20 mg/kg (extrapolated value).

5.3 Preclinical safety data

Non-clinical studies have not been conducted with clobetasol propionate with neomycin sulphate and miconazole nitrate. Clobetasol propionate, neomycin sulphate and miconazole nitrate individually have been evaluated in animal toxicity tests, and the following statements reflect the information available on the individual components**.**

Clobetasol propionate

Carcinogenicity studies have not been conducted with clobetasol propionate individually. Clobetasol propionate was not mutagenic in a range of in vitro bacterial cell assays. In fertility studies, subcutaneous administration of clobetasol propionate to rats at doses of 6.25 to 50 µg/kg/day produced no effects on mating, and fertility was only decreased at 50 µg/kg/day. Subcutaneous administration of clobetasol propionate to mice (≥100 µg/kg/day), rats (400 µg/kg/day) or rabbits (1 to 10 µg/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 µg/kg/day and survival was reduced at 400 µg/kg/day. No treatment related effects were observed in F1 reproductive performance or in the F2 generation**.**

Neomycin sulphate

Carcinogenicity studies have not been conducted with neomycin sulphate individually. Neomycin was negative in the Ames test, HGPRT mutation assay in Chinese hamster ovary (CHO) cells and mouse bone marrow micronucleus test. The effect on fertility and pregnancy of neomycin sulphate has not been evaluated in animals**.**

Miconazole nitrate

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

6 PHARMACEUTICAL PARTICULARS

6.2 List of excipients

Propylene glycol BP
Cetosteryl Alcohol BP
PEG 4000 BP
C.M. 1000 BP
Glycerine BP
Liquid Paraffin BP
Disodium EDTA BP
Di Sodium Hydrogen Phosphate BP
Steric Acid BP
Butylated hydroxy Toluene BP
Chlorocresol BP
Purified Water BP

6.3 Incompatibilities

None known

6.4 Shelf life

36 Months

6.5 Special precautions for storage

Store in a cool, dry place. Protect from light.

6.6 Nature and contents of container <and special equipment for use, administration or implantation>

15 gm Lami Tube.

6.7 Special precautions for disposal <and other handling>

No special requirement

7 APPLICANT/MANUFACTURER:

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