1. Name of the finished pharmaceutical product: SONADERM-GM CREAM

(Invented) name of the medicinal product: Clobetasol Propionate, Miconazole Nitrate & Gentamicin Sulphate Cream

1.1 Strength: Clobetasol Propionate 0.05 % w/w, Miconazole Nitrate 2.00 % w/w and Gentamicin Sulphate 0.1 % w/w.

1.2 Pharmaceutical Dosage Form: Semi-Solid dosage form (Cream)

2. Qualitative and Quantitative Composition

2.1 Qualitative declaration:

Clobetasol Propionate BP ……..… 0.05% w/w

Miconazole Nitrate BP ……...… 2.00 % w/w

Gentamicin Sulphate BP equivalent to Gentamicin ….0.1% w/w

Chlorocresol BP (as preservative) ……...… 0.1% w/w

Cream base ……..… q.s.

2.2 Quantitative declaration:

Sr.no.	Name of API	Grade	% w/w	Overages	Qty/Batch (Kg)
1.	Clobetasol Propionate	BP	0.05	--	0.05
2.	Miconazole Nitrate	BP	2.00	--	20.00
3.	Gentamicin Sulphate	BP	0.10	5.0 %	1.05

3. Pharmaceuticals Form

White to almost white smooth cream with uniform consistency, free from gritty particles & foreign matters.

10g packed in printed aluminium collapsible tube internally lacquered having sealed nozzle & fitted with a white HD poly cap having piercing needle and further packed in preprinted carton along with leaflet.

4. Clinical Particulars

4.1 Therapeutic Indication

SONADERM-GM Cream is indicated in the treatment of resistant dermatoses such as

refractory eczemas and psoriasis where secondary bacterial or fungal infection is present, suspected or likely to occur.

4.2 Posology and Method of Administration

Adults and children over 2 years: For topical administration.

Apply a thin layer of cream to the affected skin areas twice daily and rub in gently and completely. Treatment beyond 2 consecutive weeks is not recommended, and the total dosage should not exceed 50 g/week because of the potential for the drug to suppress the hypothalamic-pituitary-adrenal (HPA) axis. Repeated short courses may be used to control exacerbations.

Or, as prescribed by the physician.

4.3 Method of Administration

Topical

4.4 Contraindications

SONADERM-GM Cream is contraindicated in following cases:

- Hypersensitivity to any of the ingredients
- Rosacea
- Acne vulgaris
- Perioral dermatitis
- Perianal and genital pruritus
- Primary cutaneous viral infections (e.g. herpes simplex, chickenpox)
- Otitis externa with a perforated eardrum

4.5 Special Warnings and Precautions for Use

SONADERM-GM Cream must not come in contact with the eyes. Also, it should not be used with occlusive dressings.

Clobetasol: Use of potent topical corticosteroids including clobetasol propionate should be avoided on areas of thin and sensitive skin, such as on the face, groin or in the skin folds. As with other highly active corticosteroids, therapy should be discontinued when control has been achieved. If no improvement is seen within 2 weeks, reassessment of diagnosis may be necessary. Long-term continuous therapy should be avoided. Because of a higher

ratio of skin surface area to body mass, children are at a greater risk than adults of hypothalamic-pituitary-adrenal (HPA) axis suppression when they are treated with topical corticosteroids. They are therefore also at greater risk of adrenal insufficiency after withdrawal of treatment and of Cushing's syndrome while on treatment. Adverse effects including striae have been reported with inappropriate use of topical corticosteroids in infants and children.

Miconazole: 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.

Gentamicin: Serious adverse reactions including neurotoxicity, ototoxicity and nephrotoxicity have occurred in patients receiving systemic gentamicin therapy. Although these effects have not been reported following topical use of gentamicin, caution is advised when used concomitantly with systemic aminoglycosides.

4.6 Paediatric Population

Safety and effectiveness of this formulation has not been established in children below 2 years of age. Due to safety concerns, SONADERM-GM Cream is not recommended in paediatric patients aged less than 2 years.

4.7 Interaction with other medicinal products and other forms of interaction

Clobetasol: Interactions of clobetasol with other medicinal products have not been reported.

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.

Gentamicin: Concurrent use with other potentially nephrotoxic or ototoxic drugs should be avoided unless considered essential by the physician.

Gentamycin can intensify and prolong the respiratory depressant effects of neuromuscular blocking agents following significant systemic absorption. However, if used in accordance with the recommendations, systemic exposure to gentamycin is expected to be minimal and drug interactions are unlikely to be significant.

4.8 Additional information on special population

Geriatric Patients

Generally, no adjustment of dosage is required in the geriatric population. However, greater sensitivity of some older individuals cannot be ruled out.

4.9 Fertility, pregnancy and lactation

Pregnancy

Safety for use of SONADERM-GM Cream in pregnancy has not been established. It should only be used during pregnancy when considered mandatory by the physician, after careful assessment of the potential risks to the fetus.

Breast-feeding

It is not known whether the components of SONADERM-GM Cream are excreted in the breast milk after topical administration. Nevertheless, caution should be executed when this medication is administered to nursing women

Fertility

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

Clobetasol propionate administered subcutaneously to revealed that fertility was only decreased at the highest dose.

4.10 Effect on Ability to Drive and Use Machines

There have been no studies to investigate the effect of SONADERM-GM Cream on driving performance or the ability to operate machinery. From the adverse reaction profile of this product, effect on ability to drive and use machines is not expected with topical use of SONADERM-GM Cream.

4.11 Undesirable Effects

Generally, SONADERM-GM Cream is well tolerated. The following adverse reactions have been reported with use of this preparation. The frequency of these adverse events is unknown.

Immune System Disorders - Hypersensitivity: Local hypersensitivity reactions such as erythema, rash, pruritus, urticaria and allergic contact dermatitis may occur at the site of application and may resemble symptoms of the condition under treatment. If signs of hypersensitivity appear, application should be stopped immediately.

Endocrine Disorders - Features of Cushing's Syndrome: As with other topical corticosteroids, prolonged use especially of large amounts, or treatment of extensive areas can lead to sufficient systemic absorption to produce the features of Cushing's syndrome. This effect is more likely to occur in infants and children, and if occlusive dressings are used. In infants, the nappy may act as an occlusive dressing. Provided the weekly dosage is less than 50 g in adults, any suppression of the HPA axis is likely to be transient with a rapid return to normal values once the short course of steroid therapy has ceased. The same applies to children given proportionate dosage.

Vascular Disorders - Dilatation of the Superficial Blood Vessels: Prolonged and intensive treatment with potent corticosteroid preparations may cause dilatation of the superficial blood vessels, particularly when occlusive dressings are used, or when skin folds are involved.

Skin and Subcutaneous Tissue Disorders: Local skin burning, local atrophy, striae, thinning, pigmentation changes, hypertrichosis, exacerbation of underlying symptoms, pustular psoriasis.

Prolonged and intensive treatment with potent corticosteroid (clobetasol) preparations may cause local atrophic changes, such as thinning and striae.

4.12 Overdose

Clobetasol: 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.

Miconazole: Excessive cutaneous use can result in skin irritation, which usually disappears after discontinuation of therapy. If accidental ingestion of large quantities of the product occurs, an appropriate method of gastric emptying may be used if considered necessary.

Gentamicin: Acute overdosage of topical gentamicin is very unlikely to occur. If this is suspected, use of the product should be stopped and the patient's general status, hearing acuity, renal and neuromuscular functions should be monitored. Hemodialysis may reduce the serum level of gentamycin.

5 Pharmacological Properties

5.1 Pharmacodynamic Properties

Clobetasol Propionate

Pharmacotherapeutic group: Steroid

ATC Code: D07AD01

Clobetasol propionate is a potent corticosteroid with topical anti-inflammatory activity. The mechanism of anti-inflammatory activity of the topical corticosteroids involves induction of phospholipase A2 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 A2. The major effect of clobetasol propionate on skin is partially due to vasoconstriction and decrease in collagen synthesis.

Miconazole Nitrate

Pharmacotherapeutic group: Antifungal

ATC Code: A01AB09

Miconazole is an imidazole antifungal agent that acts by interfering with the permeability of the fungal cell membrane. It possesses a wide antifungal spectrum and has some antibacterial activity. Miconazole inhibits biosynthesis of ergosterol, damaging the fungal cell wall, which increases permeability causing leakage of nutrients.

Gentamicin Sulphate

Pharmacotherapeutic group: Antibiotic

ATC Code: J01GB03

Gentamicin, an aminoglycoside antibiotic, is bactericidal which acts by inhibiting protein synthesis. Gentamicin passes through the gram-negative membrane in an o*xygen-dependent* active transport. Once in the cytoplasm, gentamicin and other aminoglycosides bind to the 16s rRNA at the 30s ribosomal subunit, disturbing mRNA translation and, thus, leading to the formation of truncated or non-functional proteins leading to the bacteria being unable to carry out protein synthesis.

5.2 Pharmacokinetic Properties

Clobetasol: 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. 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.

Miconazole: There is little absorption through skin or mucous membranes when miconazole nitrate is applied topically. Absorbed miconazole is bound to plasma proteins (88.2%) and red blood cells (10.6%). The small amount of miconazole that is absorbed is eliminated predominantly in faeces as both unchanged drug and metabolites.

Gentamicin: Topical application of gentamicin can result in some systemic absorption. Treatment of large areas can result in plasma concentrations of up to 1µg/mL. Less than 10% of gentamicin is bound to plasma proteins. Elimination half-life is 2-3 hours in individuals with normal kidney function, but can be increased in cases of renal insufficiency. Greater than 90% of gentamicin is excreted in the urine by glomerular filtration.

5.3 Preclinical safety data

Clobetasol Propionate

Clobetasol propionate was not mutagenic in a range of in vitro bacterial cell assays.

In fertility studies, subcutaneous administration of clobetasol propionate to rats produced no effects on mating, and fertility was only decreased at the highest dose.

No treatment related effects were observed in reproductive performance.

Gentamicin Sulphate.

Gentamicin has low acute toxicity after oral administration in rodent but is more toxic following intravenous and intramuscular administration, again suggesting poor absorption after oral administration

No carcinogenicity studies are available.

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.

6. Pharmaceutical particulars

6.1 List of excipients

Sodium Acid Phosphate, Cetamacrogol 1000, Cetostearyl Alcohol, Liquid Paraffin, White Soft Paraffin, Propylene Glycol and Purified Water.

6.2 Incompatibilities

None known.

6.3 Shelf-life

30 Months

6.4 Special precaution for storage

Store below 30^0C. Do Not Freeze.

For External Use Only.

6.5 Nature and content of container

10 g's

10g packed in printed aluminium collapsible and further packed in preprinted carton along with leaflet.

6.6 Special precautions for disposal and other handling

No special requirements.

7 Marketing authorization holder

Blue Cross Laboratories Pvt. Ltd.

L – 17, Verna Industrial Estate, Verna, Goa – 403 722.

8 Marketing authorization number(s)

Rwanda FDA-HMP-MA-1182

9 Date of first authorization/renewal of the authorization

Date of authorization : 06/05/2024

10 Date of Revision of the Text

May 2024.

11. Dosimetry (If Applicable)

Not Applicable.

12. Instructions for Preparation of Radiopharmaceuticals (If Applicable)

Not Applicable.