Not to be sold by retail without the prescription of a Registered Medical Practitioner

Clobetasol Propionate, Neomycin Sulphate & Miconazole Nitrate Cream
SONADERM-NM Cream

COMPOSITION
Clobetasol Propionate BP …… 0.05% w/w
Neomycin Sulphate IP …… 0.5% w/w
Miconazole Nitrate IP ……..… 2 % w/w
Chlorocresol IP (as preservative) …… 0.1% w/w
Cream base ……..… q.s.

DOSAGE FORM
Topical cream.

INDICATIONS
SONADERM-NM Cream is indicated for resistant dermatoses where secondary bacterial and /or fungal infection is present, suspected or likely to occur.

DOSE AND METHOD OF ADMINISTRATION
For topical use in adults and children over 2 years of age.
Sufficient amount of cream should be applied to cover the affected areas twice daily (morning and evening). Rub the cream in gently and completely.
SONADERM-NM Cream shall not be used continuously for more than one week without re-evaluation by the physician. The total dosage should not exceed 50 grams per week because of the potential of the clobetasol propionate to suppress the hypothalamic-pituitary-adrenal (HPA) axis. Further, treatment beyond 2 consecutive weeks is not recommended. Repeated short courses may be used to control exacerbations.
Or, as prescribed by the physician.

USE IN SPECIAL POPULATIONS
Pregnant Women
Safety for use of SONADERM-NM 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.

Lactating Women
It is not known whether the components of SONADERM-NM Cream excrete in the breast milk after topical use. Nevertheless, caution should be executed when this medication is administered to lactating women.

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

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

CONTRAINDICATIONS
SONADERM-NM Cream is contraindicated in following cases:

- Hypersensitivity to clobetasol or to neomycin or to miconazole or to any component of the formulation.
- Rosacea.
- Acne vulgaris.
- Perioral dermatitis.
- Perianal and genital pruritus.
- Primary cutaneous viral infections (e.g., herpes simplex, chickenpox).
- Otitis externa with a perforated eardrum (because of risk of ototoxicity).

WARNINGS AND PRECAUTIONS
For external use only.
SONADERM-NM Cream must not come in contact with the eyes. Also, it should not be used with occlusive dressings. Due to the known ototoxic and nephrotoxic potential of neomycin sulphate, the use of SONADERM-NM cream in large quantities, or on large areas for prolonged periods of time is not recommended in circumstances where significant systemic absorption may occur.

Clobetasol Propionate
Use of potent topical corticosteroids, including clobetasol propionate, should be avoided on areas with 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 for 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.

Neomycin Sulphate

Neomycin can induce permanent sensorineural hearing loss due to cochlear damage, mainly destruction of hair cells in the organ of Corti (spiral organ - for hearing). The risk of ototoxicity is greater with prolonged use. Neomycin sulphate may cause cutaneous sensitization. A precise incidence of hypersensitivity reactions (primarily skin rash) due to topical neomycin is not known. Discontinue promptly if sensitization or irritation occurs.

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

Pseudomembranous Colitis: Pseudomembranous colitis has been reported with the use of antibiotics and may range in severity from mild to life-threatening. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea during or after antibiotic use. Although this is less likely to occur with topically applied neomycin, if prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further.

Miconazole Nitrate

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.

DRUG INTERACTIONS

Clobetasol Propionate

CYP3A4 inhibitor drugs such as ritonavir and itraconazole, when coadministered with corticosteroids 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 Sulphate

Following significant systemic absorption, neomycin sulphate can intensify and prolong the respiratory depressant effects of neuromuscular blocking agents. However, if used in accordance with the recommendations, systemic exposure to neomycin is expected to be minimal and drug interactions are unlikely to be significant. Concurrent use with other potentially nephrotoxic or ototoxic drugs should be avoided unless considered essential by the physician.

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.

UNDESIRABLE EFFECTS

SONADERM-NM cream is generally well tolerated. Following side effects may occur occasionally with the individual components of SONADERM-NM Cream.

Clobetasol Propionate

The following adverse reactions have been reported with use of clobetasol propionate. 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 gram 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.

Neomycin Sulphate

Neomycin occasionally causes skin sensitization. Ototoxicity and nephrotoxicity have also been reported with use of neomycin in large quantities and/or for prolonged periods.

Miconazole Nitrate

Local side effects such as itching, burning, rash, and contact dermatitis have been reported with topical miconazole therapy.

OVERDOSE

Clobetasol Propionate

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

Neomycin Sulphate

If systemic absorption of neomycin sulphate is suspected, use of the product should be stopped and the patient's general status, hearing acuity, renal and neuromuscular functions should be monitored. Blood levels of neomycin sulphate should also be determined. Haemodialysis may reduce the serum level of neomycin sulphate.

Miconazole Nitrate

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.

PHARMACODYNAMICS

Clobetasol Propionate

Like other topical corticosteroids, clobetasol propionate has anti-inflammatory, antipruritic, and vasoconstrictive properties. The major effect of clobetasol propionate on skin is a non-specific anti-inflammatory response, partially due to vasoconstriction and decrease in collagen synthesis.
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.

Neomycin Sulphate

Neomycin exerts its bactericidal effect by interfering with the protein synthesis of susceptible organisms. Neomycin is rapidly acting bactericidal agent; after diffusing through the bacterial cell membrane it binds polysomes to affect protein synthesis. Neomycin disrupts the normal cycle of ribosomal function by interfering, at least in part, with the first step of protein synthesis. Neomycin also causes a misreading of the genetic code of the mRNA template and this causes incorrect amino acids to be incorporated into the growing polypeptide chain, producing nonsense proteins.

Neomycin sulphate is bactericidal against a wide range of Gram-positive and Gram-negative bacterial pathogens including *Staphylococci, Streptococci, Escherichia, Enterobacter, Klebsiella, Hemophilus, Proteus, Salmonella* and *Shigella* species. It is also active against some strains of *Pseudomonas aeruginosa*, and against *Mycobacterium tuberculosis* and *Neisseria gonorrhea*.

Miconazole Nitrate

Miconazole is an imidazole antifungal agent that acts by interfering with the permeability of the fungal cell membrane. Miconazole inhibits biosynthesis of ergosterol, damaging the fungal cell wall, which increases permeability causing leakage of nutrients.

Miconazole possesses a wide antifungal spectrum and has some antibacterial activity. Miconazole inhibits the growth of the common dermatophytes such as *Trichophyton rubrum, Trichophyton mentagrophytes,* and *Epidermophyton floccosum*, and the yeast-like fungi such as *Candida albicans*. Also many Gram-positive bacteria including most strains of *Streptococcus* and *Staphylococcus* are susceptible to miconazole.

PHARMACOKINETICS

Clobetasol Propionate

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., metabolized primarily by the liver and then excreted by the kidneys. However, systemic metabolism of clobetasol has never been fully characterised or quantified.

Neomycin Sulphate

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. Plasma concentrations following topical application to open wounds, burns, or granulating surfaces are comparable to, or higher than, those achieved following oral preparation. Once neomycin is absorbed, it is rapidly excreted by the kidneys in active form. It has been reported to have a half-life of 2 to 3 hours.

Miconazole Nitrate

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.

INCOMPATIBILITIES

None known.

SHELF-LIFE

24 months.

PACKAGING INFORMATION

15 gram lami tube.

STORAGE AND HANDLING INSTRUCTIONS

Store at temperature below 25 ^{0}C. Do not freeze.
Keep out of reach of children.

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