

1.1 Name of the medicinal product:**CLOTRIMAZOLE, BETAMETHASONE & NEOMYCIN SULFATE CREAM****1.2 Qualitative and quantitative composition:**

Composition:

- Clotrimazole USP (1.0 % W/W)
- Betamethasone Dipropionate USP Eq. to Betamethasone (0.05 % W/W)
- Neomycin Sulfate USP (0.5 % W/W)
- Cream Base (- QS)

Sr. No.	Ingredients	Specification	Label Claim w/w	Over-ages added (In %)	Quantity in % w/w	Reason for Function
1.	Clotrimazole	USP	1.00%	2%	1.0200%	Medicament
2.	Betamethasone as Dipropionate	USP	0.05% 0.0642	2%	0.0655%	Medicament
3.	Neomycin Sulphate	USP	0.5%	20%	0.6000%	Medicament
4.	Light liquid paraffin	BP	NA	NA	12.8200%	Emollient
5.	Propylene Glycol	BP	NA	NA	4.0000%	Solvent
6.	Hard paraffin Wax	BP	NA	NA	3.0000%	Emollient
7.	Micro Crystalline Wax	IH	NA	NA	1.0000%	Thickening agent
8.	Cetostearyl Alcohol	BP	NA	NA	8.0000%	Thickening Agent, Stabilizing Agent
9.	Benzyl Alcohol	BP	NA	NA	1.0000%	Preservative
10.	Cetomacrogol 1000	IH	NA	NA	2.0000%	Emollient
11.	Chlorocresol	USP	NA	NA	0.1000%	Preservative
12.	Butylated Hydroxytoluene	BP	NA	NA	0.0500%	Preservative
13.	Purified Water	IH	NA	NA	66.3450%	Vehicle

1.3 Pharmaceutical form: Cream**Description:** White coloured cream**1.4 Clinical Particulars****4.1 Therapeutic indications**

CLOTRIMAZOLE, BETAMETHASONE & NEOMYCIN SULFATE CREAM is indicated in the treatment of variety of skin conditions (e.g., eczema, dermatitis, allergies, rash). It reduces the swelling, itching, and redness that can occur in these types of conditions.

4.2 Posology and method of administration**Route:** Topical

As directed by physician.

Method of administration

Usually for adults and children, a thin layer of **CLOTRIMAZOLE, BETAMETHASONE & NEOMYCIN SULFATE CREAM** should be rubbed into the affected area of skin twice a day.

You should always follow these instructions when using **CLOTRIMAZOLE, BETAMETHASONE & NEOMYCIN SULFATE CREAM**.

- Do not use the cream on your face for more than 5 days.
- Do not use a large amount of cream on large areas of the body, open Wounds or areas of the body where joints bend for a long time.
- Avoid getting the cream in your eyes.

4.3 Contraindications

If you previously had an allergic reaction to Clotrimazole, Betamethasone Dipropionate & Neomycin Sulfate Cream (the active ingredient in this medicine) or any of the other ingredients of this medicine.

- For eye infections
- For any other skin problem as it could make it worse especially rosacea (a skin condition affecting the face), acne, dermatitis around the mouth, genital itching, nappy rash, cold sores, chickenpox, shingles or other skin infections. Ask your doctor or pharmacist if you are not sure.

4.4 Special warnings and precautions for use

Precautions:

CLOTRIMAZOLE, BETAMETHASONE & NEOMYCIN SULFATE CREAM can cause local and systemic toxicity, which is common especially following long continued use on large areas of damaged skin and in flexures. If used on the face, courses should be limited to 5 days.

Clotrimazole, Betamethasone & Neomycin Sulfate Cream **SHOULD NOT BE USED WITH OCCLUSIVE DRESSING.**

- Topical corticosteroids may be hazardous in psoriasis for a number of reasons including rebound relapses following the development of tolerance, risk of generalised pustular psoriasis and local and systemic toxicity due to impaired barrier function of the skin.
- Any of the side effects that are reported following systemic use of corticosteroids, including adrenal suppression, manifestation of Cushing's syndrome, hyperglycemia, and glycosuria may also occur with topical steroids, especially in infants and children.
- Clotrimazole, Betamethasone & Neomycin Sulfate Cream is not intended for ophthalmic use.
- Visual disturbance may be reported with systemic and topical (including, intranasal, inhaled and intraocular) corticosteroid use. If a patient present with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes of visual disturbances which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Paediatric population

- Long term continuous therapy should be avoided in all children irrespective of age.
- Clotrimazole, Betamethasone & Neomycin Sulfate Cream should not be used with adhesive dressing.
- The safety and effectiveness of Clotrimazole, Betamethasone & Neomycin Sulfate Cream has not been established in children below the age of 12.
- If used on children, courses should be limited to 5 days.

Hypothalamic-pituitary adrenal axis suppression, Cushing's syndrome and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestation of adrenal suppression in children include linear growth retardation, delayed weight gain, low plasma cortisol levels, and absence of response to ACTH stimulation. Manifestation of intracranial hypertension include bulging fontanel's, headaches, and bilateral papilloedema.

Clotrimazole, Betamethasone & Neomycin Sulfate Cream contains:

Cetostearyl alcohol which may cause localised skin reactions (e.g. contact dermatitis).

Propylene glycol which may cause skin irritation. Because this medicine contains propylene glycol, do not use it on open wounds or large areas of broken or damaged skin (such as burns).

4.5 Interaction with other medicinal products and other forms of interaction

CLOTRIMAZOLE, BETAMETHASONE & NEOMYCIN SULFATE CREAM does not normally react with other medicines. However, tell your doctor or pharmacist if you are using or have recently used any other cream or taken any other medicines, including medicines obtained without a prescription.

Betamethasone: Betamethasone is known to interact with other drugs like Amphotericin B, carbamazepine, lofexidine, metyrosine, oxandrolone, perindopril, phenytoin (Na), rifampicin. Always consult your physician for the change of dose regimen or an alternative drug of choice that may strictly be required.

Clotrimazole: Clotrimazole is known to interact with other drugs like aliskiren. Always consult your physician for the change of dose regimen or an alternative drug of choice that may strictly be required.

Neomycin: Neomycin is known to interact with other drugs like acarbose, atracurium (Besylate), cyanocobalamin, digoxin, Doxacurium, Fluorouracil, gentamicin, gestodene, hydroxocobalamin, mecobalamin, Methotrexate, pancuronium (Br). Always consult your physician for the change of dose.

4.6 Pregnancy and Lactation

Pregnancy

There is inadequate evidence of safety in pregnancy. Clotrimazole has shown no teratogenic effect in animals but is foetotoxic at high oral doses.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate and intra-uterine growth retardation. There may therefore be a very small risk of such effects in human foetus. Hence should only be used in pregnancy if the benefit justifies the potential risk to the foetus and such use should not be extensive i.e. in large amounts or for long periods.

Lactation

It is not known whether the components of **CLOTRIMAZOLE, BETAMETHASONE & NEOMYCIN SULFATE CREAM** are excreted in human milk and therefore caution should be exercised when treating nursing mothers.

4.7 Effects on ability to drive and use machines

CLOTRIMAZOLE, BETAMETHASONE & NEOMYCIN SULFATE CREAM is not likely to affect you being able to drive or use any tools or machines.

4.8 Undesirable effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor if you notice any of the following side effects or notice any other effects not listed:

- Severe irritation or reddening of the skin where the cream has been used, or other signs of allergy during the first few days of treatment. This can affect fewer than 1 in 10 people.
- Peeling or blistering of the skin. This can affect fewer than 1 in 100 people.
- burning and stinging, maculopapular rash, oedema, paraesthesia and secondary infection.
- Reported reactions to clotrimazole include erythema, stinging, blistering, peeling, oedema, pruritus, urticaria and general irritation of the skin.
- Reactions to betamethasone dipropionate include: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hyperpigmentation, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae miliaria, capillary fragility (ecchymoses), blurred vision and sensitisation.
- In children receiving topical corticosteroids, Hypothalamic-pituitary-adrenal (HPA) axis suppression (HPA) axis suppression, Cushing's syndrome and intracranial hypertension have been reported.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your health care provider.

4.9 Overdose

Acute overdosage with topical application of **CLOTRIMAZOLE, BETAMETHASONE & NEOMYCIN SULFATE CREAM** is unlikely and would not be expected to lead to a life-threatening situation; however topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects.

If you use **CLOTRIMAZOLE, BETAMETHASONE & NEOMYCIN SULFATE CREAM** more than you should, it may cause some burning sensation, redness or swelling. If this occurs, stop using **CLOTRIMAZOLE, BETAMETHASONE & NEOMYCIN SULFATE CREAM** straight away. If you have any further questions on the use of this product, ask your doctor or pharmacist.
If you swallow the cream accidentally, rinse your mouth with plenty of water and contact your doctor.

5 Pharmacological properties

5.1 Pharmacodynamic properties

Clotrimazole is a broad-spectrum antifungal agent that inhibits the growth of pathogenic yeasts by changing the permeability of cell membranes. The action of clotrimazole is fungistatic at concentrations of drug up to 20 mcg/mL and may be fungicidal *in vitro* against *Candida albicans* and other species of the genus *Candida* at higher concentrations. Unfortunately, resistance to clotrimazole, which was rare in the past, is now common in various patient populations.

Clotrimazole is generally considered to be a fungistatic, and not a fungicidal drug, although this contrast is not absolute, as clotrimazole shows fungicidal properties at higher concentrations.

Betamethasone Dipropionate is a corticosteroids bind to the glucocorticoid receptor inhibiting pro-inflammatory signals, while promoting anti-inflammatory signals. Corticosteroids have a wide therapeutic window as patients may require doses that are multiples of what the body naturally produces. Patients who require long-term treatment with a corticosteroid should be counselled regarding the risk of hypothalamic-pituitary-adrenal axis suppression and increased susceptibility to infections.

Neomycin Sulfate mediates its bactericidal action by inhibiting bacterial protein synthesis, thereby suppressing the growth and survival of susceptible bacteria. Following oral administration, the duration of bactericidal activity of neomycin ranged from 48 to 72 hours. By decreasing colonic bacteria that produce ammonia, neomycin was shown to be effective as an adjunctive therapy in hepatic coma to improve neurologic symptoms.

Neomycin is active against both gram positive and gram negative organisms, including the major *E. coli* species resident in the colon as well as the enteropathogenic forms of *E. coli*. It is also active against *Klebsiella-Enterobacter* group. Resistant strains of *E. coli*, *Klebsiella* and *Proteus spp.* may emerge from neomycin therapy. Neomycin has no antifungal activity and has some activity against some protozoa.

5.2 Pharmacokinetic properties

CLOTRIMAZOLE, BETAMETHASONE & NEOMYCIN SULFATE CREAM is intended for treatment of skin conditions and is applied topically. Thus there are minimal pharmacokinetic aspects related to bioavailability at the site of action.

Clotrimazole penetrates the epidermis after topical administration but there is little, if any, systemic absorption.

The extent of percutaneous absorption of topical corticosteroids is determined by many factors including vehicle, integrity of skin and use of occlusion.

Systemically absorbed topical corticosteroids are bound to plasma proteins metabolised in the liver and excreted by the kidneys. Some corticosteroids and their metabolites are also excreted in the bile.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of this SmPC.

6 Pharmaceutical particulars

6.1 List of excipients

Light liquid paraffin, Propylene Glycol, Hard paraffin Wax, Micro Crystalline Wax, Cetostearyl Alcohol, Benzyl Alcohol, Cetomacrogol 1000, Chlorocresol, Butylated Hydroxytoluene, Purified Water.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

- Store at a temperature below 30° C.
- Do not freeze, Protect from direct sunlight.
- Keep all medicines out of the reach of children.
- Avoid contact with eyes.
- Keep the tube tightly close after use.

6.5 Nature and contents of container

Primary packing : 30 gm of cream filled in lami tube.

Secondary packing: Such one lami tube is packed in a carton along with leaflet.

Tertiary packing: 10 Cartons are packed in a shrink. Such 50 shrinks are packed in 5 ply shipper. Shippers to be sealed with BOPP tape.

6.6 Special precautions for disposal and other handling

None

7 Applicant / Manufacturer**Applicant**

Applicant name and address	M/s. PRIYA PHARMACEUTICAL NIG. LTD. No. C-1, Airport Road, 2F, Kano State, Nigeria.
Contact person's phone number	
Contact person's email	

Manufacturer

Manufacturer name and address	M/s. ASTAMED HEALTHCARE (I) PVT. LTD. Plot No. 2 & 3, Phase II, Genesis Ind. Complex, Kolgaon, Dist. Thane, Tal. Palghar, 401404 Maharashtra State, India
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