

1.1 Name of the medicinal product:

FAMAZORAL PLUS (Ketoconazole, Clobetasole Propionate, Neomycin Sulfate & Vitamin E Cream)

1.2 Qualitative and quantitative composition:

Composition:

- Ketoconazole USP (1.0 % W/W)
- Clobetasol Propionate USP (0.025 % W/W)
- Neomycin Sulfate USP (0.5 % W/W)
- Vitamin E (DL-alpha-tocopheryl acetate) USP (1.0 % 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.	Clobetasol Propionate	USP	0.025 %	NA	0.025%	Medicament
2.	Ketoconazole	USP	1.0%	NA	1.000%	Medicament
3.	Neomycin Sulphate	USP	0.5%	NA	0.500%	Medicament
4.	Vitamin E (DL-Alpha-Tocopheryl acetate)	USP	1.0%	NA	1.000%	Emollient
5.	Cetostearyl Alcohol	BP	NA	NA	8.000%	Thickening Agent, Stabilizing Agent
6.	Cetomacrogol 1000	IH	NA	NA	2.000%	Emollient
7.	Light liquid paraffin	BP	NA	NA	10.000%	Emollient
8.	Hard paraffin Wax	BP	NA	NA	4.200%	Emollient
9.	Propylene Glycol	BP	NA	NA	3.000%	Solvent
10.	Micro Crystalline Wax	IH	NA	NA	1.000%	Thickening agent
11.	Butylated Hydroxytoluene	BP	NA	NA	0.050%	Preservative
12.	Chlorocresol	USP	NA	NA	0.100%	Preservative
13.	Purified Water	IH	NA	NA	69.125	Vehicle

1.3 Pharmaceutical form: Cream

Description: White coloured cream

1.4 Clinical Particulars

4.1 Therapeutic indications

Ketoconazole has a potent antimycotic action against dermatophytes and yeasts. Ketoconazole acts rapidly on the pruritus, which is commonly seen in dermatophyte and yeast infections. This symptomatic improvement often occurs before the first signs of healing are observed.

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

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.

Vitamin E is used as a moisturizer to treat or prevent dry, rough, scaly, itchy skin and minor skin irritations

4.2 Posology and method of administration

Route: Topical

Apply to the affected area once a day, depending on the severity of the infection, the cream may be applied on the affected area twice daily when necessary. Generally, the duration of application depends on the type of infecting organism; Treat as bellows for die following:

Tinea Corporis 2 weeks; Tinea Cruris 2 weeks; Tinea Pedis 4 weeks; Tinea Manus 4 weeks.

Infection normally resistant to antifungal agents 4-6 weeks.

Method of administration

Topical administration only.

4.3 Contraindications

FAMAZORAL PLUS is contraindicated in patients with known hypersensitivity to any of its ingredients.

FAMAZORAL PLUS is for topical use only and cannot be used for internal or ophthalmic use. Special precautions must be observed during use on pregnant women and children.

4.4 Special warnings and precautions for use

Warning: For external use only. Avoid contact eyes. Do not exceed prescribed dosage. Read carefully before using.

- Patients with tinea cruris avoid wearing underwear that is tight-fitting or made from synthetic materials (e.g., rayon, nylon). Instead, wear loose-fitting, cotton underwear.

Patient with tinea pedis avoids wearing socks made from wool or synthetic materials (for example, rayon or nylon). Instead, wear clean, cotton socks and change them daily or more often if your feet sweat a lot. Wear well-ventilated shoes.

- If your skin problem does not improve within 2-4 weeks for cutaneous candidiasis, pityriasis versicolor, tinea corporis, or tinea cruris; or 4 weeks for seborrheic dermatitis; or if it becomes worse, check with your doctor.

- **FAMAZORAL PLUS** contains Clobetasol Propionate. If the product is administered for long term in large area or used with banding treatment it may induce the reversibility restraint of PHA axis. Cushing syndromes, hyperglycosemia. urinary glucose etc. can be occurred on some patents. So long term and large area using the product is not recommended. Banding treatments is not recommended too.

The product can be used in the cockled skin of the face, armpit and groin under the supervision of a medical doctor.

- Combining with other skin infection, the anti-infective drugs should be administrated. If the infection has not been controlled, stop using the product until the infection is controlled.

- When the local Ulcer and damage occur. Neomycin Sulfate is absorbed increasingly. The adverse reaction of aminoglycoside drug should be observed.

4.5 Interaction with other medicinal products and other forms of interaction

FAMAZORAL PLUS as a topical cream does not interact with any other product

4.6 Pregnancy and Lactation

-Pregnant and lactation women should be used with caution.

- Large area and long term using is not recommended

-It is not known whether the components of FAMAZORAL PLUS 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

FAMAZORAL PLUS has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Erythema, burning, itch, sharp pain or other stimulus symptom, folliculitis, skin atrophy, capillarectasis, etc arc commonly seen.

- Skin dryness, pilosis polytrichia, striae atrophicae and infectious susceptibility increasing can be observed.

- Adrenocortical hyper function can be induced by long term using. The symptom includes pilosis polytrichia, acne, moon face, Osteoporosis, etc.

- Allergic contact dermatitis can be seen on occasion.

4.9 Overdose

FAMAZORAL PLUS is well tolerated, no adverse effect has been observed in the event of overdosage

5 Pharmacological properties

5.1 Pharmacodynamic properties

Ketoconazole, a synthetic imidazole dioxolane derivative, has a potent antimycotic activity against dermatophytes such as *Trichophyton* sp., *Epidermophyton floccosum* and *Microsporum* sp. and against yeasts, including *Malassezia* spp and *Candida* spp. The effect on *Malassezia* spp. is very pronounced. Ketoconazole inhibits the biosynthesis of ergosterol in fungi and changes the composition of other lipid components in the membrane.

FAMAZORAL PLUS acts rapidly on pruritus which is commonly seen in dermatophyte and yeast infections, as well as skin conditions related to the presence of *Malassezia* spp. This symptomatic improvement often occurs before the first signs of healing are observed.

Clobetasol Propionate is topical corticosteroids act as anti-inflammatory agents via multiple mechanisms to inhibit late phase allergic reactions including decreasing the density of mast cells, decreasing chemotaxis and activation of eosinophils, decreasing cytokine production by lymphocytes, monocytes, mast cells and eosinophils, and inhibiting the metabolism of arachidonic acid. Topical corticosteroids, have anti-inflammatory, antipruritic, and vasoconstrictive properties.

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.

Vitamin E is an essential nutritional element and is the only lipid-soluble, chain-breaking antioxidant that prevents the propagation of free-radical reactions. Not all of the physiological effects of vitamin E are known. Alpha-tocopherol is the most active isomer of vitamin E. Vitamin E protects polyunsaturated fatty acids (PUFAs) within biological membrane and in plasma lipoproteins. Peroxyl radicals react with vitamin E 1,000 times more rapidly than they do with PUFA. Vitamin E protects red blood cells against hemolysis; it stimulates a cofactor in steroid metabolism; inhibits prostaglandin production; and suppresses platelet aggregation.

5.2 Pharmacokinetic properties

Ketoconazole: Plasma concentrations of ketoconazole were not detectable after topical administration of **FAMAZORAL PLUS** in adults on the skin.

In one study in infants with seborrheic dermatitis (n = 19), where approximately 40 g of Nizoral Cream was applied daily on 40% of the body surface area, plasma levels of ketoconazole were detected in 5 infants, ranging from 32 to 133 ng/mL.

Clobetasole Propionate:

corticosteroids can be systemically absorbed from intact healthy skin. The extent of percutaneous absorption of topical 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 nanograms/ml occurred in one study eight hours after the second application (13 h after an initial application) of 30 g clobetasol propionate 0.05 % ointment to normal individuals with healthy skin. 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. Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. They are metabolised, primarily in the liver. Topical corticosteroids are excreted by the kidneys. In addition, some corticosteroids and their metabolites are also excreted in the bile.

Neomycin Sulfate: poorly absorbed from the gastrointestinal tract. Gastrointestinal absorption of the drug may be increased if inflammatory or ulcerative gastrointestinal disease is present. The small fraction of absorbed neomycin is rapidly distributed in the tissues.

Vitamin E: Vitamin E is absorbed from the gastrointestinal tract via the same mechanisms as liposoluble substances, therefore its absorption is optimal in the presence of lipids. Vitamin E absorption from the

intestinal lumen is dependent upon biliary and pancreatic secretions, micelle formation, uptake into enterocytes, and chylomicron secretion. Vitamin E is 20% to 50% absorbed by intestinal epithelial cells in the small intestine, however the rate of absorption can vary inter-individually between 20% to 80%. Distribution of vitamin E to tissues, via the lymphatic system, occurs as a lipoprotein complex. High concentrations of vitamin E are found in the adrenals, pituitary, testes and thrombocytes. Chylomicron remnants, containing newly absorbed vitamin E, are taken up by the liver. Vitamin E is secreted from the liver in very low density lipoproteins. Plasma vitamin E concentrations depend upon the secretion of vitamin E from the liver. Vitamin E is stored unmodified in tissues (principally the liver and adipose tissue). Metabolism of vitamin E begins with CYP4F2/CYP3A4-dependent ω -hydroxylation followed β -oxidation, and forms the water-soluble end-product carboxyethylhydroxychroman. All known vitamin E hepatic metabolites can be conjugated and are excreted either via urine or faeces. Approximately 80% of vitamin E metabolites are excreted in the feces. Excess vitamin E is converted to a lactone, esterified to glucuronic acid, and subsequently excreted in the urine.

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

Cetostearyl Alcohol, Cetomacrogol 1000, Light liquid paraffin, Hard paraffin Wax, Propylene Glycol, Micro Crystalline Wax, Butylated Hydroxytoluene, Chlorocresol, 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. BRANDS PHARMA AND GENERAL ENTERPRISES A1, Umma Dantata Complex, Murtala Muhammad Way, Kano, Nigeria
Contact person's phone number	
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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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