SUMMARY OF PRODUCT CHARACTERISTICS

1.Name of the medicinal product
TERBIBACT MIXI CREAM

2.Qualitative and Quantitative composition
Each gram contains:
Ofloxacin BP.....0.75 % w/w
Ornidazole .....2.0 % w/w
Terbinafine Hydrochloride BP.....1.0 % w/w
Clobetasol Propionate BP.....0.05 % w/w

3.Pharmaceutical form
Cream.
An off white to light yellow semi solid mass filled in printed lami tube.

4.Clinical particulars
4.1 Therapeutic indications;
A multiple combination cream which exhibits anti-bacterial, anti-protozoal, anti-fungal and steroid properties to control inflammation.Ofloxacin is a broad-spectrum antibiotic that acts against many gram-positive and gram-negative bacteria. Ornidazole belongs to the nitroimidazole group of antibiotics and is used to treat amoeba and trichomonas infections. Terbinafine is a topical antifungal and antiparasitic drug. Clobetasol is a potent corticosteroid which exhibits anti-inflammatory, antipruritic and vasoconstrictive properties.

Mechanism Of Action:
Ofloxacin inhibits the DNA gyrase enzyme which is responsible for the supercoiling properties of DNA in bacterial cell. Ofloxacin and ornidazole kills the bacteria that infect inflamed skin, reduces inflammation and relieves itching. Terbinafine Hydrochloride inhibits most fungi known pathogenic to human beings. Clobetasol propionate controls the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor arachidonic acid.

Indications
TERBIBACT MIXI is used in various skin disorders including eczema, psoriasis, and lichen sclerosus. Auto-immune diseases including alopecia areata, vitiligo, lichen planus (auto immune skin nodules), and mycosis fungoides (T-cell skin lymphoma).
A fluoroquinolone antibiotic, prescribed for certain types of bacterial infections such as chronic bronchitis, pneumonia, skin and skin structure infections, and others. Intestinal and hepatic amoebiasis, Giardiasis, Trichomoniasis, Bacterial vaginosis. Anaerobic infections. An antifungal agent, prescribed for jock itch, athlete's foot and other types of ringworm infections.

4.2 Posology and method of administration

Apply a small quantity 2-3 times daily on the affected area.
Directly applied to the affected area.
A physician should be consulted if symptoms do not improve within 7 days.
Hands should be washed after application

4.3 Contraindications

Contra indicated in persons who have shown hypersensitivity to any of its components.

4.4 Special warnings and precautions for use

In Children: The experience with topical TERBIBACT MIXI in children is still limited and its use cannot therefore be recommended.
Use in the elderly: There is no evidence to suggest that elderly patients require different dosages or experience side-effects different to those of younger patients

4.5 Interaction with other medicinal products and other forms of interaction Aminophylline: Terbinafine increases the effect and toxicity of theophylline.
Caffeine: Terbinafine may increase the plasma concentration of Caffeine.
Chlorpromazine: Terbinafine may reduce the metabolism and clearance of Chlorpromazine. Consider alternate therapy or monitor for therapeutic/adverse effects of Chlorpromazine if Terbinafine is initiated, discontinued or dose changed.
Doxorubicin: Terbinafine may reduce the metabolism and clearance of Doxorubicin. Consider alternate therapy or monitor for therapeutic/adverse effects of Doxorubicin if Terbinafine is initiated, discontinued or dose changed.
Haloperidol: Terbinafine may reduce the metabolism and clearance of Haloperidol. Consider alternate therapy or monitor for therapeutic/adverse effects of Haloperidol if Terbinafine is initiated, discontinued or dose changed.
Methamphetamine: Terbinafine may reduce the metabolism and clearance of Methamphetamine. Consider alternate therapy or monitor for therapeutic/adverse effects of Methamphetamine if Terbinafine is initiated, discontinued or dose changed.

4.6 Fertility, pregnancy and lactation

Fertility:

No human studies of the effects of TERBIBACT MIXI on fertility have been performed; however, animal studies have not demonstrated any effects of the drug on fertility.

Pregnancy:

Data on a large number of exposed pregnancies indicate no adverse effects of TERBIBACT MIXI cream on pregnancy or on the health of the foetus/newborn child. To date, no other relevant epidemiological data are available.
TERBIBACT MIXI cream can be used during pregnancy, but only under the supervision of a physician or midwife.

4.7 Effects on ability to drive and use machines

TERBIBACT MIXIcream has no or negligible influence on the ability to drive or use machines

4.8 Undesirable effects

Undesirable effects are based on spontaneous reports, assigning accurate frequency of occurrence for each is not possible.

Immune system disorders: allergic reaction (syncope, hypotension, dyspnoea, urticaria).

Skin and subcutaneous tissue disorders: blisters, discomfort/pain, oedema, irritation, peeling/exfoliation, pruritus, rash, stinging/burning.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of the medicinal product is important as it allows continued monitoring of the benefit–risk balance of the medicinal product. Healthcare professionals are requested to report any suspected adverse reactions to the marketing authorisation holder or, where applicable, via the national reporting system.
https://pv.pharmacyboardkenya.org/

4.9 Overdose

Excessive application of TERBIBACT MIXI may result in severe irritation. In this event, discontinue use and wait until the skin has recovered.
Topically applied TERBIBACT MIXI is not generally absorbed in sufficient amounts to produce systemic effects. Excessive application of topically applied TERBIBACT MIXI may result in absorption of sufficient amounts to produce systemic effects.
Appropriate symptomatic measures should be taken to provide relief from irritation due to excessive application. In the event of accidental oral ingestion, gastric lavage is rarely required and should be considered only if a life-threatening amount of TERBIBACT MIXI has been ingested within the preceding hour or if clinical symptoms of overdose become apparent (e.g. dizziness, nausea or vomiting). It should be carried out only if the airway can be protected adequately.

5.Pharmacological properties

5.1 Pharmacodynamic properties

Clobetasol Like other topical corticosteroids, clobetasol has anti-inflammatory, antipruritic, and vasoconstrictive properties. It is a very high potency topical corticosteroid that should not be used with occlusive dressings. It is recommended that treatment should be limited to 2 consecutive weeks and therapy should be discontinued when adequate results have been achieved.
Clobetasol Propionate is the propionate salt form of clobetasol, a topical synthetic corticosteroid with anti-inflammatory, anti-pruritic, and vasoconstrictive properties.Clobetasol propionate exerts its effect by binding to cytoplasmic glucocorticoid receptors and subsequently activates glucocorticoid receptor

mediated gene expression. This results in synthesis of certain anti-inflammatory proteins, while inhibiting the synthesis of certain inflammatory mediators. Specifically, clobetasol propionate appears to induce phospholipase A2 inhibitory proteins, thereby controlling the release of the inflammatory precursor arachidonic acid from membrane phospholipids by phospholipase A2.

Ofloxacin is a quinolone/fluoroquinolone antibiotic. Ofloxacin is bactericidal and its mode of action depends on blocking of bacterial DNA replication by binding itself to an enzyme called DNA gyrase, which allows the untwisting required to replicate one DNA double helix into two. Notably the drug has 100 times higher affinity for bacterial DNA gyrase than for mammalian. Ofloxacin is a broadspectrum antibiotic that is active against both Gram-positive and Gram-negative bacteria.

Terbinafine is an allylamine antifungal agent and acts by inhibiting squalene epoxidase, thus blocking the biosynthesis of ergosterol, an essential component of fungal cell membranes. In vitro, mammalian squalene monooxygenase (squalene 2,3-epoxidase) is only inhibited at higher (4000 fold) concentrations than is needed for inhibition of the dermatophyte enzyme. Depending on the concentration of the drug and the fungal species test in vitro, Terbinafine may be fungicidal. However, the clinical significance of in vitro data is unknown.

Mechanism of action Terbinafine is hypothesized to act by inhibiting squalene monooxygenase, thus blocking the biosynthesis of ergosterol, an essential component of fungal cell membranes. This inhibition also results in an accumulation of squalene, which is a substrate catalyzed to 2,3-oxydo squalene by squalene monooxygenase. The resultant high concentration of squalene and decreased amount of ergosterol are both thought to contribute to terbinafine's antifungal activity.

5.2 Pharmacokinetic properties

Ornidazole is readily absorbed from the gastro-intestinal tract and peak plasma concentrations of about 30 mcg per ml have been achieved within 2 hours of a single dose of 1.5 g, falling to about 9 mcg per ml after 24 hours and 2.5 mcg per ml after 48 hours. The plasma elimination half-life of ornidazole is 12 to 14 hours. Less than 15% is bound to plasma proteins. It is widely distributed in body tissues and fluids, including the cerebrospinal fluid. Ornidazole is metabolised in the liver and is excreted in the urine, mainly as conjugates and metabolites, and to a lesser extent in the faeces; 85% of a single oral dose has been reported to be eliminated within 5 days, 63% in the urine and 22% in the faeces.3 Biliary excretion may be important in the elimination of ornidazole and its metabolites.

Clobetasol Propionate :
Absorption
Topically applied clobetasol propionate can be absorbed through normal intact skin.

Percutaneous penetration of clobetasol propionate varies among individuals and can be altered by using different vehicles. Percutaneous penetration can be increased by use of occlusive dressings and by presence of inflammation and/or other disease of the epidermal barrier (e.g., psoriasis, eczema)

Distribution

Not known whether topical clobetasol is distributed into milk.

Metabolism

Once absorbed through the skin, topically applied corticosteroids are metabolized primarily in the liver.

Elimination Route

Topical corticosteroids and metabolites are excreted by the kidneys and, to a lesser extent, in bile.

Ofloxacin

Absorption

Rapidly and almost completely absorbed from GI tract. Does not undergo appreciable first-pass metabolism. Oral bioavailability is 85–100%; peak serum concentrations attained within 0.5–2 hours. Food can decrease rate and/or extent of absorption of ofloxacin; not usually considered clinically important. Milk and yogurt do not appear to affect GI absorption.

Distribution

Widely distributed into body tissues and fluids including bone, cartilage, bile, skin, sputum, bronchial secretions, pleural effusions, tonsils, saliva, gingival mucosa, nasal secretions, aqueous humor, tears sweat, lung, blister fluid, pancreatic fluid ascitic fluid, peritoneal fluid, gynecologic tissue, vaginal fluid, cervix, ovary, semen prostatic fluid, and prostatic tissue.

Distributed into CSF following oral administration; peak CSF concentrations may be 28–87% of concurrent serum concentrations.

Crosses placenta and is distributed into cord blood and amniotic fluid. Distributed into milk. Plasma Protein Binding 20–32% bound to serum proteins. Elimination

Metabolism

<10% of a dose is metabolized; approximately 3–6% of the dose metabolized to desmethyl ofloxacin and 1–5% metabolized to ofloxacin *N*-oxide. Desmethyl ofloxacin is microbiologically active, but is less active against susceptible organisms than is ofloxacin; ofloxacin *N*-oxide has only minimal antibacterial activity.

Elimination Route

Ofloxacin and its metabolites eliminated in both urine and feces. Following a single oral dose, 65– 90% of the dose eliminated unchanged in urine within 48 hours; <5% of the dose in urine as metabolites. Approximately 4–8% of the dose excreted in feces.

Half-life

Distribution half-life averages 0.5–0.6 hours and terminal elimination half-life averages 4–8 hours.

Special Populations
In healthy geriatric adults 64–86 years of age with renal function normal for their age, half-life averages 6.4–8.5 hours. The slower elimination in geriatric individuals presumably is due to reduced renal function and clearance in this age group.
Pharmacokinetics not fully evaluated in those with hepatic impairment.
Serum concentrations are higher and half-life prolonged in adults with impaired renal function. Halflife averages 16.4 hours (range: 11–33.5 hours) in adults with Cl_{cr} 10–50 mL/minute and 21.7 hours (range: 16.9–28.4 hours) in those with Cl_{cr} <10 mL/minute. In patients with end-stage renal failure, half-life may range from 25–48 hours.

Terbinafine Hydrochloride

Absorption

Following topical application to intact skin, systemic absorption occurs and low concentrations of terbinafine are attained in plasma.

Distribution

Penetration into stratum corneum is similar following topical application of 1% cream or 1% solution. Distributed into milk following oral administration

Metabolism

Systemically absorbed drug is extensively metabolized.

Elimination Route

Approximately 75% of percutaneously absorbed drug is eliminated in urine, principally as metabolites. Half-life of percutaneously absorbed drug is approximately 21 hours.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on studies of repeated dose toxicity, genotoxicity and carcinogenicity.

6. Pharmaceutical particulars:

6.1 List of Excipients

- Cetomacrogol Emulsifying Wax
- Cetostearyl Alcohol
- Light Liquid Paraffin
- Propylene Glycol
- Disodium Edetate
- Methyl Paraben
- Propyl Paraben
- Sodium Metabisulphite
- Sodium Hydroxide
- Purified water

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
24 months

6.4 Special precautions for storage
Store at a temperature not exceeding 30^0 C. protect from light.
Do not freeze.
Keep Medicine Out of reach of Children

6.5 Nature and contents of container
The cream is filled into laminated tubes with internal lacquer coating and HDPE screw-on caps and enclosed in an outer carton. Pack sizes available are 15g. Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling
No Special requirements.

7. Marketing authorisation holder and manufacturing site address

Marketing Authorisation Holder:
Galaxy Pharmaceutical Limited

Manufacturer:
Curetech Skincare
Plot No 33 & 34, Phase-IV, Bhatoli Kalan, Baddi,
Distt: Solan (H.P) 173205, India

8. Marketing authorisation number(s)
H2022/CTD7660/14832

9. Date of first authorisation/renewal of the authorization
02/06/2022

10. Date of revision of the text
02/06/2022