TEGSOL Cream
(Terbinafine HCl)

TEGSOL Lotion
(Terbinafine HCl)

TEGSOL Tablet
(Terbinafine HCl)

ٹیگسول کریم
(ٹربینافین ایچ سی ایل)

ٹیگسول لوشن
(ٹربینافین ایچ سی ایل)

ٹیگسول ٹیبلیٹ
(ٹربینافین ایچ سی ایل)

COMPOSITION:

TEGSOL Cream
Each gram contains:
Terbinafine hydrochloride 10mg
(JP specifications)

TEGSOL Lotion
Each gram contains:
Terbinafine HCl 10mg
(JP specifications)

TEGSOL Tablet 125mg
Each tablet contains:
Terbinafine (as hydrochloride).....125mg
(BP specifications)

TEGSOL Tablet 250mg
Each tablet contains:
Terbinafine (as hydrochloride) 250mg
(BP specifications)

DESCRIPTION:

Terbinafine hydrochloride is a synthetic allylamine antifungal. It is highly lipophilic in nature and tends to accumulate in skin, nails, and fatty tissues. Like other allylamines, terbinafine inhibits ergosterol synthesis by inhibiting the fungal squalene monooxygenase (also called squalene epoxidase), an enzyme that is part of the fungal cell wall synthesis pathway.

MECHANISM OF ACTION:

Terbinafine, an allylamine antifungal, inhibits biosynthesis of ergosterol, an essential component of fungal cell membrane, via inhibition of squalene epoxidase enzyme. This results in fungal cell death primarily due to the increased membrane permeability mediated by the accumulation of high concentrations of squalene but not due to ergosterol deficiency. Depending on the concentration of the drug and the fungal species test in vitro, terbinafine hydrochloride may be fungicidal. However, the clinical significance of in vitro data is unknown. Terbinafine has been shown to be active against most strains of the following microorganisms both in vitro and in clinical infections: Trichophyton mentagrophytes Trichophyton rubrum.

INDICATIONS:

TEGSOL Cream:
Fungal infections of the skin caused by Trichophyton (e.g. T. Rubrum, T.Mentagrophytes, T. Verrucosum, T. Violaceum), Microsporum canis and Epidermophyton floccosum. Yeast infections of the skin, principally those caused by the genus Candida (e.g. C. albicans). Pityriasis (TEGSOL) versicolor due to Pityrosporum orbiculare (also known as Malassezia furfur).

TEGSOL Lotion:
Treatment for TEGSOL pedis (athlete's foot) for Adults 18 years of age and over.

TEGSOL Tablet:
Terbinafine hydrochloride tablets are indicated for the treatment of onychomycosis of the toenail or fingernail due to dermatophytes (TEGSOL unguium). Prior to initiating treatment, appropriate nail specimens for laboratory testing [potassium hydroxide (KOH) preparation, fungal culture, or nail biopsy] should be obtained to confirm the diagnosis of onychomycosis.

DOSAGE & ADMINISTRATION:

TEGSOL Cream:
TEGSOL can be applied once or twice daily. Cleanse and dry the affected areas thoroughly before application of TEGSOL. Apply the cream to the affected skin and surrounding area in a thin layer and rub in lightly. In the case of intertriginous infections (submammary, interdigital, intergluteal, inguinal) the application may be covered with a gauze strip, especially at night.

The likely durations of treatment are as follows:

Tirea pedis: **1 week**
Tirea corporis, cruris: **1 to 2 weeks**
Cutaneous candidiasis: **1 to 2 weeks**
Pityriasis versicolor: **2 weeks**

Relief of clinical symptoms usually occurs within a few days. Irregular use or premature discontinuation of treatment carries the risk of recurrence. If there are no signs of improvement after two weeks the diagnosis should be verified.

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.

Children
The experience with topical TEGSOL in children is still limited and its use cannot therefore be recommended.

TEGSOL Lotion :

For Cutaneous Use
Adults 18 years of age and over: single administration.

Duration and frequency of treatment
TEGSOL lotion should be applied once on both feet, even if lesions are visible on one foot only. This ensures elimination of the fungi (dermatophytes) that might be found in areas of the foot where no lesions are visible. Relief of clinical symptoms usually occurs within a few days. If there are no signs of improvement after one week, patients should see a doctor. There are no data on repeated treatment with TEGSOL lotion. Therefore a second treatment cannot be recommended within a particular episode of athlete's foot.

Pediatric population
TEGSOL lotion has not been studied in the pediatric population. Its use is therefore not recommended in patients below 18 years of age.

Elderly patients
There is no evidence to suggest that elderly patients require different dosages or experience side effects different from those in younger patients.

Method of Administration
Patients should wash and dry both feet and hands before applying the product. They should treat one foot, then the other. Starting between the toes, patients should apply a thin layer evenly between and all around the toes, as well as cover the sole and sides of the foot for up to 1.5 cm. The product should be applied in the same way to the other foot, even if the skin looks healthy. The product should be left to dry to a film for 1-2 minutes. Patients should then wash their hands. TEGSOL lotion should not be massaged into skin. For the best results, the treated area should not be washed for 24 hours after application. It is therefore recommended to apply TEGSOL lotion after a shower or bath and wait until the same time the following day before washing the feet again. Patients should use the quantity they need to cover both feet as instructed above. Any unused medication is to be discarded.

TEGSOL Tablet:

Assessment Prior to Initiation
Before administering terbinafine Tablets, evaluate patients for evidence of chronic or active liver disease.

Dosage
Fingernail onychomycosis: One 250 mg tablet once daily for 6 weeks.
Toenail onychomycosis: One 250 mg tablet once daily for 12 weeks.
The optimal clinical effect is seen some months after mycological cure and cessation of treatment. This is related to the period required for outgrowth of healthy nail.

PHARMACOKINETICS:

TEGSOL Tablet:
Following oral administration, terbinafine is well absorbed (greater than 70%) and the bioavailability of terbinafine tablets as a result of first-pass metabolism is approximately 40%. Peak plasma concentrations of 1 mcg/mL appear within 2 hours after a single 250 mg dose; the AUC is approximately 4.56 mcg.h/mL. An increase in the AUC of terbinafine of less than 20% is observed when terbinafine Tablets are administered with food. In plasma, terbinafine is greater than 99% bound to plasma proteins and there are no specific binding sites. At steady state, in comparison to a single dose, the peak concentration of terbinafine is 25% higher and plasma AUC increases by a factor of 2.5; the increase in plasma AUC is consistent with an effective half-life of ~36 hours. Terbinafine is distributed to the sebum and skin. A terminal half-life of 200-400 hours may represent the slow elimination of terbinafine from tissues such as skin and adipose. Prior to excretion, terbinafine is extensively metabolized by at least 7 CYP isoenzymes with major contributions from CYP2C9, CYP1A2, CYP3A4, CYP2C8, and CYP2C19. No metabolites have been identified that have antifungal activity similar to terbinafine. Approximately 70% of the administered dose is eliminated in the urine.

TEGSOL Cream:
Less than 5% of the dose is absorbed after topical application to humans; systemic exposure is therefore very slight.

TEGSOL Lotion:
Once applied to the skin, lotion forms a film on the skin. Terbinafine in the film stays on the skin for up to 72 hours. The film quickly delivers terbinafine to the stratum corneum: at 60 minutes after application, 16 to 18% of the applied dose will be present in the stratum corneum. Delivery progressively continues and terbinafine persists in the stratum corneum for up to 13 days, at levels which are in excess of the in vitro Minimum Inhibitory Concentration for terbinafine against dermatophytes. Systemic bioavailability is very low. An application of lotion on the back, on an area of 3 times the area of both feet, resulted in exposure to terbinafine of less than 0.5% of the exposure following oral administration of a 250 mg tablet.

WARNINGS & PRECAUTIONS:

TEGSOL Cream is for external use only. Contact with the eyes should be avoided. May be irritating to the eyes. In case of accidental contact with the eyes, rinse the eyes thoroughly with running water. TEGSOL lotion is not recommended to treat hyperkeratotic chronic plantar TEGSOL pedis (moccasin type). It should be used with caution in patients with lesions where alcohol could be irritating (after sun exposure or severe skin scaling). Not to be used on the face. For external use only. May be irritating to the eyes. In case of accidental contact with the eyes, rinse eyes thoroughly with running water. In the event of allergic reaction, the film should be removed with an organic solvent such as denatured alcohol and the feet washed with warm soapy water. Keep away from naked flames.

Hepatotoxicity
TEGSOL Tablets are contraindicated for patients with chronic or active liver disease. Before prescribing TEGSOL Tablets, perform liver function tests because hepatotoxicity may occur in patients with and without preexisting liver disease. Cases of liver failure, some leading to liver transplant or death, have occurred with the use of TEGSOL Tablets in individuals with and without preexisting liver disease.

Taste Disturbance Including Loss of Taste
Taste disturbance, including taste loss, has been reported with the use of TEGSOL Tablets. It can be severe enough to result in decreased food intake, weight loss, anxiety, and depressive symptoms. Taste disturbance may resolve within several weeks after discontinuation of treatment, but may be prolonged (greater than 1 year), or may be permanent. If symptoms of a taste disturbance occur, TEGSOL Tablets should be discontinued.

Smell Disturbance Including Loss of Smell
Smell disturbance, including loss of smell, has been reported with the use of TEGSOL Tablets. Smell disturbance may resolve after discontinuation of treatment, but may be prolonged (greater than 1 year), or may be permanent. If symptoms of a smell disturbance occur, TEGSOL Tablets should be discontinued.

Depressive Symptoms
Prescribers should be alert to the development of depressive symptoms, and patients should be instructed to report depressive symptoms to their physician.

Hematologic Effects
In patients with known or suspected immunodeficiency, physicians should consider monitoring complete blood counts if treatment continues for more than 6 weeks. Cases of severe neutropenia have been reported.

Serious Skin/Hypersensitivity Reactions
Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme, exfoliative dermatitis, bullous dermatitis, and drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome. Manifestations of DRESS syndrome may include cutaneous reaction (such as rash or exfoliative dermatitis), eosinophilia, and one or more organ complications such as hepatitis, pneumonitis, nephritis, myocarditis, and pericarditis. If progressive skin rash or signs/symptoms of the above drug reactions occur, treatment with TEGSOL Tablets should be discontinued.

Lupus Erythematosus
TEGSOL Tablets should be discontinued in patients with clinical signs and symptoms suggestive of lupus erythematosus.

Thrombotic Microangiopathy
Cases of thrombotic microangiopathy (TMA), including thrombotic thrombocytopenic purpura and hemolytic uremic syndrome, some fatal, have been reported with terbinafine. Discontinue terbinafine if clinical symptoms and laboratory findings consistent with TMA occur. The findings of unexplained thrombocytopenia and anemia should prompt further evaluation and consideration of diagnosis of TMA.

Pregnancy
There is no clinical experience with terbinafine in pregnant women, therefore, unless the potential benefits outweigh any potential risks, terbinafine should not be administered during pregnancy.

Breast Feeding
Terbinafine is excreted in breast milk. Therefore mothers should not receive terbinafine whilst breast-feeding. Infants must not be allowed to come into contact with any treated skin, including the breast.

SIDE EFFECTS:

Eye disorders: Visual field defects, reduced visual acuity, eye irritation.
Ear and labyrinth disorders: Hearing impairment, vertigo, and tinnitus.
Vascular disorders: Vasculitis.
Gastrointestinal disorders: Pancreatitis, vomiting
Hepatobiliary disorders: Cases of liver failure some leading to liver transplant or death, idiosyncratic and symptomatic hepatic injury. Cases of hepatitis, cholestasis, and increased hepatic enzymes have been seen with the use of TERBINAFINE Tablets.
Skin and subcutaneous tissue disorders: Serious skin reactions [e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme, exfoliative dermatitis, bullous dermatitis, and drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome], acute generalized exanthematous pustulosis, psoriasiform eruptions or exacerbation of psoriasis, photosensitivity reactions, hair loss.
Musculoskeletal and connective tissue disorders: Rhabdomyolysis, arthralgia, myalgia
General disorders and administration site conditions: Malaise, fatigue, influenza-like illness, pyrexia.
Investigations: Altered prothrombin time (prolongation and reduction) in patients concomitantly treated with warfarin and increased blood creatine phosphokinase have been reported

DRUG INTERACTIONS:

In vivo studies have shown that terbinafine is an inhibitor of the CYP450 2D6 isozyme. Drugs predominantly metabolized by the CYP450 2D6 isozyme include the following drug classes: tricyclic antidepressants, selective serotonin reuptake inhibitors, beta-blockers, antiarrhythmics class 1C (e.g., flecainide and propafenone) and monoamine oxidase inhibitors Type B.Coadministration of terbinafine Tablets should be done with careful monitoring and may require a reduction in dose of the 2D6-metabolized drug. In a study to assess the effects of terbinafine on desipramine in healthy volunteers characterized as normal metabolizers, the administration of terbinafine resulted in a 2-fold increase in C_{max} and a 5-fold increase in area under the curve (AUC). In this study, these effects were shown to persist at the last observation at 4 weeks after discontinuation of terbinafine Tablets. In studies in healthy subjects characterized as extensive metabolizers of dextromethorphan (antitussive drug and CYP2D6 probe substrate), terbinafine increases the dextromethorphan/ dextrorphan metabolite ratio in urine by 16- to 97-fold on average. Thus, terbinafine may convert extensive CYP2D6 metabolizers to poor metabolizer status.

CONTRAINDICATIONS:

Chronic or active liver disease.
History of allergic reaction and hypersensitivity to oral/topical terbinafine because of the risk of anaphylaxis.

STORAGE & INSTRUCTIONS:

store between 15-25°C. Protect from heat, sunlight and moisture. Keep away from the reach of the children.
To be sold on the prescription of a registered medical practitioner only.

HOW SUPPLIED:

TEGSOL Cream: 10g
TEGSOL Lotion: 20ml
TEGSOL Tablet 125mg: 10 Tablets
TEGSOL Tablet 250mg: 10 Tablets

خوراک وطریقہ استعمال:

ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔

ہدایات:

دوا کو ۱۵۔۲۵ ڈگری سینٹی گریڈ درجہ حرارت کے درمیان رکھیں۔ دھوپ، گرمی، نمی اور مجمد ہونے سے بچائیں۔ ریفریجریٹر میں نہ رکھیں۔ بچوں کی پہنچ سے دور رکھیں۔ صرف مستند ڈاکٹر کے نسخے پر فروخت کریں۔ صرف بیرونی استعمال کے لئے ہے۔

Manufactured by:
PHARMASOL
PRIVATE LIMITED
Plot # 549,Sundar Industrial Estate,
Lahore, Pakistan.