# MEDOFULVIN

**1. Trade Name of the Medicinal Product**

MEDOFULVIN 125mg tablets
MEDOFULVIN 500mg tablets

**2. Qualitative and Quantitative Composition**

Each tablet contains 125 mg or 500mg of griseofulvin.

**3. Pharmaceutical Form**

Tablets
White, round, flat, scored tablets.

**4. Clinical Particulars**

**4.1. Therapeutic Indications**

Treatment of dermatophytic fungi of hair, nails or skin.

**4.2. Posology and Method of Administration**

The tablets are for oral administration. They should be taken after meals.
*Adults:*
500 to 1g per day, in 2 divided doses, with meals.

*Children:*
10 to 20 mg / kg / day
The tablets should be swallowed with a full glass of water.

In children under 6 years, the tablets may be finely crushed and mixed with a liquid food.

*Duration of treatment*:
The duration of treatment is depending on the localization of the fungal infection:

- 4 to 8 weeks – for the skin fungal infection;
- 6-8 weeks – for scalp ringworm;
- 4-12 months – for nail fungal infection.

**4.3. Contraindications**

- Porphyrias;
- Allergy to griseofulvin;
- Lupus Erythematosus and related syndromes.

**4.4. Special Warnings and Precautions for Use**

- Blood count should be monitored on prolonged treatment (over one month) and high dose use (> 1.5 g daily);
- Avoid sun exposure during and immediately after the treatment;
- Patients with hepatic impairment should be closely monitored;
- Take into consideration the enzyme inducing effect of griseofulvin on many substances.
- Severe cutaneous adverse reactions (e.g. Steven-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, acute generalized exanthematous pustulosis) and erythema multiforme have been reported with griseofulvin use. These reactions may be serious and may result in hospitalization or death. If sever skin reactions occur, griseofulvin should be discontinued.

**4.5. Interactions with other Medicaments and other forms of Interaction**

**Concomitant use not recommended**

- Alcohol and drugs containing alcohol: griseofulvin has antabuse effect (warmth, redness, vomiting, tachycardia). Avoid taking alcoholic drinks and medicines containing alcohol.
- Hormonal contraceptives (oral contraceptives): griseofulvin decreases the contraceptive efficacy during the treatment and one cycle after ceasing the treatment. Another contraceptive method, particularly mechanical should be used.

**Combinations requiring precautions for use**

- Oral anticoagulants: griseofulvin decreases the effect of oral anticoagulants (it increases the hepatic catabolism); Frequent monitoring of prothrombin time and INR monitoring should be performed. Dosage adjustment of oral anticoagulants during treatment and 8 days after treatment cessation is necessary.
- Cyclosporin, tacrolimus- by extrapolation from rifampicin: griseofulvin lowers plasma levels of the immunosuppressant with decreased activity during the common use, by increasing its hepatic metabolism. In case of increased dose of the immunosuppressant, plasma levels should be checked. The dose should be reduced after cessation of the inducer.
- Estrogen- Reduced efficacy of estrogen by increasing its hepatic metabolism. Clinical monitoring and dosage adjustment of estrogen during treatment with griseofulvin and on its discontinuation may be necessary.
- Methadone: reduced plasma concentrations of methadone with risk of occurrence of withdrawal syndrome by increasing its hepatic metabolism. The frequency of methadone use should be increased 2 to 3 times a day instead of once a day.
- Zidovudine: extrapolation from rifampicin: risk of reduced efficacy of zidovudine by accelerating its hepatic metabolism. Regular clinical monitoring is recommended.

## 4.6. Pregnancy and Lactation

Pregnancy

Studies in animals have shown a teratogenic effect of griseofulvin. Clinically, the few cases of exposed pregnancies seem to evoke a teratogenic effect of griseofulvin. Further studies are needed to confirm this risk, which cannot be excluded to date.

Accordingly, the use of griseofulvin is not recommended during pregnancy. In the case where the treatment with griseofulvin is necessary, it will be initiated after birth.

In case of accidental discovery of a pregnancy after taking this medicine, this is not a systematic argument to advise abortion but leads to a cautious attitude and oriented prenatal care.

Breast-feeding

There are no data on excretion in breast milk. If breastfeeding is needed, the treatment with griseofulvin should be postponed.

## 4.7. Effects on Ability to Drive and Use Machines

There is a risk of dizziness, confusion and drowsiness associated with the use of this medicine. This is accentuated by the intake of alcoholic drinks or medications containing alcohol.

## 4.8. Undesirable Effects

- Neurological manifestations: mainly headache; rarely dizziness, insomnia or drowsiness, confusion, irritability; alcohol potentiates these disorders;
- Gastrointestinal disorders: anorexia, nausea, diarrhea, taste disturbance, feeling thirsty;
- Skin photosensitivity and exceptional allergic reactions: rare cases of bullous drug eruption (erythema multiforme or toxic epidermal necrolysis);
- Liver disorders: intrahepatic cholestasis; few cases have been reported and exceptionally, hepatitis;

- Hematologic: leukopenia, neutropenia, hypochromic anemia. These changes are infrequent and resolvent in general to treatment discontinuation;
- Peripheral neuropathy;
- Risk of worsening of systemic lupus erythematosus and related syndromes.
- Skin and subcutaneous tissue disorders: Frequency 'not known': Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, acute generalized exanthematous pustulosis, erythema multiforme.

**4.9. Overdose**

Treatment of overdosage should be symptomatic.

## 5. Pharmacological Properties

### 5.1. Pharmacodynamic Properties

Pharmacotherapeutic group: Antifungal, ATC code D01BA01.

Fungistatic antibiotic (in vivo) whose spectrum of activity is strictly limited to dermatophytes. Griseofulvin is active on the three varieties of dermatophyte fungi: microsporum, Epidermophyton and Trichophyton.

### 5.2. Pharmacokinetic Properties

**Absorption**

After oral administration of 1g of griseofulvin, the peak plasma concentration (1.5 to 3 mg/l) is reached within 2 to 4 hours.
The intestinal absorption is increased when griseofulvin is administered during a high fat meal.
The elimination half-life is 10 to 15 hours. The volume of distribution is 0.7 l/kg. The plasma protein binding is 80%.

**Biotransformation**

The liver converts largely griseofulvin to 6-demethylgriseofulvine, the principal inactive metabolite.

**Distribution**

Griseofulvin binds electively on keratin. It makes keratinized cells resistant to invasion by dermatophytes; parasitized cells are gradually replaced by healthy cells. There is a placental transfer.

**Excretion**

Much of the product is eliminated unchanged in faeces. 6-demethylgriseofulvine is eliminated in the urine, as glucuronide form. Less than 1% of the administered dose is excreted in the urine as unchanged. So there is no accumulation in renal failure.

## 6. Pharmaceutical Particulars

### 6.1. List of Excipients

MEDOFULVIN 125mg tablets
*Inactive ingredients:* Croscarmellose sodium, Povidone K25, Lactose monohydrate, Microcrystalline cellulose, Colloidal anhydrous silica, and Magnesium stearate.

MEDOFULVIN 500mg tablets
*Inactive ingredients:* Croscarmellose sodium, Povidone K25, Pregelatinised stach, Microcrystalline cellulose and Magnesium stearate.

### 6.2. Shelf life

Thirty six (36) months.

**6.3. Special Precautions for Storage**

Store below 30°C in the original package, in order to protect from light and moisture.

**6.4. Nature and Contents of Container**

MEDOFULVIN tablets are packed in PVC-Aluminium blister.
MEDOFULVIN 125mg Tablets are available in packs of 10s'x100
MEDOFULVIN 500mg Tablets are available in packs of 10s'x50 and 10s'x100

**7. Product Registration Holder:** Komedic Sdn Bhd, 4 Jalan PJS 11/14, Bandar Sunway, 46150 Petaling Jaya

**8. Manufacturer:** Medochemie Ltd (Factory AZ), 2 Michael Erakleous Street, Angios Athanassios Industrial Area, Agios Athanassios, 4101, Limassol Cyprus

**9. Date of Revision of the Text**

08/2023