

Summary of Product Characteristics

GRISOZEN 250

(Griseofulvin Tablets 250 mg)

1. Name of the medicinal product

GRISOZEN 250 (Griseofulvin Tablets 250 mg)

2. Qualitative and quantitative composition

Each tablet contains 250 mg Griseofulvin.

Excipients with known effect:

Each tablet contains 25 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Tablets.

White, circular, uncoated tablets.

4. Clinical particulars

4.1 Therapeutic indications

The treatment of dermatophytic infections of the skin, scalp, hair or nails caused by *Microsporum*, *Trichophyton* and *Epidermophyton* species, where topical therapy is considered inappropriate or has failed.

When griseofulvin is given orally for systemic treatment of fungal infections, it enables newly-formed keratin of the skin, hair and nails to resist attack by the fungi. As the new keratin extends, the old infected keratin is shed. Griseofulvin is effective against dermatophytes causing ringworm (tinea), including *Tinea pedis*, *Tinea cruris*, *Tinea corporis*, *Tinea manum*, *Tinea faciei* and *Tinea capitis*.

Griseofulvin is not effective in infections caused by *Candida albicans*, *Aspergillus* species, *Malassezia furfur* (Pityriasis versicolor) or *Nocardia* species.

4.2 Posology and method of administration

Adults

500 mg to 1 g per 24 hours. Doses of 1.5 g to 2.0 g per 24 hours may be used for short periods in severe or extensive infections. The daily dose is best divided and given at 6-hour intervals. Best results are obtained when the medicine is taken with or after meals, especially fatty meals, in order to minimise possible gastrointestinal irritation and to increase absorption.

Paediatric population

Usually 10 mg/kg (5 mg/lb) body weight daily in divided doses.

Duration of treatment

Treatment must be continued until infected tissue is replaced by normal hair, skin or nails. Therapy should continue for at least two weeks after all signs of infection have disappeared. The following durations are required:

- Skin and hair infections: 2–6 months
- Fingernails: 6–9 months
- Toenails: at least 12 months

Method of administration

Oral. Doses should be taken with or after meals; otherwise absorption is likely to be inadequate.

4.3 Contraindications

Griseofulvin is contraindicated in:

- Patients with porphyria or severe liver disease. Griseofulvin may cause liver disease to deteriorate; liver function should be monitored in such conditions.
- Patients with systemic lupus erythematosus (SLE): griseofulvin has been reported to exacerbate the condition.
- Patients with known hypersensitivity to griseofulvin or to any of the excipients listed in section 6.1.
- Pregnancy or in women intending to become pregnant within one month following cessation of treatment: griseofulvin is teratogenic in animals and some case reports of human foetal abnormalities have been observed (see section 4.6).
- Males who intend to father children within six months of treatment (see section 4.6).
- Long-term prophylactic use: long-term administration of high doses of griseofulvin with food has been reported to induce hepatomas in mice and thyroid tumours in rats but not hamsters. In view of these data, griseofulvin tablets should not be used prophylactically.

4.4 Special warnings and precautions for use

In subacute toxicity studies, orally administered griseofulvin produced hepatocellular necrosis in mice, but this has not been seen in other species. Disturbances in porphyrin metabolism have been reported in griseofulvin-treated laboratory animals.

Because the potential for adverse effects on the human fetus cannot be ruled out, additional contraceptive precautions should be taken during treatment with griseofulvin and for one month after termination of treatment. Griseofulvin should not be prescribed to women intending to become pregnant within one month following cessation of therapy.

Since griseofulvin has demonstrated genotoxic potential in vitro in bacteria, plants and fungi, and has caused aneuploidy in mammalian cells, males should not father children within six months after completing griseofulvin therapy.

Griseofulvin has a colchicine-like effect on mitosis. Griseofulvin interferes with chromosomal distribution during cell division. These effects have been demonstrated in vitro at concentrations achievable in the serum with recommended therapeutic dosages.

Suppression of spermatogenesis has been reported to occur in rats, although investigation in man has failed to confirm this.

Photosensitivity reactions have been reported. Patients should be advised to avoid exposure to intense natural or artificial sunlight during treatment.

4.5 Interaction with other medicinal products and other forms of interaction

Griseofulvin may decrease the blood level and hence efficacy of certain drugs metabolised by cytochrome P450 3A4. These include oral contraceptives, coumarin anticoagulants and ciclosporin. Appropriate monitoring should be undertaken and dosage adjusted as necessary.

Additional contraceptive precautions should be taken during griseofulvin treatment and for one month after stopping griseofulvin.

Absorption of griseofulvin is inhibited when phenobarbitone is taken concurrently. The blood level and hence efficacy of griseofulvin may also be impaired by concurrent administration of substances such as phenylbutazone and sedative and hypnotic drugs which induce metabolising enzymes.

Griseofulvin may decrease theophylline clearance by approximately 30%; theophylline serum concentrations should be monitored when co-administered.

Intermenstrual bleeding and amenorrhoea have been reported during griseofulvin therapy in patients on the oral contraceptive pill. Additional non-hormonal contraceptive measures should be used during treatment and for one month after stopping griseofulvin.

Griseofulvin may increase the prothrombin time in patients receiving warfarin; monitoring should be performed during concomitant treatment.

Decreased griseofulvin absorption has been observed with concurrent sucralfate administration. Rifampin may induce the metabolism of griseofulvin, leading to lower serum concentrations and potential failure of therapy.

Increased creatinine may occur if patients receiving ciclosporin are given griseofulvin.

Patients should be warned that griseofulvin may potentiate the effects of alcohol.

Early investigational trials revealed decreased griseofulvin absorption when co-administered with magnesium-aluminium antacids or other cations (calcium, iron, zinc) due to chelation. Concurrent sucralfate administration also reduces absorption.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is no evidence of safety in human pregnancy. Griseofulvin has been shown to be teratogenic in mice and rats following administration to pregnant animals. Some case reports suggest that it produces human foetal abnormalities. As griseofulvin is capable of inducing aneuploidy in mammalian cells exposed to the compound in vitro and in vivo, women should not take the drug during pregnancy or become pregnant within one month following cessation of treatment. Griseofulvin is contraindicated in pregnancy (see section 4.3).

Breast-feeding

It is not known if griseofulvin is excreted in human milk. Because of the potential for tumorigenicity shown for griseofulvin in animal studies, a decision should be made whether to discontinue breast-feeding or to discontinue the drug, taking into account the importance of the drug to the mother. The drug should be avoided in women who are breast-feeding.

Fertility

Males should not father children within six months of treatment with griseofulvin (see sections 4.3 and 4.4). Suppression of spermatogenesis has been reported in rats. Additionally, griseofulvin may interfere with chromosomal distribution during cell division.

4.7 Effects on ability to drive and use machines

In those cases where individuals are affected by drowsiness, dizziness or impaired coordination while taking griseofulvin, they should not drive vehicles or operate machinery.

4.8 Undesirable effects

Adverse drug reactions are classified using the following frequency convention:

Very common: $\geq 1/10$; Common: $\geq 1/100$ to $< 1/10$; Uncommon: $\geq 1/1,000$ to $< 1/100$; Rare: $\geq 1/10,000$ to $< 1/1,000$; Very rare: $< 1/10,000$; Not known: cannot be estimated from the available data.

System Organ Class	Frequency	Adverse reaction
Infections and infestations	Not known	Oral thrush (candidiasis)
Blood and lymphatic system disorders	Not known	Leucopenia with neutropenia, granulocytopenia
Immune system disorders	Very rare	Angioedema, anaphylaxis
	Not known	Exacerbation of systemic lupus erythematosus
Nervous system disorders	Common	Headache, gastric discomfort (usually disappear as treatment continues)
	Not known	Confusion, dizziness, impaired coordination, peripheral neuropathy, drowsiness
Gastrointestinal disorders	Common	Diarrhoea, nausea, vomiting
Hepatobiliary disorders	Very rare	Significant elevations in liver function tests ($> 3 \times$ ULN), cholestasis
Skin and subcutaneous tissue disorders	Uncommon	Urticaria, fixed drug eruptions, skin rashes
	Very rare	Toxic epidermal necrolysis, erythema multiforme
	Not known	Photosensitivity reactions, downgrading reactions in leprosy
Renal and urinary disorders	Very rare	Proteinuria

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to the National Regulatory Authority.

4.9 Overdose

The symptoms of overdosage consist of headache, skin rashes, dryness of the mouth, an altered sensation of taste and gastrointestinal disturbances. Angioedema, erythema multiforme, toxic epidermal necrolysis, proteinuria, leucopenia and other blood dyscrasias, candidiasis, paraesthesia, photosensitisation and severe headache have been reported occasionally. Depression, confusion, dizziness, insomnia and fatigue have also been reported. Reports of hepatotoxicity have been attributed to griseofulvin. Oral thrush, granulocytopenia or leucopenia and peripheral neuritis can also occur less frequently; in such cases the dosage should be reduced or the medicine discontinued. Treatment is supportive and symptomatic. Treatment is unlikely to be required in cases of acute overdosage.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antifungals for systemic use. ATC code: D01BA01.

Mechanism of action

Griseofulvin is an antifungal antibiotic which is active in vitro against common dermatophytes. It exerts its antifungal effect by disrupting the cell division spindle apparatus of fungal cells, thereby

arresting cell division. A prominent morphological manifestation of the action of griseofulvin is the production of multinucleate cells as the drug inhibits fungal mitosis. Griseofulvin causes disruption of the mitotic spindle by interacting with polymerised microtubules. While the effects of the drug are thus similar to those of colchicine and vinca alkaloids, its binding sites on the microtubular protein are distinct. Griseofulvin is fungistatic in vitro for various species of the dermatophytes *Microsporum*, *Epidermophyton* and *Trichophyton*.

5.2 Pharmacokinetic properties

Absorption

The absorption of griseofulvin from the gastrointestinal tract is variable and incomplete. On average, less than 50% of the oral dose is absorbed, but fatty foods and a reduction in particle size will increase the rate and extent of absorption. The site of absorption appears to be the duodenum. Peak serum concentrations (0.5–2.0 mg/l after a 500 mg dose, or 0.4–2.0 micrograms/ml after 500 mg microsize formulation) are attained 4–8 hours after administration.

Distribution

The volume of distribution is 1.2–1.4 l/kg. In plasma, griseofulvin is approximately 84% bound to plasma proteins, predominantly albumin. There is selective deposition of griseofulvin in newly formed keratin of hair, nails and skin, which gradually moves to the surface of these appendages. Concentrations in the skin and various strata have been shown to exceed serum levels but fall rapidly after drug cessation.

Elimination

A half-life in humans has ranged from 0.7 to 1.7 h with a β half-life of 9.5–21 h. The absorbed griseofulvin is metabolised extensively by the liver to 6-desmethylgriseofulvin, which is conjugated with glucuronic acid. Excretion of this metabolite is primarily in the urine (50%) and up to 30% is excreted in the faeces. Three other metabolites account for 16% of the total drug recovery after oral administration. There is considerable enterohepatic circulation of metabolites, which may also occur in humans. Kinetics in patients with hepatic dysfunction have not been fully reported; it is likely that elimination would be impaired in hepatic disease.

5.3 Preclinical safety data

Griseofulvin can induce aneuploidy and meiotic delay in mouse oocytes following oral administration of high doses (250 mg/kg or greater). In addition, griseofulvin caused increases in numerical and structural chromosome aberrations in mouse spermatocytes at doses of 500 mg/kg and above. Aneuploidy was observed at doses of 1,500 mg/kg.

Griseofulvin administered to rats and mice during pregnancy has been associated with foetotoxicity and foetal malformations. Griseofulvin has demonstrated teratogenic effects in rats at doses of 1,250–1,500 mg daily and in cats at doses of 100 mg per day or less.

Long-term administration of high doses of griseofulvin with food has been reported to induce hepatomas in mice and thyroid tumours in rats but not hamsters. The effects in mice may be due to a species-specific effect on porphyrin metabolism.

Mutagenicity of griseofulvin has not been demonstrated. Human carcinogenicity or teratogenicity has not been demonstrated. No toxic reactions of dose-related origin have been demonstrated in humans.

6. Pharmaceutical particulars

6.1 List of excipients

Lactose

Maize Starch
Microcrystalline Cellulose
Hypromellose (HPMC)
Purified Water
Purified Talc
Magnesium Stearate
Colloidal Anhydrous Silica
Croscarmellose Sodium

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at temperature not exceeding 30°C. Protect from light and moisture.

6.5 Nature and contents of container

1 ALU-PVC blister of 10 tablets; 10 blisters packed in a printed carton along with insert.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing Authorisation Holder

Marketing Authorisation Holder and Manufacturer:

ZAIN PHARMA LTD.

Plot No: 209/13741, Colchester Park,
Go-Down No. 1, 2, 3, Off Mombasa Road,
Behind Nice and Lovely House,
P.O. Box: 100167-00101, Nairobi, Kenya.

8. Marketing Authorisation Number

H2025/CTD12729/27009

9. Date of First Authorisation / Renewal of the Authorisation

03.11.2025

10. Date of Revision of the Text

03.11.2025