For the use only of Registered Medical Practitioners or a Hospital or a Laboratory

GRISOVIN - FP

1. GENERIC NAME

Griseofulvin Tablets IP 250 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains: Griseofulvin IP 250 mg

List of Excipients

Maize Starch, Gelatin, Methyl Hydroxybenzoate, Propyl Hydroxybenzoate, Purified Talc, Magnesium Stearate, Purified Water

3. DOSAGE FORM AND STRENGTH

Tablets

For information on strength(s) refer *2. Qualitative and Quantitative Composition* above.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication

GRISOVIN is indicated in the treatment of fungal infections of the skin, scalp, hair or nails caused by *Microsporum* spp., *Trichophyton* spp., *Epidermophyton* spp., where topical therapy is considered inappropriate or has failed.

4.2 Posology and Method of Administration

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

Duration of Treatment

This depends upon the thickness of keratin at the site of infection.

For hair or skin at least four weeks treatment is required, whereas toe or finger nails may need six to twelve months treatment.

Therapy should be continued for at least two weeks after all signs of infection have disappeared.

Populations

Adults (greater than or equal to 50 kg)

Normally 500 to 1,000 mg daily, but not less than 10 mg/kg bodyweight daily. A single dose daily is often satisfactory, but divided doses may be more effective in patients who respond poorly.

Children

Usually 10 mg/kg body weight daily.

The 250mg tablet should be given once daily to paediatrics of 25 - 49 kg in weight.

4.3 Contraindications

- Hypersensitivity to any ingredient of the preparation.
- Porphyria.
- Severe liver disease: griseofulvin may cause liver disease to deteriorate, and liver function should be monitored in such conditions.
- Systemic lupus erythematosus: griseofulvin has been reported to exacerbate the condition.
- There is no evidence of the safety of griseofulvin in human pregnancy.
- Griseofulvin is teratogenic in animals and some case reports of human foetal abnormalities have been observed. Therefore, griseofulvin should not be used in pregnancy, or in women intending to become pregnant within one month following cessation of treatment.
- Males should not father children within six months of treatment with griseofulvin.
- 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 clinical significance of these findings in man is not known. In view of these data, griseofulvin should not be used prophylactically.

4.4 Special Warnings and Precautions for Use

Customary hygienic measures should be adopted to minimise the risk of re-infection, and concurrent use of a topical fungicide may be helpful to minimise any spread of infective material.

While data from an epidemiology study have suggested an increased risk of breast cancer in patients receiving three or more prescriptions of griseofulvin (odds ratio = 1.59, 95% confidence interval 1.11-2.27), this finding has not been confirmed in other studies.

4.5 Drug Interactions

Griseofulvin may decrease the blood level and hence efficacy of certain drugs, which are metabolised by cytochrome P450 3A4. These include oral contraceptives, coumarin anticoagulants and cyclosporin. Appropriate monitoring should be undertaken and dosage should be adjusted as necessary. Additional contraceptive precautions should be taken during griseofulvin treatment and for a 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 reduced as the result of concurrent administration of substances such as phenylbutazone and sedative and hypnotic drugs which induce metabolising enzymes.

Patients should be warned that an enhancement of the effects of alcohol by griseofulvin has been reported.

4.6 Use in Special Populations

Pregnancy

There is no evidence of griseofulvin safety in human pregnancy (*see 4.3 Contraindications*). Griseofulvin administered to rats and mice during pregnancy has been associated with foetotoxicity and foetal malformations.

As griseofulvin is capable of inducing aneuploidy (abnormal segregation of chromosomes following cell division) in mammalian cells exposed to the compound *in vitro* and *in vivo*, women should be warned that they should not take the drug during pregnancy or become pregnant within one month following cessation of treatment.

Additionally, males should not father children within six months of treatment.

Lactation

It is not known if griseofulvin is excreted in human milk. Safety in children of mothers who are breast-feeding has not been established.

4.7 Effects on Ability to Drive and Use Machines

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

4.8 Undesirable Effects

Diarrhoea, nausea and vomiting are common adverse events.

Headache and gastric discomfort sometimes occur, but usually disappear as treatment continues.

On rare occasions urticarial reactions, skin rashes and precipitation of systemic lupus erythematosus have been reported.

Toxic epidermal necrolysis and erythema multiforme have been reported.
Significant elevations in LFTs (greater than three times the upper limit of normal) have been reported very rarely.

There have been reports of central nervous system effects e.g. confusion, dizziness, impaired co-ordination and peripheral neuropathy.

Leucopenia with neutropenia has been reported.

Photosensitivity reactions can occur on exposure to intense natural or artificial sunlight.

Drowsiness.

4.9 Overdose

Treatment is unlikely to be required in cases of acute overdosage.

5. PHARMACOLOGICAL PROPERTIES

5.1 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.

5.2 Pharmacodynamic Properties

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.

Microbiology:

Griseofulvin is effective against the dermatophytes causing ringworm (tinea), including: *Microsporum canis, T. verrucosum, T. mentagrophytes, E. floccosum and T. rubrum*.

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

5.3 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 the absorption.

After oral dosing there is a phase of rapid absorption followed by slower prolonged absorption. Peak plasma levels (0.5 to 1.5 micrograms after a 500 mg oral dose) are achieved by 4 h and are maintained for 10 to 20 h.

Distribution

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.

Metabolism

6 - desmethylgriseofulvin or its glucuronide conjugate are metabolites of griseofulvin.

Elimination

The absorbed griseofulvin is excreted in the urine mainly as 6 - desmethylgriseofulvin or its glucuronide conjugate. The terminal plasma half-life ranges from 9.5 to 21 h, there being considerable intersubject variability.

6. NONCLINICAL PROPERTIES

Genotoxic Potential:

The mode of action of griseofulvin as a fungicide is to interfere with microtubule assembly; this also has the potential for disruption of the cell division spindle apparatus. This disruption can lead to abnormal chromosome segregation at cell division. *In vitro* and *in vivo* genotoxicity studies have demonstrated that griseofulvin causes structural and numerical chromosome aberrations, including aneuploidy.

Carcinogenic Potential:

Long-term administration of griseofulvin showed no carcinogenic potential in the hamster but induced hepatomas in mice and thyroid tumours in rats. Both of these tumour types are considered to be induced by species specific mechanisms and therefore are thought not to represent a carcinogenic risk to humans.

7. DESCRIPTION

Each uncoated tablet contains: Griseofulvin IP 250 mg

List of Excipients

Maize Starch, Gelatin, Methyl Hydroxybenzoate, Propyl Hydroxybenzoate, Purified Talc, Magnesium Stearate, Purified Water

8. PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

There are no relevant data available.

8.2 Shelf Life

The expiry date is indicated on the label and packaging.

8.3 Packaging Information

Blister strips in a carton.

8.4 Storage and Handling Instructions

Store at temperature below 30º C

Keep out of reach of children.

9. PATIENT COUNSELLING INFORMATION

Registered Medical Practitioners may counsel their patients (and/or their patients' caregiver as applicable) about the special warnings and precautions for use, drug interactions, undesirable effects, and any relevant contraindications of *GRISOVIN*. Patients (and/or the patients' caregiver) may also be informed about posology, method of administration and storage/handling information as applicable.

10. DETAILS OF MANUFACTURER

The Manufacturing Site details are mentioned on the label and packaging.

For further information please contact:
GlaxoSmithKline Pharmaceuticals Limited.
Registered Office:
Dr. Annie Besant Road, Worli
Mumbai 400 030, India.

11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE

Manufacturing License number is indicated on the label and packaging.

12. DATE OF REVISION

13-JUL-2023

Version: GRI/PI/IN/2023/01

Adapted from: Griseofulvin GDS v13 dated 03 August 2010