SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Griseofulvin 500mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Griseofulvin BP 500.0 mg

Excipient(s) with known effect:
Each tablet contains 1.55 mg propylene glycol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

The treatment of fungal infections of the skin, scalp, hair or nails 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 the dermatophytes causing ringworm (tinea), including: *Microsporum canis and T. Verrucosum.*

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

4.2 Posology and method of administration

Posology

Adults
Normally 500 to 1000 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.

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

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 fingernails may need six to twelve months treatment. Therapy should be continued for at least two weeks after all signs of infection have disappeared.

Method of administration
For oral administration.

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

4.3 Contraindications

Porphyria or 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.

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

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 tablets should not be used prophylactically.

4.4 Special warnings and precautions for use

None.

4.5 Interaction with other medicinal products and other forms of interaction

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 ciclosporin. 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 impaired 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.

Excipients
This medicine contains 1.55 mg propylene glycol in each tablet.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is no evidence of its safety in human pregnancy (see contraindications). 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 (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.

Breast-feeding
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 has been reported.

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 via the Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9. Overdose

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.

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 the absorption.

Distribution
After oral dosing there is a phase of rapid absorption followed by slower prolonged absorption. Peak plasma levels (0.5 - 1.5 micrograms after a 500mg oral dose) are achieved by 4 hours and are maintained for 10 - 20 hours. The terminal plasma half-life ranges from 9.5 - 21 hours, there being considerable intersubject variability. In plasma griseofulvin is approximately 84% bound to plasma proteins, predominantly albumin.

Elimination
The absorbed griseofulvin is excreted in the urine mainly as 6-desmethylgriseofulvin or its glucuronide conjugate.

There is selective deposition of griseofulvin in newly formed keratin of hair, nails and skin, which gradually moves to the surface of these appendages.

5.3. Pre-clinical Safety Data

Griseofulvin can induce aneuploidy and meiotic delay in mouse oocytes following oral administration of high doses, i.e. 250mg/kg or greater. In addition, griseofulvin caused increases in numerical and structural chromosome aberrations in mouse spermatocytes at doses of 500mg/kg and above. Aneuploidy was observed at doses of 1500mg/kg. Griseofulvin administered to rats and mice during pregnancy has been associated with foetotoxicity and foetal malformations. 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 (see contraindications). The

effects in mice may be due to a species specific effect on porphyrin metabolism.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium laurilsulfate
Povidone
Maize starch
Potato starch
Microcrystalline cellulose
Magnesium stearate
Purified water

Film Coating:
Hypromellose
Ethylcellulose
Acetylated monoglyceride
Polysorbate 80
Propylene glycol (E 1520)
Methylene chloride
Isopropyl alcohol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years

6.4 Special Precautions for Storage

Do not store above 25°C. Store in the original container.

6.5. Nature and Content of Container

100 tablets in a tubular glass vial with a polythene snap plug closure or, tamper evident polypropylene container with a low density polyethylene lid.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Chemidex Pharma Ltd,
Trading as Essential Generics,
8a Crabtree Road,
Egham, Surrey
TW20 8RN

8. MARKETING AUTHORISATION NUMBER(S)

PL 17736/0083

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

28th June 2005

10 DATE OF REVISION OF THE TEXT

12/08/2024