Issued to the Medical Professions only

FULCIN TABLETS

Trade Mark

Presentation

FULCIN Tablets are presented as tablets, each containing 500 mg griseofulvin Ph. Eur.

Product Description

Fulcin 500 tablet is presented as white, round, biconvex tablet which may imprinted F on one face and plain on reverse face. Each tablet containing 500 mg griseofulvin. The tablet is for oral administration

Indications

FULCIN is effective against the dermatophytes causing ringworm (tinea) including *Microsporum canis*, *Trichophyton rubrum*, *Trichophyton verrucosum* and *Epidermophyton spp*.

FULCIN is indicated for the treatment of fungal infections of the skin, hair and nails, where topical therapy is considered inappropriate or has failed.

Dosage and administration

Adults (including elderly patients)

The usual dosage is 500 mg daily in single or divided doses after food. In severe conditions, up to twice this amount may be given, reducing to the lower level when a clinical response has occurred.

Children

The daily dosage is 10 mg griseofulvin per kg bodyweight in single or divided doses after food. The duration of treatment depends on the type of infection and the time required for normal replacement of infected tissues. Up to twelve months may be required for recalcitrant infections.

For complete eradication of infection, FULCIN treatment should be combined with general measures of care and hygiene with particular attention to reservoirs of infection.

Contraindications

FULCIN is contra-indicated in patients with established porphyria, hepatocellular failure or lupus erythematosus and related conditions.

FULCIN is contra-indicated in pregnancy (see section *Preclinical safety data relevant to the prescriber*).

Precautions

Griseofulvin is capable of producing aneuploidy (abnormal segregation of chromosomes following cell division) in mammalian cells exposed to the compound in vitro and in viva. Griseofulvin may damage sperm cells; males should not father children during treatment or within six months of completion of treatment.

There is no evidence of the safety of griseofulvin in human pregnancy. Griseofulvin administered to rats during pregnancy has been associated with foetotoxicity and tail deformities at high dosages. Some case reports of human foetal abnormalities have been observed. Therefore, women should not become pregnant during or within one month of treatment with griseofulvin; if they do, they should seek genetic advice.
Long-term administration of high doses of griseofulvin with food has been reported to induce hepatomas in mice and thyroid tumors in rats. The clinical significance of these findings in man is not known. In view of these data, FULCIN should not be used prophylactically.

Interactions with other medicaments and other forms of interaction

FULCIN may decrease the response to coumarin anticoagulants administered concomitantly.

Liver enzyme inducing drugs, such as barbiturates, may reduce the effectiveness of FULCIN therapy.

Barbiturates can reduce the effectiveness of FULCIN therapy by interfering with gastrointestinal absorption of the drug.

Breakthrough bleeding, amenorrhoea and failure of contraceptive therapy have been reported in patients taking griseofulvin and oral contraceptive steroids. It may be advisable to consider additional contraceptive precautions during FULCIN therapy and for up to one month afterwards.

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

Griseofulvin may falsely elevate urinary levels of VMA.

Pregnancy and lactation

FULCIN is contra-indicated in pregnancy. There is no evidence of the safety of FULCIN in human pregnancy (see *Precautions*).

It is not known if griseofulvin is excreted in breast milk. Safety in children of nursing mothers has not been established.

Effect on ability to drive or operate machinery

FULCIN may impair the ability of some individuals to drive and operate machinery. There have been occasional reports of dizziness and confusion with impaired co-ordination and griseofulvin has been reported to enhance the effects of alcohol.

Possible adverse drug reactions

FULCIN is generally well tolerated. Urticarial reactions and skin rashes have been noted in a few cases. There have been occasional complaints of headache and gastric discomfort, which, in most cases, have regressed during treatment. Dizziness, fatigue, granulocytopenia and leucopenia have also been reported. Photosensitivity associated with griseofulvin therapy has been recorded and there have been rare reports of precipitation of systemic lupus erythematosus and related conditions, erythema multiforme, toxic epidermal necrolysis and related conditions, peripheral neuropathy, confusion with impaired co-ordination and of oral candidiasis. FULCIN may rarely cause cholestasis, increased liver enzymes and hepatitis.

Overdose

In the event of overdosage, symptomatic treatment should be given.

Pharmacological properties

Pharmacodynamic properties

Griseofulvin inhibits fungal cell mitosis by causing disruption of the mitotic spindle structure, thereby arresting the metaphase of cell division. It is deposited in varying degrees in the keratin precursor cells of skin, hair and nails, rendering the keratin resistant to fungal invasion. As the infected keratin is shed, it is replaced with healthy tissue.

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

Pharmacokinetic properties

Following oral administration, griseofulvin is absorbed principally from the duodenum. Peak plasma concentrations of the drug (approximately 1-2 µg/ml) occur about 4 hours after dosing.

Concentrations of approximately 12-25 µg/g are maintained in skin during long term administration, whilst concurrent serum levels remain at 1-2 µg/ml. When the drug is discontinued, the drug is not detectable after 2 days in the skin and after 4 days in the plasma.

The drug has an elimination half-life of 9-24 hours and it is metabolised in the liver, the major metabolite being 6-demethylgriseofulvin, which is microbiologically inactive. The metabolites are excreted mainly in the faeces. Griseofulvin is also excreted in sweat.

Pre-clinical safety data relevant to the prescriber

Griseofulvin can induce aneuploidy and meiotic delay in mouse oocytes. These effects were demonstrated 17 hours after oral administration of very high doses of griseofulvin. Griseofulvin administered to rats during pregnancy has been associated with foetotoxicity and tail deformities at high doses.

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

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.

Pharmaceutical precautions

Store below 30°C. Protected from moisture.

Excipient Lists

Calcium carboxymethyl cellulose

Maize starch
Polyvinylpyrrolidone
Magnesium stearate
Purified water

Packings

FULCIN 500 mg, in container of 2strips @ 14 tablets (Reg. No.:)

Shelf Life

5 years

HARUS DENGAN RESEP DOKTER
OBAT KERAS

Manufactured by:
PT Boehringer Ingelheim Indonesia, Bogor Indonesia.
Under license from AstraZeneca UK Limited

Marketing authorization holder

AstraZeneca Indonesia
Techno Park Blok B1A – B1B, Jababeka Industrial Park Cikarang, Bekasi

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