Griseofulvin may impair the ability to drive or operate machinery, and has been reported to enhance the effects of alcohol.

Porphyria. Griseofulvin has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Interactions

Phenobarbital has been reported to decrease the gastrointestinal absorption of griseofulvin. Plasma concentrations of griseofulvin have also been reported to be reduced by drugs that induce metabolising enzymes.

Griseofulvin may increase the rate of metabolism and diminish the effects of some drugs such as coumarin anticoagulants and oral contraceptives.

Griseofulvin may enhance the effects of alcohol.

Alcohol. In addition to reports of griseofulvin enhancing the effects of alcohol, a severe disulfiram-like reaction to alcohol has been reported in a patient taking griseofulvin.[1]

1. Fett DL, Vukov LF. An unusual case of severe griseofulvin-alcohol interaction. *Ann Emerg Med* 1994; **24:** 95–7.

Bromocriptine. For a report that griseofulvin can block the response to bromocriptine, see p.800.

Salicylates. Griseofulvin has been reported to reduce plasma concentrations of salicylate in a patient taking aspirin, see p.23.

Antimicrobial Action

Griseofulvin is a fungistatic antibiotic that inhibits fungal cell division by disruption of the mitotic spindle structure. It may also interfere with DNA production. It is active against the common dermatophytes, including some species of *Epidermophyton*, *Microsporum*, or *Trichophyton*.

Pharmacokinetics

Absorption of griseofulvin from the gastrointestinal tract is variable and incomplete, but is enhanced by reducing the particle size or when given with a fatty meal. Peak plasma concentrations are reached within 4 hours and are maintained for 10 to 20 hours.

Griseofulvin is about 84% bound to plasma proteins. It is deposited in keratin precursor cells and is concentrated in the stratum corneum of the skin and in the nails and hair, thus preventing fungal invasion of newly formed cells. Concentrations of 12 to 25 micrograms/g are maintained in skin during long-term use, while plasma concentrations remain at about 1 to 2 micrograms/mL. Griseofulvin has an elimination half-life of 9 to 24 hours, and is metabolised by the liver mainly to 6-demethylgriseofulvin and its glucuronide conjugate which are excreted in the urine. A large amount of a dose of griseofulvin of reduced particle size appears unchanged in the faeces; less than 1% is excreted unchanged in the urine; some is excreted in the sweat.

Uses and Administration

Griseofulvin is an antifungal used orally in the treatment of dermatophyte infections. It is generally given when such infections involve the scalp, hair, nails, and skin and do not respond to topical treatment (see Skin Infections, p.521); infections of the soles of the feet, the palms of the hands, and the nails respond slowly.

The usual dose of griseofulvin has been 0.5 to 1 g daily in single or divided doses; children have been given 10 mg/kg daily. These doses are for preparations of griseofulvin of reduced particle size, sometimes known as microcrystalline or microsize griseofulvin. Doses have been reduced by about one-quarter when preparations, available in some countries, containing ultramicrocrystalline or ultramicrosize griseofulvin are used. Griseofulvin should be given with or after meals.

The duration of treatment depends on the thickness of the keratin layer: 2 to 8 weeks for infections of the hair and skin, up to 6 months for infections of the fingernails, and 12 months or more for infections of the toenails.

Griseofulvin is also used as a 1% topical spray in tinea pedis.

◊ Reviews.

1. Fleece D, *et al*. Griseofulvin versus terbinafine in the treatment of tinea capitis: a meta-analysis of randomized, clinical trials. *Pediatrics* 2004; **114:** 1312–15.
2. Gupta AK, *et al*. Meta-analysis: griseofulvin efficacy in the treatment of tinea capitis. *J Drugs Dermatol* 2008; **7:** 369–72.

Non-infective skin disorders. Lichen planus is usually treated with corticosteroids or retinoids (see p.1580) but griseofulvin has been suggested as an alternative to topical corticosteroids in erosive disease.[1] However, some researchers have found it to be of no value.[2]

Dramatic responses of pigmented purpuric dermatoses to griseofulvin 500 to 750 mg daily have been reported in 5 patients.[3]

1. Lamey P-J, Lewis MAO. Oral medicine in practice: white patches. *Br Dent J* 1990; **168:** 147–52.
2. Bagan JV, *et al*. Treatment of lichen planus with griseofulvin. *Oral Surg Oral Med Oral Pathol* 1985; **60:** 608–10.
3. Tamaki K, *et al*. Successful treatment of pigmented purpuric dermatosis with griseofulvin. *Br J Dermatol* 1995; **132:** 159–60.

Preparations

BP 2008: Griseofulvin Tablets;
USP 31: Griseofulvin Capsules; Griseofulvin Oral Suspension; Griseofulvin Tablets; Ultramicrosize Griseofulvin Tablets.

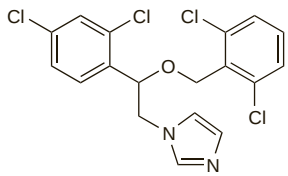
Proprietary Preparations (details are given in Part 3)
Arg.: Grisovin; ***Austral.:*** Griseostatin†; Grisovin; ***Austria:*** Griseomed†; Grisovin; ***Braz.:*** Fulcin; Sporostatin; ***Canad.:*** Fulvicin†; ***Chile:*** Fulvistatin P/G†; ***Fr.:*** Grisefuline; ***Ger.:*** Fulcin S†; Gricin; Griseo; Likuden M; ***India:*** Grisactin; Walavin; ***Indon.:*** Fulcin; Fungistop; Griseofort; Mycostop; ***Irl.:*** Fulcin†; ***Israel:*** Grifulin; ***Ital.:*** Fulcin; Grisovina FP; ***Malaysia:*** Grisuvin; Grivin; Krisovin; Medofulvin†; Myconil†; ***Mex.:*** Fulcin; Fulsivin; Fulvina†; Grisovin; ***Philipp.:*** Grisovin; ***Port.:*** Fulcin†; Grisomicon†; Grisovin; ***S.Afr.:*** Microcidal; ***Singapore:*** Grivin†; Krisovin; Medofulvin†; ***Spain:*** Fulcin; Greosin†; ***Switz.:*** Grisol†; ***Thai.:*** Aofen; Grifulvin; Grisflavin; Grivin; Neofulvin; Trivanex; ***Turk.:*** Gefulvin; Grisovin; ***UK:*** Grisol; Grisovin†; ***USA:*** Gris-PEG; ***Venez.:*** Fulvin†; Grisovin.

Multi-ingredient: ***Arg.:*** Griseoplus.

Isoconazole *(BAN, USAN, rINN)*

Isoconazol; Isoconazolum; Isokonatsoli; Isokonazol; Izokonazol; Izokonazolas. 1-[2,4-Dichloro-β-(2,6-dichlorobenzyloxy)phenethyl]imidazole.

Изоконазол
$C_{18}H_{14}Cl_4N_2O$ = 416.1.
CAS — 27523-40-6.
ATC — D01AC05; G01AF07.
ATC Vet — QD01AC05; QG01AF07.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Isoconazole). A white or almost white powder. Practically insoluble in water; freely soluble in alcohol; very soluble in methyl alcohol. Protect from light.

Isoconazole Nitrate *(BANM, rINNM)*

Isoconazole, bitrate d'; Isoconazole, Nitrate d'; Isoconazoli nitras; Isokonatsolinitraatti; Isokonazolnitrat; Isokonazol-nitrát; Izokonazol Nitrat; Izokonazol-nitrát; Izokonazolo nitratas; Nitrato de isoconazol; R-15454.

Изоконазола Нитрат
$C_{18}H_{14}Cl_4N_2O,HNO_3$ = 479.1.
CAS — 24168-96-5 (isoconazole mononitrate); 40036-10-0 (isoconazole nitrate).
ATC — D01AC05; G01AF07.
ATC Vet — QD01AC05; QG01AF07.

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Isoconazole Nitrate). A white or almost white powder. Very slightly soluble in water; slightly soluble in alcohol; soluble in methyl alcohol. Protect from light.

Adverse Effects and Precautions

Local reactions including burning or itching may occur after application of isoconazole.

Intravaginal preparations of azole antifungals may damage latex contraceptives and additional contraceptive measures are therefore necessary during local application.

For a discussion of the caution needed when using azole antifungals during pregnancy, see under Pregnancy in Precautions of Fluconazole, p.532.

Antimicrobial Action

Isoconazole is an imidazole antifungal active against a wide spectrum of fungi including *Candida* spp., dermatophytes, and *Malassezia furfur*. It is also active against some Gram-positive bacteria.

Uses and Administration

Isoconazole is an imidazole antifungal used locally as the nitrate in the treatment of vaginal mycoses, particularly due to *Candida* spp. (p.518) and in fungal skin infections (p.521). For vaginal infections it is usually given as pessaries in a single dose of 600 mg or 300 mg daily for 3 days, or as a 1% vaginal cream daily for 7 days. For skin infections a 1% or 2% cream or other topical formulation has been used.

Preparations

BP 2008: Isoconazole Pessaries.

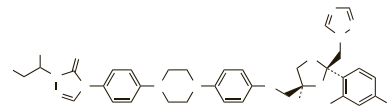
Proprietary Preparations (details are given in Part 3)
Arg.: Isomicot; Mupaten; ***Austria:*** Gyno-Travogen; Travogen; ***Belg.:*** Travogen; ***Braz.:*** Gino Monipax†; Gino-Isomax; Ginotrax; Gyno Icaden; Gyno-Mycel†; Gynoplus†; Icaden; Isomax; Micaden; Mycel Gyno; Neo Isocaden; ***Chile:*** Ufarin; ***Fr.:*** Fazol; Fazol G; ***Ger.:*** Travogen†; ***Gr.:*** Travogen; ***Hong Kong:*** Gyno-Travogen†; Travogen; ***Israel:*** Isogen; ***Ital.:*** Isogyn; Travogen; ***Malaysia:*** Travogen; ***Mex.:*** Icaden; Nocazin; ***Philipp.:*** Travogen; ***Pol.:*** Gyno-Travogen; Travogen; ***Port.:*** Gino-Travogen; ***Rus.:*** Gyno-Travogen (Гино-травоген); Travogen (Травоген); ***Singapore:*** Gyno-Travogen; Travogen; ***Switz.:*** Gyno-Travogen; Travogen; ***Thai.:*** Nacozil†; Travogen; ***Turk.:*** Gyno-Travogen; Travogen; ***Venez.:*** Icaden; Noginox.

Multi-ingredient: ***Arg.:*** Scheriderm; ***Austria:*** Travocort; ***Belg.:*** Travocort; ***Ger.:*** Bi-Vaspit†; Travocort; ***Gr.:*** Travocort; ***Hong Kong:*** Travocort; ***Indon.:*** Travocort; ***Irl.:*** Travocort; ***Israel:*** Isocort; Tevaderm; ***Ital.:*** Travocort; ***Malaysia:*** Isoradin; Travocort; ***Mex.:*** Scheriderm; ***Philipp.:*** Travocort; ***Pol.:*** Travocort; ***Port.:*** Travocort; ***Rus.:*** Travocort (Травокорт); ***S.Afr.:*** Travocort; ***Singapore:*** Travocort; ***Switz.:*** Travocort; ***Thai.:*** Travocort; ***Turk.:*** Travazol; Travocort.

Itraconazole *(BAN, USAN, rINN)*

Itraconazol; Itraconazolum; Itrakonatsoli; Itrakonazol; Itrakonazolas; Oriconazole; R-51211. (±)-2-*sec*-Butyl-4-[4-(4-{4-[(2*R**,4*S**)-2-(2,4-dichlorophenyl)-2-(1*H*-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-4-ylmethoxy]phenyl}-piperazin-1-yl)phenyl]-2,4-dihydro-1,2,4-triazol-3-one.

Итраконазол
$C_{35}H_{38}Cl_2N_8O_4$ = 705.6.
CAS — 84625-61-6.
ATC — J02AC02.
ATC Vet — QJ02AC02.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Itraconazole). A white or almost white powder. Practically insoluble in water; very slightly soluble in alcohol; freely soluble in dichloromethane; sparingly soluble in tetrahydrofuran. Protect from light.

Adverse Effects

The most common adverse effects associated with itraconazole include dyspepsia, abdominal pain, nausea, vomiting, constipation, diarrhoea, headache, and dizziness. Others include allergic reactions such as pruritus, rash, urticaria, and angioedema. Isolated cases of the Stevens-Johnson syndrome have been associated with itraconazole.

An increase in liver enzyme values has occurred in some patients and cases of hepatitis and cholestatic jaundice have been observed, especially in those treated for more than one month. There have been rare cases of liver failure and death.

Heart failure and pulmonary oedema have been reported rarely and serious cardiovascular events including arrhythmias and sudden death have been attributed to drug interactions in patients receiving itraconazole (see Interactions, below).

Alopecia, oedema, and hypokalaemia have also been associated with prolonged use. Menstrual disorders and peripheral neuropathy have been reported in a few patients.

Incidence of adverse effects. Itraconazole 50 to 400 mg daily for a median of 5 months was considered to be well tolerated in 189 patients with systemic fungal infections.[1] Of 86 patients with