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

◊ References.

1. del Palacio A, *et al.* A double-blind randomized comparative trial: eberconazole 1% cream versus clotrimazole 1% cream twice daily in Candida and dermatophyte skin infections. *Mycoses* 2001; **44:** 173–80.
2. Repiso Montero T, *et al.* Eberconazole 1% cream is an effective and safe alternative for dermatophytosis treatment: multicenter, randomized, double-blind, comparative trial with miconazole 2% cream. *Int J Dermatol* 2006; **45:** 600–4.

Preparations

Proprietary Preparations (details are given in Part 3)
Spain: Ebernet; Ebertop; Ebesupol.

Econazole *(BAN, USAN, rINN)*

Econazol; Éconazole; Econazolum; Ekonatsoli; Ekonazol; Ekonazolas. 1-[2,4-Dichloro-β-(4-chlorobenzyloxy)phenethyl]imidazole.

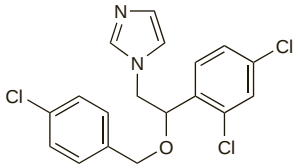
Эконазол

$C_{18}H_{15}Cl_3N_2O$ = 381.7.

CAS — 27220-47-9.

ATC — D01AC03; G01AF05.

ATC Vet — QD01AC03; QG01AF05.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Econazole). A white or almost white powder. M.p. 88° to 92°. Practically insoluble in water; very soluble in alcohol and in dichloromethane. Protect from light.

Econazole Nitrate *(BANM, USAN, rINNM)*

C-C2470; Éconazole, nitrate d'; Econazoli nitras; Ekonatsolinitraatti; Ekonazolnitrat; Ekonazol-nitrát; Ekonazolo nitratas; Nitrato de econazol; R-14827; SQ-13050. (±)-1-[2,4-Dichloro-β-(4-chlorobenzyloxy)phenethyl]imidazole nitrate.

Эконазола Нитрат

$C_{18}H_{15}Cl_3N_2O,HNO_3$ = 444.7.

CAS — 24169-02-6 (econazole nitrate); 68797-31-9 ((±)-econazole nitrate).

ATC — D01AC03; G01AF05.

ATC Vet — QD01AC03; QG01AF05.

Pharmacopoeias. In *Chin., Eur.* (see p.vii), and *US.*
Ph. Eur. 6.2 (Econazole Nitrate). A white or almost white crystalline powder. Very slightly soluble in water; slightly soluble in alcohol; sparingly soluble in dichloromethane; soluble in methyl alcohol. Protect from light.
USP 31 (Econazole Nitrate). A white or practically white, crystalline powder, with not more than a slight odour. Very slightly soluble in water and in ether; slightly soluble in alcohol; sparingly soluble in chloroform; soluble in methyl alcohol. Protect from light.

Adverse Effects and Precautions

Local reactions including burning and irritation may occur when econazole nitrate is applied topically. Contact dermatitis has been reported rarely.

Intravaginal preparations of econazole 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.

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

Antimicrobial Action

Econazole is an imidazole antifungal with antimicrobial activity similar to that of ketoconazole (p.539).

Pharmacokinetics

Absorption is not significant when econazole nitrate is applied to the skin or vagina.

Uses and Administration

Econazole is an imidazole antifungal used topically in the treatment of superficial candidiasis (see p.518) and in dermatophytosis and pityriasis versicolor (see Skin Infections, p.521).

Econazole nitrate is applied topically up to 3 times daily as a 1% cream, lotion, powder, or solution in the treatment of fungal skin infections. Treatment is continued for 2 to 4 weeks. It is also used in the treatment of vaginal candidiasis as pessaries of 150 mg once daily at bedtime for 3 consecutive nights; a single dose of 150 mg in a long-acting formulation has also been used. Intravaginal use of 5 g of a 1% cream once daily at night has been given for 2 weeks. A 1% cream may be used concurrently for the treatment of vulval infections or for the treatment of balanitis in a male partner.

In the treatment of fungal infections of the nails, a 1% cream or lotion is applied once daily and covered with an occlusive dressing.

Econazole nitrate has also been used as eye or ear drops.

Econazole sulfosalicylate has also been used.

Preparations

BP 2008: Econazole Cream; Econazole Pessaries.

Proprietary Preparations (details are given in Part 3)
Arg.: Dermocitran; Micocide; Micofitex†; Micolis; Micotex; Novo Paramicon; Sinamida Econazol; ***Austral.:*** Dermazole; Pevaryl; ***Austria:*** Gyno-Pevaryl; Pevaryl; ***Belg.:*** Gyno-Pevaryl; Pevaryl; ***Braz.:*** Dermazol; Micostyl; ***Canad.:*** Ecostatin; ***Chile:*** Micolis; ***Cz.:*** Gyno-Pevaryl; Pevaryl; ***Denm.:*** Pevaryl; ***Fin.:*** Pevaryl; ***Fr.:*** Dermazol; Fongeryl; Gyno-Pevaryl; Mycoapaisyl; Pevaryl; ***Ger.:*** Epi-Pevaryl; Epi-Pevaryl Pv; Gyno-Pevaryl; ***Gr.:*** Bismultin; Mycobacter; Nectarmicin†; Penicomb; Pevaryl; Unifungin; ***Hong Kong:*** Dermazole†; Econite; Ecosone; Gyno-Pevaryl†; Heads Shampoo; Pevaryl†; ***Hung.:*** Gyno-Pevaryl; Pevaryl; ***India:*** Ecanol; ***Irl.:*** Ecostatin; Gyno-Pevaryl; Pevaryl†; ***Israel:*** Gyno-Pevaryl; Pevaryl; ***Ital.:*** Chemionazolo†; Dermazol†; Eccelium†; Eco Mi; Ecodergin; Ecorex; Ecosteril; Ganazolo; Ifenec; Micos; Pevaryl; Polinazolo; ***Malaysia:*** Ecoderm†; Gyno-Pevaryl; Pevaryl†; Zoliderm†; ***Mex.:*** Micostyl; Pevaryl; ***Neth.:*** Pevaryl; ***Norw.:*** Pevaryl; ***NZ:*** Dermazole†; Ecreme; Gyno-Pevaryl†; Pevaryl; ***Philipp.:*** Pevaryl; ***Pol.:*** Gyno-Pevaryl; Pevaryl; Pevazol; ***Port.:*** Gyno-Pevaryl; Pevaryl; ***Rus.:*** Ecalin (Экалин); Ecodax (Экодакс); Ecomikole (Экомикол)†; Gyno-Pevaryl (Гино-Певарил); Ifenec (Ифенек); ***S.Afr.:*** Ecoderm; Econal-C; Gyno-Pevaryl; Pevaryl; ***Singapore:*** Dermazole†; Gyno-Pevaryl; Pevaryl†; ***Spain:*** Ecotam; Gyno-Pevaryl; Micoespec; Pevaryl; ***Swed.:*** Pevaryl; ***Switz.:*** Gyno-Pevaryl; Pevaryl; Sebolith; ***Thai.:*** Econ; ***UK:*** Ecostatin; Gyno-Pevaryl; Pevaryl; ***USA:*** Spectazole; ***Venez.:*** Gyno-Pevaryl; Gynomiconax†; Miconax; Mizol†; Pevaryl.

Multi-ingredient: ***Arg.:*** Diflunazol†; Filoderma Plus; Griseocrem; Griseoplus; Novo Bacticort Complex†; ***Austria:*** Pevaryl; Pevisone; ***Belg.:*** Pevisone; ***Denm.:*** Pevisone; ***Fin.:*** Pevisone; ***Fr.:*** Pevisone; ***Ger.:*** Epi-Pevaryl Heilpaste†; Epipevisone; ***Gr.:*** Pevison; ***Hong Kong:*** Pevisone; Triconazole; ***India:*** Cobederm-H; Ecodax†; ***Israel:*** Pevisone; ***Ital.:*** Pevisone; ***Malaysia:*** Ecocort; Econazine; Pevisone†; ***Norw.:*** Pevisone; ***Philipp.:*** Nizolex; Pevaryl HP; Pevisone; ***Pol.:*** Pevisone; ***Port.:*** Pevisone; ***S.Afr.:*** Pevisone; ***Singapore:*** Ecocort; Econazine; Pevisone†; ***Swed.:*** Pevisone; ***Switz.:*** Pevaryl; Pevisone; ***Thai.:*** Ecocort; Ecoderm; Pevisone†; Tricozole; ***UK:*** Econacort.

Enilconazole *(BAN, USAN, rINN)*

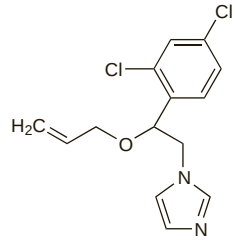
Enilconazol; Énilconazole; Enilconazolum; Enilkonatsoli; Enilkonazol; R-23979. (±)-1-(β-Allyloxy-2,4-dichlorophenethyl)imidazole.

Энилконазол

$C_{14}H_{14}Cl_2N_2O$ = 297.2.

CAS — 35554-44-0.

ATC Vet — QD01AC90.



Pharmacopoeias. In *Eur.* (see p.vii) for veterinary use only.
Ph. Eur. 6.2 (Enilconazole for Veterinary Use; Enilconazole BP(Vet) 2008). A clear, yellowish, oily liquid or solid mass. Very slightly soluble in water; freely soluble in alcohol, in methyl alcohol, and in toluene. Store in airtight containers. Protect from light.

Profile

Enilconazole is an imidazole antifungal used topically in veterinary medicine for the treatment of fungal skin infections in cattle, horses, and dogs. It is also used by inhalation for the treatment of aspergillosis in ostriches.

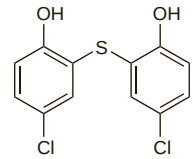
Fenticlor *(BAN, USAN, rINN)*

D-25; Fenticloro; Fenticlorum; HL-1050; NSC-4112; Ph-549; S-7. 2,2′-Thiobis(4-chlorophenol).

Фентиклор

$C_{12}H_8Cl_2O_2S$ = 287.2.

CAS — 97-24-5.



Profile

Fenticlor is an antifungal that has been applied topically in the treatment of dermatophyte infections.

Photosensitivity reactions have been reported.

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Spain:*** Dermisdin†.

Fenticonazole Nitrate *(BANM, USAN, rINNM)*

Fenticonazole, nitrate de; Fenticonazoli nitras; Fentikonatsolinitraatti; Fentikonazolnitrat; Fentikonazol-nitrát; Fentikonazolo nitratas; Nitrato de fenticonazol; Rec-15/1476. (±)-1-[2,4-Dichloro-β-{[p-(phenylthio)benzyl]oxy}phenethyl]imidazole mononitrate.

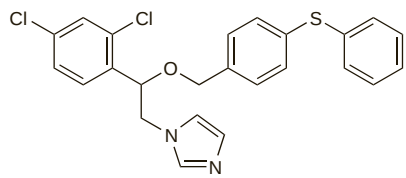
Фентиконазола Нитрат

$C_{24}H_{20}Cl_2N_2OS,HNO_3$ = 518.4.

CAS — 72479-26-6 (fenticonazole); 73151-29-8 (fenticonazole nitrate).

ATC — D01AC12; G01AF12.

ATC Vet — QD01AC12; QG01AF12.



(fenticonazole)

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Fenticonazole Nitrate). A white or almost white, crystalline powder. Practically insoluble in water; sparingly soluble in dehydrated alcohol; freely soluble in dimethylformamide and in methyl alcohol. Protect from light.

Adverse Effects and Precautions

Burning and itching have been reported after the application of fenticonazole nitrate.

Intravaginal preparations of fenticonazole 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

Fenticonazole is an imidazole antifungal active against a range of organisms including dermatophyte pathogens, *Malassezia furfur,* and *Candida albicans.*

Uses and Administration

Fenticonazole is an imidazole antifungal used locally as the nitrate in the treatment of vulvovaginal candidiasis (p.518). A 200-mg pessary is inserted into the vagina at bedtime for 3 nights or a 600-mg pessary is inserted once only at bedtime. Fenticonazole nitrate is also applied topically as a 2% cream or solution for the treatment of fungal skin infections.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Lomexin†; ***Austria:*** Lomexin; ***Braz.:*** Fentizol; Lomexin; ***Cz.:*** Lomexin; ***Fr.:*** Lomexin; Terlomexin; ***Ger.:*** Fenizolan; Lomexin; ***Gr.:*** Lomexin; ***Hung.:*** Gynoxin; ***Ital.:*** Falvin; Fentiderm†; Fentigyn†; Lomexin; ***Mex.:*** Lomexin; ***Neth.:*** Gynoxin; ***Pol.:*** Gynoxin; ***Port.:*** Lomexin; ***S.Afr.:*** Lomexin†; ***Singapore:*** Lomexin†; ***Spain:*** Laurimic; Lomexin; Micofulvin; ***Switz.:*** Mycodermil; ***Turk.:*** Gyno-Lomexin; ***UK:*** Lomexin†; ***Venez.:*** Mycofentin.

Fluconazole *(BAN, USAN, rINN)*

Fluconazol; Fluconazolum; Flukonatsoli; Flukonazol; UK-49858. 2-(2,4-Difluorophenyl)-1,3-bis(1*H*-1,2,4-triazol-1-yl)propan-2-ol.

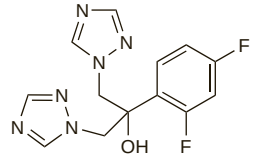
Флуконазол

$C_{13}H_{12}F_2N_6O$ = 306.3.

CAS — 86386-73-4.

ATC — D01AC15; J02AC01.

ATC Vet — QD01AC15; QJ02AC01.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *US.*

Ph. Eur. 6.2 (Fluconazole). A white or almost white, hygroscopic, crystalline powder. It exhibits polymorphism. Slightly soluble in water; freely soluble in methyl alcohol; soluble in acetone. Store in airtight containers.

USP 31 (Fluconazole). A white or almost white, crystalline powder. Slightly soluble in water; soluble in alcohol and in acetone; sparingly soluble in chloroform and in isopropyl alcohol; freely soluble in methyl alcohol; very slightly soluble in toluene. Store in airtight containers at a temperature below 30°.

Incompatibility and stability. References.

1. Lor E, *et al.* Visual compatibility of fluconazole with commonly used injectable drugs during simulated Y-site administration. *Am J Hosp Pharm* 1991; **48:** 744–6.
2. Couch P, *et al.* Stability of fluconazole and amino acids in parenteral nutrient solutions. *Am J Hosp Pharm* 1992; **49:** 1459–62.
3. Hunt-Fugate AK, *et al.* Stability of fluconazole in injectable solutions. *Am J Hosp Pharm* 1993; **50:** 1186–7.
4. Ishisaka DY. Visual compatibility of fluconazole with drugs given by continuous infusion. *Am J Hosp Pharm* 1994; **51:** 2290 and 2292.

Adverse Effects

Adverse effects reported with fluconazole most commonly affect the gastrointestinal tract and include abdominal pain, diarrhoea, flatulence, nausea and vomiting, and taste disturbance. Other adverse effects include headache, dizziness, leucopenia, thrombocytopenia, hyperlipidaemias, and raised liver enzyme values. Serious hepatotoxicity has been reported in patients with severe underlying disease such as AIDS or malignancy. Anaphylaxis and angioedema have been reported rarely.

Skin reactions are rare but exfoliative cutaneous reactions such as toxic epidermal necrolysis and Stevens-Johnson syndrome have occurred, more commonly in patients with AIDS.

Alopecia. Alopecia has occasionally been reported in patients receiving fluconazole, especially during prolonged use.[1,2]

1. Weinroth SE, Tuazon CU. Alopecia associated with fluconazole treatment. *Ann Intern Med* 1993; **119:** 637.
2. Pappas PG, *et al.* Alopecia associated with fluconazole therapy. *Ann Intern Med* 1995; **123:** 354–7.

Effect on electrolyte balance. Hypokalaemia was associated with fluconazole in 3 patients with acute myeloid leukaemia.[1]

1. Kidd D, *et al.* Hypokalaemia in patients with acute myeloid leukaemia after treatment with fluconazole. *Lancet* 1989; **i:** 1017.

Effects on the heart. Prolonged QT interval and torsade de pointes have been reported rarely in patients receiving fluconazole.[1-5]

1. Wassmann S, *et al.* Long QT syndrome and torsade de pointes in a patient receiving fluconazole. *Ann Intern Med* 1999; **131:** 797.
2. Tholakanahalli VN, *et al.* Fluconazole-induced torsade de pointes. *Ann Pharmacother* 2001; **35:** 432–4.
3. Khazan M, Mathis AS. Probable case of torsades de pointes induced by fluconazole. *Pharmacotherapy* 2002; **22:** 1632–7.
4. Pham CP, *et al.* Long QTc interval and torsade de pointes caused by fluconazole. *Ann Pharmacother* 2006; **40:** 1456–61.
5. McMahon JH, Grayson ML. Torsades de pointes in a patient receiving fluconazole for cerebral cryptococcosis. *Am J Health-Syst Pharm* 2008; **65:** 619–23.

Effects on the liver. Although severe hepatic reactions to fluconazole are rare they have been reported, especially in patients with severe underlying diseases or hepatic dysfunction.[1,2] Elevated liver enzymes are commonly found and there have been reports of jaundice.[3,4] Hepatic necrosis has been seen rarely post mortem in patients with severe underlying disease who had received fluconazole. In one such patient, hepatotoxicity was concluded to be dose-dependent.[5]

1. Wells C, Lever AML. Dose-dependent fluconazole hepatotoxicity proven on biopsy and rechallenge. *J Infect* 1992; **24:** 111–12.
2. Jacobson MA, *et al.* Fatal acute hepatic necrosis due to fluconazole. *Am J Med* 1994; **96:** 188–90.
3. Holmes J, Clements D. Jaundice in HIV positive haemophiliac. *Lancet* 1989; **i:** 1027.
4. Franklin IM, *et al.* Fluconazole-induced jaundice. *Lancet* 1990; **336:** 565.
5. Bronstein J-A, *et al.* Fatal acute hepatic necrosis due to dose-dependent fluconazole hepatotoxicity. *Clin Infect Dis* 1997; **25:** 1266–7.

Hypersensitivity. Desensitisation has been successfully carried out in a patient with AIDS who exhibited hypersensitivity to both fluconazole and itraconazole.[1] Gradually increasing oral doses of fluconazole (starting at 5 mg daily) were given over 7 days; thereafter dosage was maintained at 400 mg daily. No adverse reactions were noted during the desensitisation period or in the 3 months up to the publication of the report.

1. Takahashi T, *et al.* Desensitization to fluconazole in an AIDS patient. *Ann Pharmacother* 2001; **35:** 642–3.

Precautions

Fluconazole should be used with caution in patients with impaired hepatic or renal function. Abnormalities in haematological, hepatic, and renal-function tests have been observed in patients with serious underlying diseases such as AIDS or malignancy. Cases of torsade de pointes and QT prolongation have been reported rarely and caution is advised when giving fluconazole to patients with proarrhythmic conditions.

Teratogenicity has occurred in *animals* given high doses of fluconazole and its use is not recommended in pregnancy (see under Pregnancy, below).

Breast feeding. Fluconazole is distributed into breast milk, achieving concentrations similar to those found in maternal plasma,[1] and its use in women who are breast feeding is not recommended by licensed product information.

In one report,[2] no untoward effects, other than a slight increase in lactase dehydrogenase level, were seen in an infant who was exposed to fluconazole in breast milk for 6 weeks.

The American Academy of Pediatrics considers that the use of fluconazole is usually compatible with breast feeding.[3]

1. Force RW. Fluconazole concentrations in breast milk. *Pediatr Infect Dis J* 1995; **14:** 235–6.
2. Bodley V, Powers D. Long-term treatment of a breastfeeding mother with fluconazole-resolved nipple pain caused by yeast: a case study. *J Hum Lact* 1997; **13:** 307–11.
3. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 21/06/05)

Pregnancy. High (toxic) doses of *fluconazole*, *itraconazole*, and *ketoconazole* have been reported to be teratogenic in *rodents.* Although there is little information about the use of these drugs in human pregnancy, there is a report of a woman who took fluconazole 400 mg daily throughout pregnancy and who gave birth to an infant with severe craniofacial and limb abnormalities.[1] The abnormalities resembled those associated with the Antley-Bixler syndrome, a genetic disorder, but a teratogenic effect could not be excluded. Although prescription-event-monitoring studies of fluconazole did not reveal adverse effects on the fetus,[2-4] congenital abnormalities have occurred in infants whose mothers were given high doses of fluconazole for 3 months or more. Data collected by the manufacturer,[5] relating to 198 women exposed to itraconazole during the first trimester of pregnancy, indicated that the malformation rate for both exposed women and matched controls was within the expected baseline risk for the general population. Nevertheless, the manufacturers recommend that fluconazole, itraconazole, and ketoconazole should be avoided during pregnancy.

Licensed product information states that doses of *voriconazole* equivalent to those used therapeutically have been shown to be teratogenic and embryotoxic in *rodents*. It therefore recommends that voriconazole should be avoided during pregnancy and that women of child bearing potential should use effective contraception during treatment. Similar recommendations have been made for *posaconazole*.

Other azole antifungals including butoconazole, clotrimazole, econazole, miconazole, sulconazole, terconazole, and tioconazole are reported to be embryotoxic but not teratogenic in *rodents* given high doses. Many of these drugs are used topically or intravaginally and the systemic absorption from these routes of administration varies. While these drugs may not necessarily be contra-indicated in pregnancy, consideration should be given to these potential risks when choosing antifungal therapy for such patients.

1. Lee BE, *et al.* Congenital malformations in an infant born to a woman treated with fluconazole. *Pediatr Infect Dis J* 1992; **11:** 1062–4.
2. Rubin PC, *et al.* Fluconazole and pregnancy: results of a prescription event-monitoring study. *Int J Gynecol Obstet* 1992; **37** (suppl): 25–7.
3. Inman W, *et al.* Safety of fluconazole in the treatment of vaginal candidiasis: a prescription-event monitoring study, with special reference to the outcome of pregnancy. *Eur J Clin Pharmacol* 1994; **46:** 115–18.
4. Sørensen HT, *et al.* Risk of malformations and other outcomes in children exposed to fluconazole in utero. *Br J Clin Pharmacol* 1999; **48:** 234–8.
5. Bar-Oz B, *et al.* Pregnancy outcome after in utero exposure to itraconazole: a prospective cohort study. *Am J Obstet Gynecol* 2000; **183:** 617–20.

Renal impairment. For dose adjustments in renal impairment, see Administration in Renal Impairment, under Uses and Administration, below.

Interactions

In general, fewer interactions are considered to occur with fluconazole than with either itraconazole or ketoconazole.

Use of rifampicin with fluconazole results in reduced plasma concentrations of fluconazole. Use of hydrochlorothiazide and fluconazole has resulted in clinically insignificant increases in plasma-fluconazole concentrations.

Fluconazole may interfere with the metabolism of some other drugs, mainly through inhibition of the cytochrome P450 isoenzymes CYP3A4 and CYP2C9. This may account for the reported increases in plasma concentrations of bosentan, ciclosporin, midazolam, nevirapine, amitriptyline, nortriptyline, phenytoin, rifabutin, sulfonylurea hypoglycaemics and nateglinide, selective cyclo-oxygenase-2-inhibitors such as celecoxib and parecoxib, tacrolimus, triazolam, warfarin, and zidovudine; fluconazole may inhibit the formation of a toxic metabolite of sulfamethoxazole.

Increases in terfenadine concentrations following high doses of fluconazole have been associated with ECG abnormalities. A similar effect may be anticipated with astemizole. Use of fluconazole with cisapride could result in increased cisapride concentrations and associated toxicity. The use of fluconazole with astemizole, cisapride, or terfenadine should therefore be avoided because of the risk of cardiac arrhythmias. Syncope attributed to increased amitriptyline concentrations has occurred when amitriptyline was given with fluconazole.

Fluconazole may also reduce the clearance of theophylline. The concentration of contraceptive steroids has been reported to be both increased and decreased in patients receiving fluconazole and the efficacy of oral contraceptives may be affected.

For further information on interactions between drugs metabolised by the cytochrome P450 isoenzyme CYP3A and azoles, see under Itraconazole, p.537.

Antineoplastics. For the effect of azole antifungals on *cyclophosphamide* metabolism, see p.703.

Fluoroquinolones. Both *levofloxacin* and fluconazole can cause a prolonged QT interval. The simultaneous use of intravenous levofloxacin and fluconazole resulted in an episode of torsade de pointes in a patient on haemodialysis.[1]

1. Gandhi PJ, *et al.* Fluconazole- and levofloxacin-induced torsades de pointes in an intensive care unit patient. *Am J Health-Syst Pharm* 2003; **60:** 2479–83.

Nitrofurans. For a report of pulmonary and hepatic toxicity due to a possible interaction between *nitrofurantoin* and fluconazole, see p.308.

Antimicrobial Action

Fluconazole is a triazole antifungal drug which in sensitive fungi inhibits cytochrome P450-dependent enzymes, resulting in impairment of ergosterol synthesis in fungal cell membranes. It is active against *Blastomyces dermatitidis*, *Candida* spp., *Coccidioides immitis*, *Cryptococcus neoformans*, *Epidermophyton* spp., *Histoplasma capsulatum*, *Microsporum* spp., and *Trichophyton* spp.

Resistance has developed in some *Candida* spp. following long-term prophylaxis with fluconazole, and cross-resistance with other azoles has been reported.

Microbiological interactions. A synergistic antifungal effect was seen *in vitro* with terbinafine and fluconazole against strains