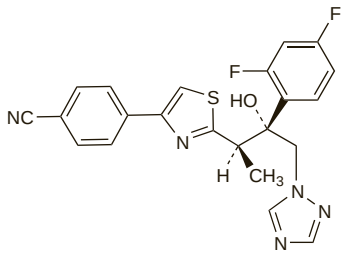
Ravuconazole *(pINN)*

BMS-207147; ER-30346; Ravuconazol; Ravuconazolum. 4-{2-[(1*R*,2*R*)-2-(2,4-Difluorophenyl)-2-hydroxy-1-methyl-3-(1*H*-1,2,4-triazol-1-yl)propyl]-4-thiazolyl}-benzonitrile.

Равуконазол

$C_{22}H_{17}F_2N_5OS$ = 437.5.

CAS — 182760-06-1.



Profile
Ravuconazole is a triazole antifungal said to possess a broader spectrum of activity than fluconazole or itraconazole. It is under investigation for the treatment of systemic fungal infections.

Sertaconazole Nitrate *(BANM, rINNM)*

Nitrato de sertaconazol; Sertaconazole, nitrate de; Sertaconazoli nitras; Sertakonatsolinitraatti; Sertakonazol Nitrat; Sertakonazol-nitrat; Sertakonazol-nitrát; Sertakonazolo nitratas; Szertakonazol-nitrát. (±)-1-{2,4-Dichloro-β-[(7-chlorobenzo[*b*]thien-3-yl)-methoxy]phenethyl}imidazole nitrate.

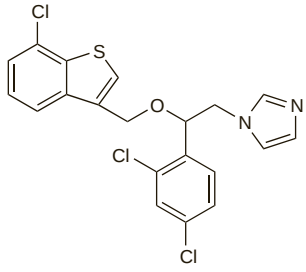
Сертаконазола Нитрат

$C_{20}H_{15}Cl_3N_2OS,HNO_3$ = 500.8.

CAS — 99592-32-2 (sertaconazole); 99592-39-9 (sertaconazole nitrate).

ATC — D01AC14.

ATC Vet — QD01AC14.



(sertaconazole)

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Sertaconazole Nitrate). A white or almost white powder. Practically insoluble in water; sparingly soluble in alcohol and in dichloromethane; soluble in methyl alcohol. Protect from light.

Profile
Sertaconazole is an imidazole antifungal used topically as the nitrate as a 2% cream, gel, solution, or powder in the treatment of superficial candidiasis, dermatophytosis, seborrhoeic dermatitis, and pityriasis versicolor. In the treatment of vaginal candidiasis it is used as a 2% vaginal cream daily for 7 or 8 days or as a single dose of a 300-mg or 500-mg pessary.

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

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Zalain†; ***Austria:*** Zalain†; ***Braz.:*** Gyno Zalain; Zalain; ***Chile:*** Tromderm; Zalain; ***Cz.:*** Zalain†; ***Ger.:*** Mykosert; Zalain; ***Gr.:*** Fuganol†; ***Hong Kong:*** Zalain; ***Hung.:*** Zalain; ***Indon.:*** Dermofix; ***Ital.:*** Sertacream; Sertaderm; Sertadie; Sertagyn; Zalain†; ***Malaysia:*** Zalain†; ***Philipp.:*** Zalain; ***Port.:*** Dermofix; Sertopic; ***Rus.:*** Zalain (Залаин); ***Singapore:*** Zalain; ***Spain:*** Dermofix; Dermoseptic; Gine Zalain; Ginedermofix; Zalain; ***Thai.:*** Zalain; ***Turk.:*** Zalain; ***USA:*** Ertaczo; ***Venez.:*** Zalain.

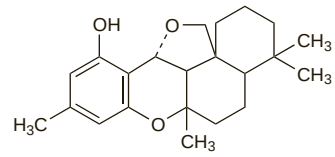
Siccanin *(rINN)*

Sicanina; Siccanine; Siccaninum. (13a*S*)-1,2,3,4,4a*β*,-5,6,6a,11b*β*,13b*β*-Decahydro-4-4-6a*β*9-tetramethyl-13*H*-benzo[*a*]furo[2,3,4-*mn*]xanthen-11-ol.

Сикканин

$C_{22}H_{30}O_3$ = 342.5.

CAS — 22733-60-4.



Pharmacopoeias. In *Jpn.*

Profile
Siccanin is obtained from *Helminthosporium siccans*, a parasitic organism of rye grass It has antifungal activity and is used topically as a 1% ointment for dermatophyte infections.

Sodium Parachlorobenzoate

Sodium *p*-Chlorobenzoate.

Натрий Парахлорбензоат

$C_7H_4ClNaO_2$ = 178.5.

CAS — 3686-66-6.

Profile
Sodium parachlorobenzoate has antifungal activity and is used as a 4% powder in the treatment of fungal skin infections (p.521).

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Hung.:*** Mycosid.

Sulconazole Nitrate *(BANM, USAN, rINNM)*

Nitrato de sulconazol; RS-44872; RS-44872-00-10-3; Sulconazole, Nitrate de; Sulconazoli Nitras; Sulkonazol Nitrat. 1-[2,4-Dichloro-β-(4-chlorobenzyl)thiophenethyl]imidazole nitrate.

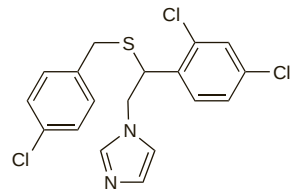
Сульконазола Нитрат

$C_{18}H_{15}Cl_3N_2S,HNO_3$ = 460.8.

CAS — 61318-90-9 (sulconazole); 61318-91-0 (sulconazole nitrate).

ATC — D01AC09.

ATC Vet — QD01AC09.



(sulconazole)

Pharmacopoeias. In *Fr.* and *US.*
USP 31 (Sulconazole Nitrate). A white to off-white crystalline powder. Soluble 1 in 3333 of water, 1 in 100 of alcohol, 1 in 130 of acetone, 1 in 333 of chloroform, 1 in 286 of dichloromethane, 1 in 2000 of dioxan, 1 in 71 of methyl alcohol, 1 in 10 of pyridine, and 1 in 2000 of toluene. Protect from light.

Adverse Effects and Precautions
Local reactions including blistering, burning, itching, and erythema have been reported after sulconazole use.

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

Antimicrobial Action
Sulconazole is an imidazole antifungal with activity against dermatophytes, *Candida* spp., and *Malassezia furfur.*

Uses and Administration
Sulconazole is an imidazole antifungal used topically as the nitrate once or twice daily as a 1% cream or solution in the treatment of fungal skin infections including dermatophyte infections and pityriasis versicolor (p.521), and candidiasis (p.518).

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Antifungal; Minot†; ***Belg.:*** Myk-1; ***Fr.:*** Myk; ***Irl.:*** Exelderm†; ***Neth.:*** Myk-1; ***Turk.:*** Exelderm; ***UK:*** Exelderm; ***USA:*** Exelderm.

Terbinafine *(BAN, USAN, rINN)*

SF-86-327; SF-86327; Terbinafiini; Terbinafin; Terbinafina; Terbinafinum. (*E*)-6,6-Dimethylhept-2-en-4-ynl(methyl)-(1-naphthylmethyl)amine.

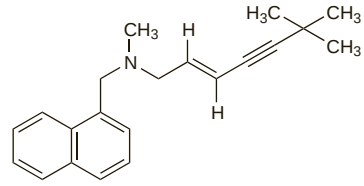
Тербинафин

$C_{21}H_{25}N$ = 291.4.

CAS — 91161-71-6.

ATC — D01AE15; D01BA02.

ATC Vet — QD01AE15; QD01BA02.



Terbinafine Hydrochloride *(BANM, rINNM)*

Hidrocloruro de terbinafina; Terbinafiinihydrokloridi; Terbinafin Hidroklorür; Terbinafine, chlorhydrate de; Terbinafin-hydrochlorid; Terbinafinhydroklorid; Terbinafini hydrochloridum; Terbinafiny chlorowodorek.

Тербинафина Гидрохлорид

$C_{21}H_{26}ClN$ = 327.9.

CAS — 78628-80-5.

ATC — D01AE15; D01BA02.

ATC Vet — QD01AE15; QD01BA02.

Pharmacopoeias. In *Eur.* (see p.vii) and *US.*
Ph. Eur. 6.2 (Terbinafine Hydrochloride). A white or almost white powder. Very slightly or slightly soluble in water; freely soluble in dehydrated alcohol and in methyl alcohol; slightly soluble in acetone. Protect from light.
USP 31 (Terbinafine Hydrochloride). A white or off-white powder. Very slightly or slightly soluble in water; freely soluble in dehydrated alcohol and in methyl alcohol; slightly soluble in acetone; Protect from light.

Adverse Effects
The most frequent adverse effects after oral use of terbinafine hydrochloride are gastrointestinal disturbances such as nausea, diarrhoea, and mild abdominal pain. Loss or disturbance of taste may occur and occasionally may be severe enough to lead to anorexia and weight loss. Other frequent adverse effects include headache and skin reactions, including rash or urticaria, sometimes with arthralgia or myalgia. Severe skin reactions including angioedema, photosensitivity, Stevens-Johnson syndrome, and toxic epidermal necrolysis have occurred rarely. Liver dysfunction with isolated reports of cholestasis, hepatitis, and jaundice, has occurred and there have also been rare cases of hepatic failure, sometimes leading to death or needing liver transplantation, in patients both with and without pre-existing liver disease. Other rare adverse effects include paraesthesia, hypoaesthesia, dizziness, malaise, fatigue, and alopecia. Haematological disorders including neutropenia, thrombocytopenia, and agranulocytosis, psychiatric disturbances such as depression and anxiety, and precipitation or exacerbation of cutaneous and systemic lupus erythematosus have been reported very rarely.

There may be local reactions after topical use of terbinafine.

Incidence of adverse effects. Postmarketing surveillance of about 10 000 patients[1] suggested the following incidences of adverse effects to oral terbinafine: gastrointestinal symptoms, 4.7%; dermatological effects, 3.3%; CNS symptoms (commonly headache), 1.8%; taste disturbances, 0.6%; and transient disturbances in liver function, 0.1%. Serious adverse effects possibly or probably related to terbinafine included angioedema, bronchospasm, erythema multiforme, extended stroke, and unilateral leg oedema. Combined data from 25 884 patients from this and 3 further studies[2] generally confirmed these results. Overall, adverse effects were reported in 10.5% of patients and caused treatment to be stopped in 5.3%. Serious adverse effects probably or possibly related to terbinafine occurred in 12 patients (0.046%).

1. O'Sullivan DP, *et al.* Postmarketing surveillance of oral terbinafine in the UK: report of a large cohort study. *Br J Clin Pharmacol* 1996; **42:** 559–65.
2. O'Sullivan DP. Terbinafine: tolerability in general medical practice. *Br J Dermatol* 1999; **141** (suppl 56): 21–5.

Effects on the blood. Up to August 2006, the Australian Adverse Drug Reactions Advisory Committee had received 16 reports of blood dyscrasias attributed to oral terbinafine including agranulocytosis (7 reports), neutropenia (7), and pancytopenia (2).[1] The reactions generally occurred within 4 to 6 weeks of starting therapy. Eleven patients recovered, 4 within one week of stopping treatment. However, a 79-year-old patient who developed agranulocytosis about 2 months after starting terbinafine died from septic shock.

1. Adverse Drug Reactions Advisory Committee (ADRAC). Life threatening blood dyscrasias with oral terbinafine. *Aust Adverse Drug React Bull* 2006; **25:** 15. Also available at: http://www.tga.gov.au/adr/aadrb/aadr0608.htm (accessed 02/05/08)

Effects on the eyes. The US manufacturer has noted that changes in the lens and retina of the eye have sometimes been associated with oral terbinafine, although the significance of these changes is not known.

Effects on the salivary glands. Bilateral parotid swelling was associated with terbinafine in a 38-year-old man.[1] Information from the manufacturer and the UK CSM indicated that this effect had occurred in other patients but was very rare. More recently, severe sialadenitis as a complication of drug reaction with eosinophilia and systemic complications (DRESS—a type of hypersensitivity reaction) was reported in an 80-year-old woman treated with terbinafine.[2] She also had severe xerostomia, lachrymal gland swelling, dry eyes, and keratitis.

1. Torrens JK, McWhinney PH. Parotid swelling and terbinafine. *BMJ* 1998; **316:** 440–1.
2. Abecassis S, *et al.* Severe sialadenitis: a new complication of drug reaction with eosinophilia and systemic symptoms. *J Am Acad Dermatol* 2004; **51:** 827–30.

Effects on the skin. Serious skin reactions are occasionally reported in patients receiving terbinafine and have included erythema multiforme,[1,2] erythroderma,[1] severe urticaria,[1] pityriasis rosea,[1] worsening of pre-existing psoriasis,[1,3] acrodermatitis continua of Hallopeau,[4] bullous pemphigoid,[5] acute generalised exanthematous pustulosis,[6] and lupus erythematosus.[7-10] Several of these patients had a history of auto-immune disease[2,9] and it has been suggested that this could be a risk factor for developing severe reactions.[2]

1. Gupta AK, *et al.* Cutaneous adverse effects associated with terbinafine therapy: 10 case reports and a review of the literature. *Br J Dermatol* 1998; **138:** 529–32.
2. Goeteyn V, *et al.* Is systemic autoimmune disease a risk factor for terbinafine-induced erythema multiforme? *Br J Dermatol* 2000; **142:** 578–9.
3. Wilson NJE, Evans S. Severe pustular psoriasis provoked by oral terbinafine. *Br J Dermatol* 1998; **139:** 168.
4. Nishiwaki F, *et al.* Acrodermatitis continua of Hallopeau due to oral terbinafine. *Br J Dermatol* 2007; **157:** 1073–4.
5. Aksakal BA, *et al.* Oral terbinafine-induced bullous pemphigoid. *Ann Pharmacother* 2003; **37:** 1625–7.
6. Beltraminelli HS, *et al.* Acute generalized exanthematous pustulosis induced by the antifungal terbinafine: case report and review of the literature. *Br J Dermatol* 2005; **152:** 780–3.
7. Murphy M, Barnes L. Terbinafine-induced lupus erythematosus. *Br J Dermatol* 1998; **138:** 708–9.
8. Brooke R, *et al.* Terbinafine-induced subacute cutaneous lupus erythematosus. *Br J Dermatol* 1998; **139:** 1132–3.
9. Holmes S, Kemmett D. Exacerbation of systemic lupus erythematosus induced by terbinafine. *Br J Dermatol* 1998; **139:** 1133.
10. Hill VA, *et al.* Subacute lupus erythematosus-like eruption due to terbinafine: report of three cases. *Br J Dermatol* 2003; **148:** 1056.

Effects on taste. Disturbance and loss of taste have been reported in about 0.6% of patients taking terbinafine. While this usually resolves gradually once the drug is withdrawn, persistent impairment of taste has been reported.[1,2]

1. Bong JL, *et al.* Persistent impairment of taste resulting from terbinafine. *Br J Dermatol* 1998; **139:** 747–8.
2. Duxbury AJ, *et al.* Persistent impairment of taste associated with terbinafine. *Br Dent J* 2000; **188:** 295–6.

Precautions

Terbinafine should not be used in patients with existing liver disease and liver function tests should be performed in all patients before starting oral therapy. Terbinafine should be stopped if clinical or biochemical evidence of hepatotoxicity develops. It should also be stopped if any progressive skin rash occurs and should be used with caution in patients with psoriasis.

Terbinafine should be given in reduced doses to patients with renal impairment (see Administration in Renal Impairment, under Uses and Administration, below).

Breast feeding. Terbinafine is excreted in breast milk and licensed product information states that it should be avoided during breast feeding.

Interactions

Plasma concentrations of terbinafine may be increased by drugs that inhibit its metabolism by cytochrome P450, such as cimetidine, and decreased by drugs that induce cytochrome P450 enzymes, such as rifampicin. Menstrual disturbances including breakthrough bleeding have been reported in patients taking oral contraceptives and terbinafine.

Terbinafine has been shown *in vitro* to inhibit metabolism mediated by the cytochrome P450 isoenzyme CYP2D6. Hence it may affect the plasma concentrations of drugs predominantly metabolised by this enzyme such as tricyclic antidepressants, beta blockers, SSRIs, and type B MAOIs.

For the effects of terbinafine on some other drugs, see carbamazepine (p.475), ciclosporin (p.1826), nortriptyline (p.380), and warfarin (p.1429).

Antimicrobial Action

Terbinafine is an allylamine derivative reported to have a broad spectrum of antifungal activity. It is considered to act through inhibition of fungal sterol synthesis. Terbinafine is fungicidal against dermatophytes, moulds, and certain dimorphic fungi and some yeasts.

Microbiological interactions. Additive and synergistic activity was reported with terbinafine plus fluconazole or itraconazole against strains of *Candida albicans* that had reduced susceptibility to azoles *in vitro*.[1] Terbinafine was also reported to enhance the activity of azoles against *Scedosporium prolificans*[2] and against the protozoan *Leishmania braziliensis*.[3]

1. Barchiesi F, *et al.* In vitro activities of terbinafine in combination with fluconazole and itraconazole against isolates of Candida albicans with reduced susceptibility to azoles. *Antimicrob Agents Chemother* 1997; **41:** 1812–14.
2. Meletiadis J, *et al.* In vitro interaction of terbinafine with itraconazole against clinical isolates of Scedosporium prolificans. *Antimicrob Agents Chemother* 2000; **44:** 470–2.
3. Rangel H, *et al.* Naturally azole-resistant Leishmania braziliensis promastigotes are rendered susceptible in the presence of terbinafine: comparative study with azole-susceptible Leishmania mexicana promastigotes. *Antimicrob Agents Chemother* 1996; **40:** 2785–91. Correction. *ibid*. 1997; **41:** 496.

Pharmacokinetics

Terbinafine hydrochloride is well absorbed from the gastrointestinal tract. The bioavailability is about 40% because of first-pass hepatic metabolism. Mean peak plasma concentrations of about 1 microgram/mL occur within 2 hours of a single oral dose of 250 mg. Steady state concentrations are about 25% higher than those seen after a single dose and are reached in 10 to 14 days. Terbinafine is extensively bound to plasma proteins. Terbinafine is distributed into the stratum corneum of the skin, the nail plate, and hair where it reaches concentrations considerably higher than those found in plasma. It appears in breast milk.

Terbinafine is metabolised in the liver to inactive metabolites which are excreted mainly in the urine. A plasma elimination half-life varying from 17 to 36 hours has been reported and a terminal elimination half-life of up to 400 hours in patients given prolonged therapy, probably representing elimination from skin and adipose tissue. Fungicidal concentrations in nails are maintained for several weeks after therapy is stopped. The elimination rate may be altered in patients with liver or kidney disease. Less than 5% of a topical dose of terbinafine hydrochloride is absorbed.

◊ References.

1. Kovarik JM, *et al.* Multiple-dose pharmacokinetics and distribution in tissue of terbinafine and metabolites. *Antimicrob Agents Chemother* 1995; **39:** 2738–41.

Uses and Administration

Terbinafine is an allylamine antifungal given by mouth as the hydrochloride in the treatment of dermatophyte infections of the skin and nails (p.521). Oral doses are stated in terms of the base. Terbinafine hydrochloride 1.13 g is equivalent to about 1 g of terbinafine. It is also applied, as the hydrochloride, to the skin in dermatophytoses, in pityriasis versicolor (see Skin Infections, p.521), and in cutaneous candidiasis (p.518).

An oral dose of 250 mg is given once daily for 2 to 4 weeks for tinea cruris; treatment may be continued for up to 6 weeks for tinea pedis infections; a 4-week course is used in tinea corporis infections. A cream, gel, or solution containing 1% terbinafine hydrochloride is applied once or twice daily for 1 to 2 weeks to treat tinea corporis and tinea cruris; a 1-week course is recommended for tinea pedis. A 2-week course of treatment is used in cutaneous candidiasis and pityriasis versicolor.

Dermatophyte infections of the nails are treated with the equivalent of terbinafine 250 mg orally once daily for 6 to 12 weeks although longer treatment may be necessary in toe-nail infections.

Dosage should be reduced in patients with renal impairment (see below).

◊ References.

1. Balfour JA, Faulds D. Terbinafine: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential in superficial mycoses. *Drugs* 1992; **43:** 259–84.
2. Abdel-Rahman SM, Nahata MC. Oral terbinafine: a new antifungal agent. *Ann Pharmacother* 1997; **31:** 445–56.
3. McClellan KJ, *et al.* Terbinafine: an update of its use in superficial mycoses. *Drugs* 1999; **58:** 179–202.
4. Darkes MJ, *et al.* Terbinafine: a review of its use in onychomycosis in adults. *Am J Clin Dermatol* 2003; **4:** 39–65.
5. 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.
6. Gupta AK, *et al.* The use of terbinafine in the treatment of onychomycosis in adults and special populations: a review of the evidence. *J Drugs Dermatol* 2005; **4:** 302–8.
7. Revankar SG, *et al.* Use of terbinafine in rare and refractory mycoses. *Future Microbiol* 2008; **3:** 9–17.

Administration in children. Although terbinafine is not currently licensed in the UK for use in children, the *BNFC* suggests the following oral doses for the treatment of tinea capitis in children over 1 year of age:

- in those weighing 10 to 20 kg: the equivalent of terbinafine 62.5 mg once daily
- in those weighing 20 to 40 kg: 125 mg once daily
- in those weighing over 40 kg: 250 mg once daily Treatment is usually given for 4 weeks for tinea capitis, 2 to 4 weeks for tinea cruris, 4 weeks for tinea corporis, and may be continued for up to 6 weeks in tinea pedis. Infections of the nails are treated for 6 weeks to 3 months, although longer treatment may occasionally be required for toe-nail infections.

Similar regimens have been reported in the literature.[1,2] A review on the use of terbinafine in children considered it both safe and effective in the management of tinea capitis and onychomycosis.[3]

1. Jones TC. Overview of the use of terbinafine (Lamisil) in children. *Br J Dermatol* 1995; **132:** 683–9.
2. Fuller LC, *et al.* A randomized comparison of 4 weeks of terbinafine vs 8 weeks of griseofulvin for the treatment of tinea capitis. *Br J Dermatol* 2001; **144:** 321–7.
3. Gupta AK, *et al.* The efficacy and safety of terbinafine in children. *J Eur Acad Dermatol Venereol* 2003; **17:** 627–40.

Administration in renal impairment. The UK licensed product information recommends that in patients with renal impairment (creatinine clearance less than 50 mL/minute or serum creatinine greater than 300 micromol/litre) usual oral doses should be halved to the equivalent of 125 mg of terbinafine daily.

Leishmaniasis. An inadvertent beneficial response has been reported[1] in an HIV-positive patient with cutaneous leishmaniasis (p.824) who was taking terbinafine 250 mg daily for tinea corporis and onychomycosis. Beneficial results were also reported in a pilot study[2] in which patients with cutaneous leishmaniasis took either terbinafine 125 mg twice daily (those aged 5 to 15 years), or terbinafine 250 mg twice daily (those over 15 years), for 4 weeks.

1. González-Rupérez J, *et al.* Remission of localized cutaneous leishmaniasis in a HIV-positive patient using systemic terbinafine. *Dermatology* 1997; **194:** 85–6.
2. Bahamdan KA, *et al.* Terbinafine in the treatment of cutaneous leishmaniasis: a pilot study. *Int J Dermatol* 1997; **36**: 59–60.

Non-dermatophyte fungal infections. Beneficial responses to oral terbinafine have been reported in candidal infections of the nails and mouth,[1-3] aspergillosis, chromoblastomycosis, paracoccidioidomycosis, and sporotrichosis.[3]

1. Nolting S, *et al.* Terbinafine in onychomycosis with involvement by non-dermatophytic fungi. *Br J Dermatol* 1994; **130** (suppl 43): 16–21.
2. Segal R, *et al.* Treatment of Candida nail infection with terbinafine. *J Am Acad Dermatol* 1996; **35:** 958–61.
3. Pérez A. Terbinafine: broad new spectrum of indications in several subcutaneous and systemic and parasitic diseases. *Mycoses* 1999; **42** (suppl 2): 111–4.

Seborrhoeic dermatitis. Terbinafine has been tried in the treatment of seborrhoeic dermatitis (p.1584). In one study, 60 patients were randomised to receive oral terbinafine 250 mg daily or a placebo cream applied twice daily for 4 weeks.[1] Clinical improvement, maintained 8 weeks after completing treatment, in the terbinafine group led the investigators to conclude that oral terbinafine is an effective treatment for seborrhoeic dermatitis, and to suggest that this might be due to its activity against *Malassezia ovalis* (*Pityrosporum ovale*) as well as to some anti-inflammatory action. However, the methodology of this study has been questioned[2] and further investigation is needed. A further, uncontrolled, study[3] of 661 patients who received oral terbinafine 250 mg daily for 12 days each month for 3 months concluded

that intermittent oral terbinafine could be effective for seborrhoeic dermatitis, at least in severe or recalcitrant forms. It has also been tried topically as a 1% cream.[4]

1. Scaparro E, *et al*. Evaluation of the efficacy and tolerability of oral terbinafine (Daskil) in patients with seborrhoeic dermatitis: a multicentre, randomized, investigator-blinded, placebo-controlled trial. *Br J Dermatol* 2001; **144:** 854–7.
2. Faergemann J. Treatment of seborrhoeic dermatitis with oral terbinafine? *Lancet* 2001; **358:** 170.
3. Cassano N, *et al*. Oral terbinafine for the treatment of seborrheic dermatitis in adults. *Int J Dermatol* 2002; **41:** 821–2.
4. Gündüz K, *et al*. Efficacy of terbinafine 1% cream on seborrhoeic dermatitis. *J Dermatol* 2005; **32:** 22–5.

Preparations

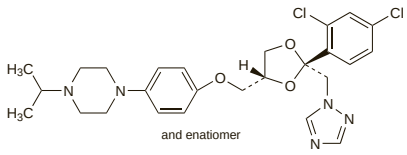
Proprietary Preparations (details are given in Part 3)
Arg.: Fungueal; Lamisil; Maditez; Piecidex NF; Tacna; Terbi-Derm; Terekol; Terfin; ***Austral.:*** Lamisil; SolvEasy; Tamsil; Zabel; ***Austria:*** Daskil; Lamisil; ***Belg.:*** Lamisil; ***Braz.:*** Binafin†; Finex†; Funtyl; Lamisil; Micosil; ***Canad.:*** Lamisil; ***Chile:*** Dermoxyl; Dicil; Elater; Finex; Lamisil; Micoset; Micostop†; Terfex; ***Cz.:*** Atifan; Brinaf†; Lamisil; Mycodekan; Onychon; Tefine; Terbihexal; Terbisil; Terbistad; Terfimed; Verbinaf; ***Denm.:*** Lamisil; ***Fin.:*** Lamisil; ***Fr.:*** Lamisil; Lamisilate; LamisilDermgel; ***Ger.:*** Amiada; Dermatin; Lamisil; Myconormin; Onymax; Terbiderm; Terbigalen; ***Gr.:*** Anaplas; Chemiderm; Demsil; Drogenil; Ealk; Flixid; Frezylin; Fungitherapy; Lamigen; Lamisil; Mycutol; Optimus; Pavlinox; Pro-Misil; Romiver; Seralon; Soluteb; Terbafin; Terbigram; Terbin; Terbiprol; Terbiskin; Terbisol; Terfinil; Terfinor; Termisil; Thateron; Vifaderm; ***Hong Kong:*** Lamisil; Terbifin; ***Hung.:*** Lamisil; Terbigen; Terbisil; Terfin; Tineal; ***India:*** Exifine; Lamisil†; Terbifin; ***Indon.:*** Interbi; Lamisil; Termisil; ***Irl.:*** Fungafine; Fungasil; Lamisil; Lanafine; Nailderm; Ternaf; ***Israel:*** Lamisil; ***Ital.:*** Daskil; Lamisil; ***Malaysia:*** Dermafin; Exifine; Lamisil; Lisim; ***Mex.:*** Binafex; Erbitrax; Fyterdin; Lamisil; Losil-T; Mycelvan; Unasal; Xilatril; ***Neth.:*** Binanidda; Finanidda; Finavita†; Fungitif; Lamisil; Niddafin; Niddavita; Terbiderm; Terbinavita; Terfungin; Tiebinafin; Vitabin; ***Norw.:*** Lamisil; ***NZ:*** Lamisil†; Terbafin; ***Philpp.:*** Lamifen; Lamisil; ***Pol.:*** Afugin; Lamisil; Lamisilatt; Myconafine; Onymax; Tenasil; Terbiderm; TerbiGen; Terbisil; ***Port.:*** Daskyl; Lamisil; ***Rus.:*** Binafin (Бинафин); Exifine (Экзифин); Fungoterbine (Фунготербин); Lamican (Ламикан); Lamisil (Ламизил); Medofloran (Медофлоран); Terbinox (Тербинокс); Terbisil (Тербизил); Termicon (Термикон); ***S.Afr.:*** Dermax; Lamisil; Terbicil; ***Singapore:*** Lamisil; ***Spain:*** Lamicosil; Lamisil; ***Swed.:*** Lamisil; ***Switz.:*** Lamisil; Myconormin; Onymax; Terbifil; Tineafine; ***Thai.:*** EU 2000; Lamisil; ***Turk.:*** Lamisil; Mycocur; Terafin; Terbin; Terbisil; Tigal; ***UK:*** Lamisil; ***USA:*** DesenexMax; Lamisil; ***Venez.:*** Exifine†; Funtopic†; Lamisil; Nafina; Terfex.

Terconazole *(BAN, USAN, rINN)*

R-42470; Terconazol; Terconazolum; Terkonatsoli; Terkonazol; Terkonazolas; Triaconazole. 1-{4-[[2-(2,4-Dichlorophenyl)-*r*-2-(1*H*-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-*c*-4-yl]methoxy]phenyl}-4-isopropylpiperazine.

Терконазол

$C_{26}H_{31}Cl_2N_5O_3$ = 532.5.
CAS — 67915-31-5.
ATC — G01AG02.
ATC Vet — QG01AG02.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Terconazole). A white or almost white powder. It exhibits polymorphism. Practically insoluble in water; sparingly soluble in alcohol; soluble in acetone; freely soluble in dichloromethane. Protect from light.

Adverse Effects

Local reactions including burning and itching have been reported with vaginal use of terconazole. Other adverse effects have included dysmenorrhoea and genital, body, and abdominal pain. A flu-like syndrome with headache, fever, chills, and hypotension has been reported in some patients and may be more prevalent with vaginal pessaries providing doses larger than 80 mg.

Flu-like syndrome. References.

1. Moebius UM. Influenza-like syndrome after terconazole. *Lancet* 1988; **ii:** 966–7.

Precautions

Intravaginal preparations of terconazole 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

Terconazole is a triazole derivative that is thought to disrupt normal fungal cell membrane permeability. Terconazole is active *in vitro* against *Candida* spp. and other fungi. It has some antibacterial activity *in vitro* but not against usual vaginal flora such as lactobacilli.

Pharmacokinetics

After intravaginal use, 5 to 16% of terconazole is absorbed. Systemically absorbed drug is metabolised by the liver and excreted in urine and faeces.

Uses and Administration

Terconazole is a triazole antifungal used in the local treatment of vulvovaginal candidiasis (p.518). Intravaginal dosage regimens are terconazole 40 mg (as 0.8% vaginal cream) or 80 mg (as a pessary) at bedtime for 3 nights or 20 mg (as 0.4% cream) at bedtime for 7 nights.

Preparations

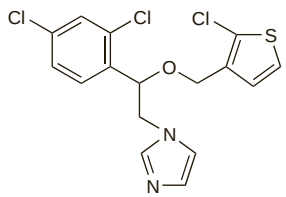
Proprietary Preparations (details are given in Part 3)
Belg.: Gyno-Terazol†; ***Braz.:*** Ginconazol†; Gyno-Fungix; ***Canad.:*** Terazol; ***Mex.:*** Fungistat; ***S.Afr.:*** Terazol; ***Switz.:*** Gyno-Terazol; ***USA:*** Terazol; Zazole; ***Venez.:*** Fungistat.

Tioconazole *(BAN, USAN, rINN)*

Tioconazol; Tioconazolum; Tiokonatsoli; Tiokonazol; Tiokonazolas; UK-20349. 1-[2,4-Dichloro-β-(2-chloro-3-thenyloxy)phenethyl]imidazole.

Тиоконазол

$C_{16}H_{13}Cl_3N_2OS$ = 387.7.
CAS — 65899-73-2.
ATC — D01AC07; G01AF08.
ATC Vet — QD01AC07; QG01AF08.



Pharmacopoeias. In *Eur.* (see p.vii) and *US*.
Ph. Eur. 6.2 (Tioconazole). A white or almost white crystalline powder. Very slightly soluble in water; freely soluble in alcohol; very soluble in dichloromethane. Protect from light.
USP 31 (Tioconazole). Store in airtight containers.

Adverse Effects and Precautions

Local reactions to tioconazole including burning, itching, and erythema have been reported.

Intravaginal preparations of tioconazole 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.

Hypersensitivity. Tioconazole, an imidazole antifungal widely used in Finland, appeared to be an important cause of contact allergy in that country, since an incidence of more than 1% was reported in patients undergoing routine patch testing.[1] There may be cross-reactivity with other commonly used imidazole derivatives.

1. Heikkilä H, *et al.* A study of 72 patients with contact allergy to tioconazole. *Br J Dermatol* 1996; **134:** 678–80.

Antimicrobial Action

Tioconazole is an imidazole antifungal with a broad spectrum of activity including action against dermatophytes, *Malassezia furfur*, and *Candida albicans*. Tioconazole is active *in vitro* against some Gram-positive bacteria.

Uses and Administration

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

For vaginal candidiasis it is used as pessaries or vaginal ointment usually as a single 300-mg dose.

It has been used topically as a 1% cream, lotion, or powder in the treatment of superficial fungal infections. Tioconazole has also been used for nail infections as a 28% w/w topical solution, although systemic treatment is generally preferred.

Preparations

BP 2008: Tioconazole Cream; Tioconazole Nail Solution.

Proprietary Preparations (details are given in Part 3)
Arg.: Honguil; Niofen; Tiomicol; Trosyd; ***Austria:*** Trosyd; ***Braz.:*** Gino Conazol; Gino Tralen; Neo Tionazol; Tioconax; Tionazen; Tralen; ***Canad.:*** Gynecure†; Trosyd†; ***Chile:*** Telset; ***Fin.:*** Gyno-Trosyd; Trosyd; ***Fr.:*** Gyno-Trosyd; Trosyd; ***Ger.:*** Mykontral; ***Gr.:*** Cotinazin; ***Hong Kong:*** Gyno-Trosyd; Trosyd; ***Indon.:*** Prodermal; Trosyd; ***Irl.:*** Trosyl; ***Ital.:*** Gino-Trosyd†; Trosyd; ***Malaysia:*** Gyno-Trosyd; Trosyd; ***NZ:*** Gyno-Trosyd†; ***Philipp.:*** Trosyd; ***Port.:*** Gino-Trosyd; Trosyd; ***S.Afr.:*** Gyno-Trosyd; Trosyd; ***Singapore:*** Gyno-Trosyd; Trosyd; ***Spain:*** Trosderm; Trosid; ***Switz.:*** Gyno-Trosyd; Trosyd; ***Thai.:*** Trosyd; ***Turk.:*** Dermo-Rest; Dermo-Trosyd; Gyno-Trosyd; Tiocan; Tiocell; ***UK:*** Trosyl; ***USA:*** Vagistat-1; ***Venez.:*** Gino-Tralen; Tralen.

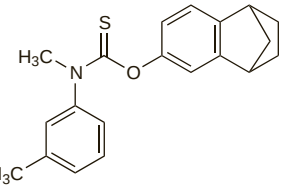
Multi-ingredient: ***Braz.:*** Cartrax; Duozol; Gynomax; Gynopac; Seczol; Takil; Travogyn; ***Fin.:*** Trosycort; ***Mex.:*** Fasigyn VT; ***Switz.:*** Trosyd†.

Tolciclate *(USAN, rINN)*

K-9147; KC-9147; Tolciclato; Tolciclatum. *O*-(1,2,3,4-Tetrahydro-1,4-methano-6-naphthyl) *m,N*-dimethylthiocarbanilate.

Тольциклат

$C_{20}H_{21}NOS$ = 323.5.
CAS — 50838-36-3.
ATC — D01AE19.
ATC Vet — QD01AE19.



Profile

Tolciclate is an antifungal with activity against *Epidermophyton*, *Microsporum*, and *Trichophyton* spp. It is used topically as a 1% cream or lotion, or as a 0.5% powder in the treatment of various dermatophyte infections and in pityriasis versicolor.

Preparations

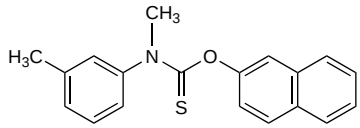
Proprietary Preparations (details are given in Part 3)
Braz.: Tolmicol†; ***Ger.:*** Fungifos†; ***Gr.:*** Tolmicil†; ***Ital.:*** Tolmicen†; ***Mex.:*** Kilmicen†; ***NZ:*** Tolmicen; ***Port.:*** Tolmicen†.

Tolnaftate *(BAN, USAN, rINN)*

Sch-10144; Tolnaftaatti; Tolnaftát; Tolnaftat; Tolnaftatas; Tolnaftato; Tolnaftatum. *O*-2-Naphthyl *m,N*-dimethylthiocarbanilate.

Тольнафтат

$C_{19}H_{17}NOS$ = 307.4.
CAS — 2398-96-1.
ATC — D01AE18.
ATC Vet — QD01AE18.



Pharmacopoeias. In *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Tolnaftate). A white or yellowish-white powder. Practically insoluble in water; very slightly soluble in alcohol; freely soluble in acetone and in dichloromethane. Protect from light.
USP 31 (Tolnaftate). A white to creamy-white, fine powder, with a slight odour. Practically insoluble in water; slightly soluble in alcohol; freely soluble in acetone and in chloroform; sparingly soluble in ether. Store in airtight containers.

Adverse Effects

Skin reactions occur rarely with tolnaftate and include irritation and contact dermatitis.

Antimicrobial Action

Tolnaftate inhibits the growth of the dermatophytes *Epidermophyton*, *Microsporum*, *Trichophyton* spp., and *Malassezia furfur*, but is not active against *Candida* spp. or bacteria.

Uses and Administration

Tolnaftate is an antifungal used topically as a 1% gel, solution, powder, ointment, or cream in the treatment or prophylaxis of superficial dermatophyte infections and of pityriasis versicolor (see Skin Infections, p.521). Tolnaftate is applied twice daily for 2 to 6 weeks. Repeat treatment may be required.

Preparations

USP 31: Tolnaftate Cream; Tolnaftate Gel; Tolnaftate Topical Aerosol; Tolnaftate Topical Powder; Tolnaftate Topical Solution.

Proprietary Preparations (details are given in Part 3)
Arg.: Athletes Foot†; Tinaderm†; ***Austral.:*** Antifungal Foot Deodorant†; Curatin; Ringworm Ointment; Tinaderm; Tineafax; ***Canad.:*** Absorbine Jr Antifungal; Footworks; Pitrex; Scholl Athlete's Foot; Tinactin; ZeaSorb AF; ***Chile:*** Tinaderm; ***Fr.:*** Sporiline†; ***Ger.:*** Tinatox; Tonoftal; ***Hong Kong:*** Aftate; ***Hung.:*** Athletes Foot†; Chinofungin; Digifungin; ***India:*** Tinaderm; Tolnaderm; ***Indon.:*** Naftate; ***Irl.:*** Mycil; Tinaderm†; ***Israel:*** Athletes Foot; Pitrex; Tinasol; ***Ital.:*** Tinaderm†; ***Malaysia:*** Dermoplex Antifungal; Myco-Aid; Tinaderm†; Tolnaderm; ***Mex.:*** Excelsior†; Tinaderm; Tinoxal; ***NZ:*** Tinaderm†; ***Philipp.:*** Tinactin; Tolnaderm; ***Port.:*** Tinaderme; ***S.Afr.:*** Tinaderm; ***Singapore:*** Tinaderm†; ***Spain:*** Micoisdin†; Tinaderm; ***Thai.:*** Ezon-T; Tono; ***Turk.:*** Mikoderm; ***UK:*** Mycil; Scholl Athlete's Foot; Tinaderm;