a dose of 1.5 g daily is given in single or divided doses for 5 days; children may be given 30 mg/kg daily.

◊ References.

1. Gillis JC, Wiseman LR. Secnidazole: a review of its antimicrobial activity, pharmacokinetic properties and therapeutic use in the management of protozoal infections and bacterial vaginosis. *Drugs* 1996; **51:** 621–38.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Flagentyl; ***Braz.:*** Decnazol†; Deprozol; Neodazol; Secnaxidol; Secni-Plus; Secnics; Secnidal; Secnidalin; Secnihexal†; Secnitec; Secnitrol†; Secnix; Secnizol†; Tecnid; Unigyn; ***Fr.:*** Secnol; ***India:*** Entosec; Noameba-DS; Secnil; ***Indon.:*** Sentyl; ***Mex.:*** Gisistin; Minovag; Sabima; Secnidal; ***Philipp.:*** Flagentyl; ***Port.:*** Flagentyl; ***Turk.:*** Flagentyl; ***Venez.:*** Ambese; Daksol; Fazol; Secnidal; Secnivax; Seczol; Unidazol.

Multi-ingredient: ***Arg.:*** Gynerium; Gynerium UD; ***Braz.:*** Gynopac; ***India:*** Safkit; ***Mex.:*** Sepia; Sporasec; ***Venez.:*** Sporasec.

Semduramicin *(BAN, USAN, rINN)*

Semduramicina; Semduramicine; Semduramicinum; UK-61689; UK-61689-2 (semduramicin sodium). (2*R*,3*S*,4*S*,5*R*,6*S*)-Tetrahydro-2,4-dihydroxy-6-{(*R*)-1-[(2*S*,5*R*,7*S*,8*R*,9*S*)-9-hydroxy-2,8-dimethyl-2-{(2*S*,2′*R*,3′*S*,5′*R*)-octahydro-2-methyl-5′-[(2*S*,3*S*,5*R*,6*S*)-tetrahydro-6-hydroxy-3,5,6-trimethyl-2*H*-pyran-2-yl]-3′-[(2*S*,5*S*,6*R*)-tetrahydro-5-methoxy-6-methyl-2*H*-pyran-2-yloxy]-2,2′-bifuran-5-yl}-1,6-dioxaspiro[4.5]dec-7-yl]ethyl}-5-methoxy-3-methyl-2*H*-pyran-2-ylacetic acid.

Семдурамицин

$C_{45}H_{76}O_{16}$ = 873.1.

CAS — 113378-31-7 (semduramicin); 119068-77-8 (semduramicin sodium).

Profile

Semduramicin is an antiprotozoal used in veterinary practice for the prevention of coccidiosis in poultry. It is also used as the sodium salt.

Suramin Sodium *(rINN)*

Antrypol; Bayer-205; CI-1003; Fourneau-309; Naganinum; Naganol; Suramin Hexasodium *(USAN)*; Suramina sódica; Suramine Sodique; Suraminum Natricum. The symmetrical 3″-urea of the sodium salt of 8-(3-benzamido-4-methylbenzamido)naphthalene-1,3,5-trisulphonic acid; Hexasodium 8,8′-{carbonylbis[imino-3,1-phenylenecarbonylimino(4-methyl-3,1-phenylene)carbonylimino]}bis(1,3,5-naphthalenetrisulfonate).

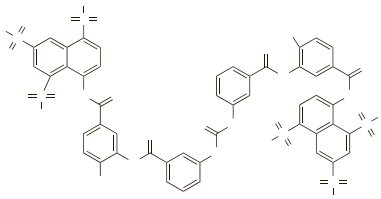
Сурамин Натрий

$C_{51}H_{34}N_6Na_6O_{23}S_6$ = 1429.2.

CAS — 145-63-1 (suramin); 129-46-4 (suramin sodium).

ATC — P01CX02.

ATC Vet — QP51AE02.



(suramin)

Pharmacopoeias. In *Fr.*, *Int.*, and *It.*

Adverse Effects

An immediate and potentially fatal reaction, with nausea, vomiting, shock, seizures, and loss of consciousness, may follow the injection of suramin sodium in some patients and thus it is usual practice to give a small test dose before starting treatment.

Abdominal pain, mouth ulceration, and skin reactions such as urticaria and pruritus may occur. The risk of hypersensitivity reactions is reported to be greater when onchocerciasis is present.

Other adverse effects include paraesthesia, hyperaesthesia of the palms and soles, skin eruptions, blood dyscrasias, fever, polyuria, increased thirst, raised liver enzyme values, fatigue, and effects on the eye including photophobia and lachrymation. Proteinuria is common; haematuria and casts in the urine may also occur. There have been occasional reports of adrenal insufficiency.

Effects on the blood. Thrombocytopenia has been reported in patients receiving suramin, generally during treatment for AIDS or cancer.[1-4] An immune-mediated mechanism has been proposed[3] although there is evidence that multiple mechanisms may be involved.[4] Other adverse effects on the blood include neutropenia,[1,5] anaemia,[1] deterioration of pre-existing lymphocytopenia,[5] and fatal myelosuppression.[5] Agranulocytosis and haemolytic anaemia have occurred rarely.

1. Levine AM, *et al.* Suramin antiviral therapy in the acquired immunodeficiency syndrome. *Ann Intern Med* 1986; **105:** 32–7.
2. Arlt W, *et al.* Suramin in adrenocortical cancer: limited efficacy and serious toxicity. *Clin Endocrinol (Oxf)* 1994; **41:** 299–307.
3. Seidman AD, *et al.* Immune-mediated thrombocytopenia secondary to suramin. *Cancer* 1993; **71:** 851–4.
4. Tisdale JF, *et al.* Severe thrombocytopenia in patients treated with suramin: evidence for an immune mechanism in one. *Am J Hematol* 1996; **51:** 152–7.
5. Rosen PJ, *et al.* Suramin in hormone-refractory metastatic prostate cancer: a drug with limited efficacy. *J Clin Oncol* 1996; **14:** 1626–36.

Effects on the eyes. Late effects on the eyes associated with suramin include photophobia, lachrymation, and palpebral oedema. Keratopathy characterised by corneal deposits has been reported in patients receiving suramin. In a study of 114 patients receiving suramin for prostatic cancer, 13 developed corneal deposits similar to those reported with chloroquine therapy after 34 to 98 days of therapy.[1] Symptoms in 10 of the 13 included lachrymation and foreign body sensation. The remaining 3 patients were asymptomatic. Shifts in refractive error were also found. Keratopathy has also been reported in patients with AIDS receiving suramin.[2] In patients treated with suramin for ocular onchocerciasis, the incidence of optic atrophy was higher after 3 years than in untreated patients.[3] A prolonged inflammatory response to dying microfilariae in the optic nerve might be responsible, although a direct toxic or allergic effect could not be ruled out.

1. Hemady RK, *et al.* Ocular symptoms and signs associated with suramin sodium treatment for metastatic cancer of the prostate. *Am J Ophthalmol* 1996; **121:** 291–6.
2. Teich SA, *et al.* Toxic keratopathy associated with suramin therapy. *N Engl J Med* 1986; **314:** 1455–6.
3. Thylefors B, Rolland A. The risk of optic atrophy following suramin treatment of ocular onchocerciasis. *Bull WHO* 1979; **57:** 479–80.

Effects on the kidneys. In addition to the proteinuria commonly seen during suramin therapy, there have been reports of individual cases of renal glycosuria[1] and of acute renal dysfunction.[2]

1. Awadzi K, *et al.* The chemotherapy of onchocerciasis XVIII: aspects of treatment with suramin. *Trop Med Parasitol* 1995; **46:** 19–26.
2. Figg WD, *et al.* Acute renal toxicity associated with suramin in the treatment of prostate cancer. *Cancer* 1994; **74:** 1612–14.

Effects on the nervous system. Neurological disorders reported in patients receiving suramin include paraesthesia and polyneuropathy. Severe polyneuropathy with generalised flaccid paralysis has generally been associated with serum-suramin concentrations greater than 350 micrograms/mL,[1,2] but motor neuropathy was reported in 8 patients with serum concentrations of 275 micrograms/mL.[3]

1. La Rocca RV, *et al.* Suramin-induced polyneuropathy. *Neurology* 1990; **40:** 954–60.
2. Arlt W, *et al.* Suramin in adrenocortical cancer: limited efficacy and serious toxicity. *Clin Endocrinol (Oxf)* 1994; **41:** 299–307.
3. Bitton RJ, *et al.* Pharmacologic variables associated with the development of neurologic toxicity in patients treated with suramin. *J Clin Oncol* 1995; **13:** 2223–9.

Effects on the skin. Pruritus and urticaria may occur as hypersensitivity reactions to suramin. Late skin reactions include erythematous maculopapular rashes.[1] Severe reactions including erythema multiforme,[2] exfoliative dermatitis, and fatal toxic epidermal necrolysis[3,4] have been reported.

1. O'Donnell BP, *et al.* Suramin-induced skin reactions. *Arch Dermatol* 1992; **128:** 75–9.
2. Katz SK, *et al.* Erythema multiforme induced by suramin. *J Am Acad Dermatol* 1995; **32:** 292–3.
3. May E, Allolio B. Fatal toxic epidermal necrolysis during suramin therapy. *Eur J Cancer* 1991; **27:** 1338.
4. Falkson G, Rapoport BL. Lethal toxic epidermal necrolysis during suramin treatment. *Eur J Cancer* 1992; **28A:** 1294.

Precautions

Suramin sodium should be used under close supervision, and the general condition of patients improved as far as possible before treatment starts. Patients who have a severe reaction to the first dose should never receive suramin again. It should not be used in elderly or infirm patients or in the presence of severe hepatic or renal disease. The urine should be tested before treatment starts and weekly during treatment; dosage should be reduced if moderate proteinuria develops and stopped if it becomes severe or if casts appear in the urine.

Pregnancy. Suramin has been reported to be teratogenic in *mice* but not in *rats*.[1] WHO[2] recommends that when necessary suramin should be used in pregnant women with *T. b. rhodesiense* trypanosomiasis, even those with meningoencephalitic disease, because melarsoprol is contra-indicated; in onchocerciasis, suramin treatment should be delayed until after delivery.

1. Mercier-Parot L, Tuchmann-Duplessis H. Action abortive et tératogène d'un trypanocide, la suramine. *C R Soc Biol* 1973; **167:** 1518–22.
2. WHO. *WHO model formulary.* Geneva: WHO, 2004.

Pharmacokinetics

After intravenous injection, suramin becomes bound to plasma proteins and plasma concentrations over 100 micrograms/mL are maintained for several weeks. Unbound suramin is excreted in the urine. Penetration of suramin into the CSF appears to be poor.

◊ The clinical pharmacokinetics of suramin were studied in 4 patients with AIDS given 6.2 g intravenously over 5 weeks.[1] Suramin accumulated during treatment and plasma concentrations exceeded 100 micrograms/mL for several weeks. After the last dose the terminal half-life of suramin ranged from 44 to 54 days. At least 99.7% was bound to plasma proteins. Renal clearance accounted for most of the elimination of suramin from the body. There appeared to be little or no metabolism of suramin.

In another study,[2] ten male patients with onchocerciasis received weekly infusions of suramin for 6 weeks, according to the dose regimen recommended by WHO (see below). In these patients the median elimination half-life was about 92 days, and in each case, the maximum plasma concentration remained below 300 micrograms/mL.

1. Collins JM, *et al.* Clinical pharmacokinetics of suramin in patients with HTLV-III/LAV infection. *J Clin Pharmacol* 1986; **26:** 22–6.
2. Chijioke CP, *et al.* Clinical pharmacokinetics of suramin in patients with onchocerciasis. *Eur J Clin Pharmacol* 1998; **54:** 249–51.

Uses and Administration

Suramin is a trypanocide used in the treatment of African trypanosomiasis and as an anthelmintic in the treatment of onchocerciasis.

Suramin is given as suramin sodium by slow intravenous injection, usually as a 10% solution. Because of the danger of severe reactions it is advisable to give a test dose before starting treatment.

In African trypanosomiasis suramin is used mainly for the early (haematolymphatic) stages of *Trypanosoma brucei rhodesiense* infection; pentamidine may be preferred for early-stage treatment of *T. b. gambiense* infection. Suramin is not used as sole therapy for late-stage infections with CNS involvement. Early-stage trypanosomiasis may be treated with a dose of 5 mg/kg of suramin on day 1, 10 mg/kg on day 3, then 20 mg/kg on days 5, 11, 17, 23, and 30. Another schedule consists of 5 doses of 1 g given over 3 weeks after a test dose of 100 to 200 mg. In late-stage trypanosomiasis injections of suramin are often given before starting treatment with melarsoprol; 5 and 10 mg/kg are given on days 1 and 3 respectively, and in some regimens 20 mg/kg is also given on day 5.

For doses used in onchocerciasis see below.

Malignant neoplasms. Suramin is reported to have antineoplastic activity and has been studied in a number of malignant neoplasms, in particular hormone-resistant prostatic cancer (p.671). However, its clinical usefulness is hindered by dose-limiting toxicity and problems in developing a simple dose schedule. It has also been investigated as a chemosensitiser.

References.

1. Stein CA, *et al.* Suramin: an anticancer drug with a unique mechanism of action. *J Clin Oncol* 1989; **7:** 499–508.
2. Kilbourn RG. Suramin: new therapeutic concepts for an old drug. *Cancer Bull* 1991; **43:** 265–7.
3. Rapoport BL, *et al.* Suramin in combination with mitomycin C in hormone-resistant prostate cancer: a phase II clinical study. *Ann Oncol* 1993; **4:** 567–73.
4. Woll PJ, *et al.* Suramin for breast and prostate cancer: a pilot study of intermittent short infusions without adaptive controls. *Ann Oncol* 1994; **5:** 597–600.
5. Arlt W, *et al.* Suramin in adrenocortical cancer: limited efficacy and serious toxicity. *Clin Endocrinol (Oxf)* 1994; **41:** 299–307.
6. Eisenberger MA, Reyno LM. Suramin. *Cancer Treat Rev* 1994; **20:** 259–73.
7. Rosen PJ, *et al.* Suramin in hormone-refractory metastatic prostate cancer: a drug with limited efficacy. *J Clin Oncol* 1996; **14:** 1626–36.
8. Small EJ, *et al.* Suramin therapy for patients with symptomatic hormone-refractory prostate cancer: results of a randomized phase III trial comparing suramin plus hydrocortisone to placebo plus hydrocortisone. *J Clin Oncol* 2000; **18:** 1440–50.
9. Chen D, *et al.* Nontoxic suramin as a chemosensitizer in patients: dosing nomogram development. *Pharm Res* 2006; **23:** 1265–74.

Onchocerciasis. Although suramin is the only drug in clinical use for onchocerciasis that is effective against adult worms, its use is restricted because of the frequency of associated compli-

cations and its intrinsic toxicity. Treatment of onchocerciasis (p.137) is currently based on continuous suppression of microfilariae by regular use of ivermectin. WHO[1] advises that suramin should only be considered for the curative treatment of individuals in areas without transmission of onchocerciasis and of individuals leaving an endemic area, and for severe hyperreactive onchodermatitis where symptoms are not adequately controlled with ivermectin. WHO[2] also recommends that it should not be used to treat onchocerciasis in the elderly or infirm, in patients with severe liver or renal disease, in totally blind patients (unless they require relief from intensely itchy lesions), or in pregnant women (who should be treated after delivery).

A total dose of 66.7 mg/kg in six incremental weekly doses is recommended.[1,2] The first (test) dose of suramin sodium 3.3 mg/kg should be given very cautiously by slow intravenous injection; this is followed at weekly intervals by incremental doses of 6.7 mg/kg, 10.0 mg/kg, 13.3 mg/kg, 16.7 mg/kg and 16.7 mg/kg.[2]

1. WHO. Onchocerciasis and its control: report of a WHO expert committee. *WHO Tech Rep Ser 852* 1995.
2. WHO. *WHO model formulary.* Geneva: WHO, 2004.

African trypanosomiasis. Suramin is used in the treatment of the early haematolymphatic phase of African trypanosomiasis (p.827) caused by *Trypanosoma brucei rhodesiense* and for *T. b. gambiense* infections which are resistant to pentamidine.[1] In some regions, suramin is used with pentamidine for *T. b. gambiense* infections but it has not been shown to be clinically superior to pentamidine alone.[2] Although suramin does not reach sufficient concentrations in the CSF to produce a cure in the meningoencephalitic phase, it is used to reduce the number of trypanosomes in the blood and lymph before treatment with melarsoprol.[1] Case reports have suggested that suramin with metronidazole[3] or eflornithine[4] could be useful in *T. b. rhodesiense* infections, although response to suramin plus eflornithine was disappointing in a study involving 6 patients.[5]

1. WHO. *WHO model formulary.* Geneva: WHO, 2004.
2. Pépin J, Khonde N. Relapses following treatment of early-stage Trypanosoma brucei gambiense sleeping sickness with a combination of pentamidine and suramin. *Trans R Soc Trop Med Hyg* 1996; **90:** 183–6.
3. Foulkes JR. Metronidazole and suramin combination in the treatment of arsenical refractory rhodesian sleeping sickness—a case study. *Trans R Soc Trop Med Hyg* 1996; **90:** 422.
4. Taelman H, *et al.* Combination treatment with suramin and eflornithine in late stage rhodesian trypanosomiasis: case report. *Trans R Soc Trop Med Hyg* 1996; **90:** 572–3.
5. Clerinx J, *et al.* Treatment of late stage rhodesiense trypanosomiasis using suramin and eflornithine: report of six cases. *Trans R Soc Trop Med Hyg* 1998; **92:** 449–50.

Preparations

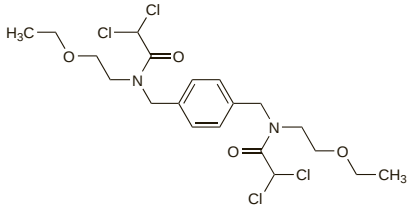
Proprietary Preparations (details are given in Part 3)
Ger.: Germanin.

Teclozan *(USAN, rINN)*

NSC-107433; Téclozan; Teclozán; Teclozanum; Win-13146. *NN′-p*-Phenylenedimethylenebis[2,2-dichloro-*N*-(2-ethoxyethyl)-acetamide].

Теклозан

$C_{20}H_{28}Cl_4N_2O_4$ = 502.3.
CAS — 5560-78-1.
ATC — P01AC04.



Profile
Teclozan, a dichloroacetamide derivative, is a luminal amoebicide with actions and uses similar to those of diloxanide furoate (p.832). It has been given orally in the treatment of intestinal amoebiasis.

Preparations

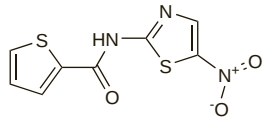
Proprietary Preparations (details are given in Part 3)
Braz.: Falmonox; ***Venez.:*** Falmonox.

Tenonitrozole *(rINN)*

TC-109; Tenonitrozol; Ténonitrozole; Tenonitrozolum; Thenitrazole. *N*-(5-Nitrothiazol-2-yl)thiophene-2-carboxamide.

Тенонитрозол

$C_8H_5N_3O_3S_2$ = 255.3.
CAS — 3810-35-3.
ATC — P01AX08.



Profile
Tenonitrozole is an antiprotozoal given in the treatment of trichomoniasis (p.827). It is given orally in a dose of 250 mg twice daily with meals, for 4 days.

Preparations

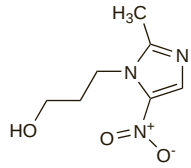
Proprietary Preparations (details are given in Part 3)
Fr.: Atrican; ***Rus.:*** Atrican (Атрикан); ***Venez.:*** Detricant†.

Ternidazole *(rINN)*

Ternidazol; Ternidazolum. 2-Methyl-5-nitroimidazole-1-propanol.

Тернидазол

$C_7H_{11}N_3O_3$ = 185.2.
CAS — 1077-93-6.



Profile
Ternidazole is a 5-nitroimidazole antiprotozoal with properties similar to those of metronidazole (p.837). It has been an ingredient of preparations used for the treatment of vaginitis.

Preparations

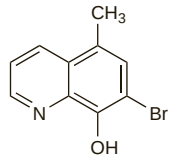
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Rus.:*** Tergynan (Тержинан).

Tilbroquinol *(pINN)*

Tilbroquinolum. 7-Bromo-5-methylquinolin-8-ol.

Тильброхинол

$C_{10}H_8BrNO$ = 238.1.
CAS — 7175-09-9.
ATC — P01AA05.



Profile
Tilbroquinol is a halogenated hydroxyquinoline antiprotozoal with properties similar to those of diiodohydroxyquinoline (p.832). It has been used with tiliquinol (below) in the treatment of intestinal infections including amoebiasis but less toxic drugs are preferred.

Adverse effects. A report of neurotoxicity, considered to be subacute myelo-opticoneuropathy, in a patient who had taken tilbroquinol with tiliquinol for 4 years.[1] Hepatotoxicity has also been reported[2] with this combination.

1. Soffer M, *et al.* Oxyquinoline toxicity. *Lancet* 1983; **i:** 709.
2. Caroli-Bosc F-X, *et al.* Hépatite aiguë due à l'association de tiliquinol et tilbroquinol (Intétrix). *Gastroenterol Clin Biol* 1996; **20:** 605–6.

Preparations

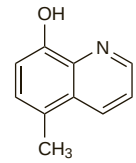
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Fr.:*** Intetrix; ***Rus.:*** Intetrix (Интетрикс).

Tiliquinol *(rINN)*

Tiliquinolum. 5-Methylquinolin-8-ol.

Тилихинол

$C_{10}H_9NO$ = 159.2.
CAS — 5541-67-3.



Profile
Tiliquinol has been used with tilbroquinol (above) in the treatment of intestinal infections including amoebiasis but less toxic drugs are preferred.

Preparations

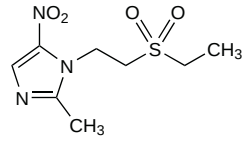
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Fr.:*** Intetrix; ***Rus.:*** Intetrix (Интетрикс).

Tinidazole *(BAN, USAN, rINN)*

CP-12574; Tinidatsoli; Tinidazol; Tinidazolas; Tinidazolum; Tynidazol. 1-[2-(Ethylsulphonyl)ethyl]-2-methyl-5-nitroimidazole.

Тинидазол

$C_8H_{13}N_3O_4S$ = 247.3.
CAS — 19387-91-8.
ATC — J01XD02; P01AB02.
ATC Vet — QJ01XD02; QP51AA02.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US.*
Ph. Eur. 6.2 (Tinidazole). An almost white or pale yellow, crystalline powder. Practically insoluble in water; soluble in acetone and in dichloromethane; sparingly soluble in methyl alcohol. Protect from light.
USP 31 (Tinidazole). An almost white or pale yellow crystalline powder. Practically insoluble in water; soluble in acetone and in dichloromethane; sparingly soluble in methyl alcohol. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

As for Metronidazole, p.837.

Breast feeding. The American Academy of Pediatrics[1] considers that the use of tinidazole by mothers during breast feeding may be of concern, since it is mutagenic *in vitro*. After single-dose therapy, breast feeding may be stopped for 12 to 24 hours to allow excretion of the dose.

1. 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 03/06/04)

Porphyria. Tinidazole is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *in-vitro* systems.

Shock. An acute severe toxic reaction, considered not to be allergic, occurred in a healthy subject shortly after the intravenous infusion of tinidazole 1.6 g over 80 minutes.[1] He fainted for about 10 seconds and low blood pressure, nausea, and tiredness persisted for several hours. Spasms in the left arm were also experienced but no generalised convulsions. Anaphylactic shock has also been reported,[2] with severe bronchospasm and subsequent development of Stevens-Johnson syndrome, in a patient who had reactions of increasing severity after 3 separate exposures to tinidazole.

1. Aase S, *et al.* Severe toxic reaction to tinidazole. *Eur J Clin Pharmacol* 1983; **24:** 425–7.
2. Singbal SS, Rataboli PV. Anaphylaxis and hypersensitivity syndrome reactions in increasing severity following repeated exposure to tinidazole. *J Postgrad Med* 2005; **51:** 243–4.

Interactions

Tinidazole may, like metronidazole (p.838), produce a disulfiram-like reaction with alcohol.