Pharmacokinetics

The pharmacokinetics of tinidazole resemble those of metronidazole although the half-life is longer.

Tinidazole is rapidly and almost completely absorbed after oral doses and, typically, a peak plasma concentration of about 40 micrograms/mL is achieved 2 hours after a single 2-g dose, falling to about 10 micrograms/mL at 24 hours and 2.5 micrograms/mL at 48 hours; concentrations above 8 micrograms/mL are maintained by daily maintenance doses of 1 g. Comparable concentrations are achieved with equivalent intravenous doses. The plasma elimination half-life of tinidazole is 12 to 14 hours.

Tinidazole is widely distributed and concentrations similar to those in plasma have been achieved in bile, breast milk, CSF, saliva, and a variety of body tissues; it crosses the placenta readily. Only 12% is reported to be bound to plasma proteins. An active hydroxy metabolite has been identified.

Unchanged drug and metabolites are excreted in the urine and, to a lesser extent, in the faeces.

◊ References.

1. Wood BA, *et al.* The pharmacokinetics, metabolism and tissue distribution of tinidazole. *J Antimicrob Chemother* 1982; **10** (suppl A): 43–57.
2. Karhunen M. Placental transfer of metronidazole and tinidazole in early human pregnancy after a single infusion. *Br J Clin Pharmacol* 1984; **18:** 254–7.
3. Evaldson GR, *et al.* Tinidazole milk excretion and pharmacokinetics in lactating women. *Br J Clin Pharmacol* 1985; **19:** 503–7.
4. Wood SG, *et al.* Pharmacokinetics and metabolism of C-tinidazole in humans. *J Antimicrob Chemother* 1986; **17:** 801–9.

Renal impairment. Single-dose studies indicate that the pharmacokinetics of tinidazole in patients with chronic renal failure are not significantly different from those in healthy subjects and that no modification of tinidazole dosage is necessary. However, tinidazole is rapidly removed by haemodialysis.[1,2]

1. Flouvat BL, *et al.* Pharmacokinetics of tinidazole in chronic renal failure and in patients on haemodialysis. *Br J Clin Pharmacol* 1983; **15:** 735–41.
2. Robson RA, *et al.* Tinidazole pharmacokinetics in severe renal failure. *Clin Pharmacokinet* 1984; **9:** 88–94.

Uses and Administration

Tinidazole is a 5-nitroimidazole derivative. It has the antimicrobial actions of metronidazole and is used similarly (see p.839) in the treatment of susceptible protozoal infections and in the treatment and prophylaxis of anaerobic bacterial infections. It has also been used in regimens for the eradication of *Helicobacter pylori* in peptic ulcer disease.

Tinidazole is usually given as a single daily oral dose with or after food; it is also given by intravenous infusion and as vaginal pessaries.

In invasive **amoebiasis**, tinidazole is usually given with a luminal amoebicide. In intestinal amoebiasis, a single daily dose of 2 g is given orally for 2 or 3 days; in hepatic amoebiasis, 1.5 to 2 g as a single daily dose may be given for 3 days or occasionally up to 6 days. Children are given 50 to 60 mg/kg daily for 3 or 5 days respectively.

A single dose of tinidazole 2 g is given orally in the treatment of **giardiasis**, **trichomoniasis**, and acute necrotising **ulcerative gingivitis**; 50 to 75 mg/kg as a single dose is given to children with giardiasis or trichomoniasis. It may sometimes be necessary to repeat this dose once. In trichomoniasis, sexual partners should also be treated.

In **bacterial vaginosis**, a single 2-g dose of tinidazole is usually given orally, although higher cure rates have been achieved with a 2-g dose on 2 successive days or 1 g daily for 5 days.

For the treatment of most **anaerobic bacterial infections**, tinidazole is given orally, usually for 5 or 6 days, in an initial dose of 2 g followed on subsequent days by 1 g daily or 500 mg twice daily. If oral therapy is not possible, tinidazole may be given intravenously, 800 mg being infused as 400 mL of a 2 mg/mL solution at a rate of 10 mL/minute; this initial dose is followed by 800 mg daily or 400 mg twice daily until oral therapy can be substituted. For the *prevention* of postoperative anaerobic bacterial infections, 2 g is given by mouth about 12 hours before surgery. Alternatively 1.6 g is given as a single intravenous infusion before surgery.

In regimens for the treatment of **peptic ulcer disease**, tinidazole 500 mg twice daily has been given with clarithromycin and omeprazole for 7 days.

◊ Reviews.

1. Manes G, Balzano A. Tinidazole: from protozoa to Helicobacter pylori—the past, present and future of a nitroimidazole with peculiarities. *Expert Rev Anti Infect Ther* 2004; **2:** 695–705.
2. Fung HB, Doan TL. Tinidazole: a nitroimidazole antiprotozoal agent. *Clin Ther* 2005; **27:** 1859–84.
3. Nailor MD, Sobel JD. Tinidazole for bacterial vaginosis. *Expert Rev Anti Infect Ther* 2007; **5:** 343–8.

Administration in renal impairment. The elimination of tinidazole is largely unchanged in patients with impaired renal function (see under Pharmacokinetics, above) and dosage adjustment is not generally considered necessary. However tinidazole is removed by haemodialysis, and patients may need additional doses to compensate.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Fasigyn; Gynormal; Ladylen Duo; ***Austral.:*** Fasigyn; Simplotan; ***Belg.:*** Fasigyn; ***Braz.:*** Amplium; Facyl; Fasigyn; Ginosutin; Pletil; Tinoral; Trinizol†; ***Chile:*** Fasigyn; Triconidazol†; Troxxil; ***Fr.:*** Fasigyne; ***Ger.:*** Simplotan†; ***Gr.:*** Fasigyn; ***Hong Kong:*** Fasigyn; ***India:*** Amebamagma; Enidazol; Fasigyn; Tiniba; Tinidafyl; Tinidol†; Tinifas; Tinvista; ***Indon.:*** Fasigyn; Flatin; ***Israel:*** Fasigyn; Protocide; ***Ital.:*** Fasigin; Trimonase; ***Malaysia:*** Fasigyn†; Tindol; ***Mex.:*** Amebysol; Ametricid†; Estovyn-T; Fasigyn; Induken†; Trinigyn; Triseptil; ***Neth.:*** Fasigyn†; ***NZ:*** Dyzole; ***Port.:*** Fasigyn; ***Rus.:*** Fasigyn (Фазижин); Tiniba (Тиниба); ***S.Afr.:*** Fasigyn; ***Singapore:*** Fasigyn; ***Spain:*** Tricolam; ***Swed.:*** Fasigyn; ***Switz.:*** Fasigyne; ***Thai.:*** Asiazole-TN; Fasigyn; Funida; Idazole; Sporinex; Tinazole; Tini†; Tonid; Trichonas; Tricogyn; Tricozone; Trigyn†; ***UK:*** Fasigyn; ***USA:*** Tindamax; ***Venez.:*** Cinabel†; Fasigyn; Pangamil.

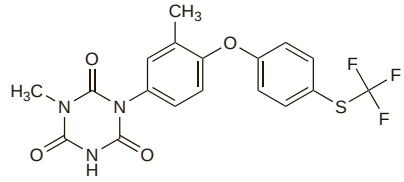
Multi-ingredient: ***Arg.:*** Aduar; Fasigyn Nistatina; Gynormal; Helmint Compuesto; Ladylen; Mebutar Compuesto; Nistinol; Tru Compuesto; ***Braz.:*** Amplium-G; Anfugine; Cartrax; Colpolase; Duozol; Facyl M; Ginec†; Gino Pletil; Ginometrim Oral†; Ginosutin M; Gynomax; Gynopac; Poliginax; Seczol; Takil; Tizonil M†; Travogyn; Trinizol M†; ***Chile:*** Doxifen; Famidal; Famidal Ad†; Ginecopast; Ginecopast Dual; Ginedazol; Ginedazol Dual; Medidos; Mizonase; ***India:*** Biocip-TZ; Bioflox-TZ; Candizole-T; Cipgen TZ; Ciplox TZ; Ciptini; Citizol; Entrolate†; Forcan TZ; Genflox TZ; Helipac; Nor T; Norflox TZ; Normax TZ; Ofler-TZ; Oflox TZ; Olfi TZ; OTC HP Kit; Parabact; Pylokit; Tinidafyl Plus; Tinvista-CF; Tinvista-NF; Wotinex; ***Indon.:*** Fasigyn-Nystatin; ***Ital.:*** Fasigin N; ***Malaysia:*** Pylobact Combi; ***Mex.:*** Afumix; Fasigyn VT; Mebeciclol; ***Rus.:*** Pylobact (Пилобакт).

Toltrazuril *(BAN, USAN, rINN)*

Bay-Vi-9142; Toltrazurilo; Toltrazurilum. 1-Methyl-3-(4-{*p*-[(trifluoromethyl)thio]phenoxy}-*m*-tolyl)-*s*-triazine-2,4,6(1*H*,3*H*,5*H*)-trione.

Толтразурил

$C_{18}H_{14}F_3N_3O_4S$ = 425.4.
CAS — 69004-03-1.
ATC Vet — QP51AJ01.



Profile

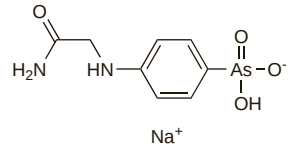
Toltrazuril is an antiprotozoal used in veterinary practice for the treatment of coccidiosis in poultry and piglets, and for the treatment of isosporiasis in piglets.

Tryparsamide *(rINN)*

Glyphenarsine; Triparsamida; Tryparsam.; Tryparsamidum; Tryparsone. Sodium hydrogen 4-(carbamoylmethylamino)-phenylarsonate hemihydrate.

Трипарсамид

$C_8H_{10}AsN_2NaO_4 \cdot H_2O$ = 305.1.
CAS — 554-72-3 (anhydrous tryparsamide); 6159-29-1 (tryparsamide hemihydrate).



(anhydrous tryparsamide)

Profile

Tryparsamide, a pentavalent arsenical compound, is a trypanocide which penetrates into the CSF and has been used with suramin in the treatment of late-stage African trypanosomiasis due to *Trypanosoma brucei gambiense*, as an alternative to melarsoprol or eflornithine (see p.827). However, because of its toxicity, especially the risk of blindness resulting from damage to the optic nerve, melarsoprol or eflornithine are preferred.

For the adverse effects of arsenic and their treatment, see Arsenic Trioxide, p.2260. Like melarsoprol, tryparsamide can cause encephalopathy.
