Effects on the pancreas. Pancreatitis has been associated with sodium stibogluconate treatment.[1-3] Withdrawing treatment usually resulted in resolution of pancreatitis.

1. Donovan KL, *et al.* Pancreatitis and palindromic arthropathy with effusions associated with sodium stibogluconate treatment in a renal transplant recipient. *J Infect* 1990; **21:** 107–10.
2. Gasser RA, *et al.* Pancreatitis induced by pentavalent antimonial agents during treatment of leishmaniasis. *Clin Infect Dis* 1994; **18:** 83–90.
3. Domingo P, *et al.* Treatment of Indian kala-azar with pentavalent antimony. *Lancet* 1995; **345:** 584–5.

Pharmacokinetics

The pentavalent antimony compounds are poorly absorbed from the gastrointestinal tract. After intravenous doses an initial distribution phase is followed by biexponential elimination by the kidneys. The elimination half-life of the initial phase is about 1.7 hours and that of the slow terminal phase is about 33 hours. The corresponding half-lives after intramuscular doses are reported to be 2 hours and 766 hours respectively. The slow elimination phase may reflect reduction to trivalent antimony. Accumulation occurs on daily use and maximum tissue concentrations may not be reached for 7 days or more. Antimony has been detected in breast milk (see Breast Feeding, above).

◊ References.

1. Rees PH, *et al.* Renal clearance of pentavalent antimony (sodium stibogluconate). *Lancet* 1980; **ii:** 226–9.
2. Chulay JD, *et al.* Pharmacokinetics of antimony during treatment of visceral leishmaniasis with sodium stibogluconate or meglumine antimoniate. *Trans R Soc Trop Med Hyg* 1988; **82:** 69–72.
3. Al Jaser M, *et al.* Pharmacokinetics of antimony in patients treated with sodium stibogluconate for cutaneous leishmaniasis. *Pharm Res* 1995; **12:** 113–16.

Uses and Administration

Pentavalent antimony, as sodium stibogluconate or meglumine antimonate, is used as first-line treatment for all forms of leishmaniasis except *Leishmania aethiopica* infections.

For systemic use, sodium stibogluconate is given by intramuscular or intravenous injection as a solution containing the equivalent of pentavalent antimony 100 mg/mL. Intramuscular injection is generally preferable. Intravenous injections must be given very slowly (over at least 5 minutes) and preferably through a fine needle to avoid thrombophlebitis; as with trivalent antimony compounds, they should be stopped immediately if coughing, vomiting, or substernal pain occurs. Meglumine antimonate is given by deep intramuscular injection as a solution containing the equivalent of pentavalent antimony 85 mg/mL. Doses are expressed in terms of the equivalent amount of pentavalent antimony.

Local variations exist in treatment schedules but WHO recommends the following regimens:

- In **visceral leishmaniasis**, initial treatment is based on daily intramuscular injection of pentavalent antimony 20 mg/kg to a maximum of 850 mg (but see below) for at least 20 days. The length of treatment varies from one endemic area to another, but is continued until no parasites are detected in consecutive splenic aspirates taken at 14-day intervals. Patients who relapse are re-treated at the same dose.
- Early non-inflamed lesions of **cutaneous leishmaniasis** due to all forms of *Leishmania* except *L. aethiopica*, *L. amazonensis*, and *L. braziliensis* may be treated by infiltration with intralesional injections of 1 to 3 mL of sodium stibogluconate or meglumine antimonate (about 100 to 300 mg of pentavalent antimony), repeated once or twice if necessary at intervals of 1 to 2 days. Systemic therapy with intramuscular pentavalent antimony 10 to 20 mg/kg daily is given if the lesions are more severe and continued until a few days after clinical and parasitological cure is achieved.

  Cutaneous leishmaniasis due to *L. aethiopica* is not responsive to antimonials at conventional doses. In cutaneous leishmaniasis due to *L. braziliensis*, prolonged systemic treatment with intramuscular pentavalent antimony 20 mg/kg daily for a minimum of 4 weeks is indicated. Similar doses are required for **diffuse cutaneous leishmaniasis** due to *L. amazonensis* and are continued for several months after clinical improvement occurs. Relapses should be expected until immunity develops.
- In **mucocutaneous leishmaniasis**, daily doses of intramuscular pentavalent antimony 20 mg/kg are given for a minimum of 4 weeks; if the response is poor, 10 to 15 mg/kg may be given every 12 hours for the same period. Relapses are well known and have generally been associated with inadequate or interrupted treatment; they are treated with the same drug given for at least twice as long as the original treatment. Only when that fails should alternative treatment be given.

Leishmaniasis. The main treatment for leishmaniasis (p.824) is a pentavalent antimony compound such as sodium stibogluconate. Higher doses of antimony compounds than those recommended by WHO (see above) have been tried in order to overcome the unresponsiveness of leishmaniasis to therapy. In the USA, the use of 20 mg/kg daily of pentavalent antimony has been recommended, without restriction to an 850-mg maximum daily dose.[1,2] At 20 mg/kg daily the most common adverse effects are musculoskeletal disorders, elevated liver enzyme values, and T-wave changes on the ECG, and the CDC recommends that the ECG, blood chemistry, and blood count should be monitored throughout therapy if resources permit.[1] Severe cardiotoxicity is rare at this dose but fatal cardiac toxicity has been reported with doses of up to 60 mg/kg daily (see under Effects on the Heart, above). Drug-resistant strains of *Leishmania infantum* have been associated with unresponsiveness to treatment with meglumine antimonate.[3] It was suggested[4] that the use of suboptimal doses may be increasing the prevalence of drug-resistant strains of the parasite. However, low doses of antimony compounds (5 mg/kg daily for 30 days) have produced long-term cure in patients with cutaneous *L. braziliensis* infection followed for up to 10 years.[5]

INTRALESIONAL ADMINISTRATION. Intralesional infiltration of 3 doses of sodium stibogluconate on alternate days or once weekly was more effective than daily treatment in a study of 96 patients in Saudi Arabia.[6] Local infiltration of meglumine antimonate in usual doses of 150 to 900 mg (maximum 1500 mg) once each week for up to 6 weeks produced microbiological and clinical cures in all of 45 patients in Italy with cutaneous leishmaniasis.[7]

1. Herwaldt BL, Berman JD. Recommendations for treating leishmaniasis with sodium stibogluconate (Pentostam) and review of pertinent clinical studies. *Am J Trop Med Hyg* 1992; **46:** 296–306.
2. Abramowicz M, ed. *Drugs for parasitic infections*. 1st ed. New Rochelle NY: The Medical Letter, 2007.
3. Faraut-Gambarelli F, *et al.* In vitro and in vivo resistance of Leishmania infantum to meglumine antimoniate: a study of 37 strains collected from patients with visceral leishmaniasis. *Antimicrob Agents Chemother* 1997; **41:** 827–30.
4. Grogl M, *et al.* Drug resistance in leishmaniasis: its implication in systemic chemotherapy of cutaneous and mucocutaneous disease. *Am J Trop Med Hyg* 1992; **47:** 117–26.
5. Oliveira-Neto MP, *et al.* A low-dose antimony treatment in 159 patients with American cutaneous leishmaniasis: extensive follow-up studies (up to 10 years). *Am J Trop Med Hyg* 1997; **57:** 651–5.
6. Tallab TM, *et al.* Cutaneous leishmaniasis: schedules for intralesional treatment with sodium stibogluconate. *Int J Dermatol* 1996; **35:** 594–7.
7. Aste N, *et al.* Intralesional treatment of cutaneous leishmaniasis with meglumine antimoniate. *Br J Dermatol* 1998; **138:** 370–1.

Preparations

BP 2008: Sodium Stibogluconate Injection.

Proprietary Preparations (details are given in Part 3)
Braz.: Glucantime; ***Fr.:*** Glucantime; ***Israel:*** Pentostam; ***Ital.:*** Glucantim†; ***Spain:*** Glucantime; ***UK:*** Pentostam; ***Venez.:*** Glucantime.

Atovaquone *(BAN, USAN, rINN)*

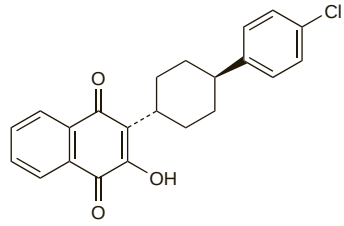
Atovacuona; Atovakon; Atovakvon; Atovakvoni; Atovaquonum; BW-A566C; BW-566C; BW-566C80; 566C; 566C80. 2-[*trans*-4-(4-Chlorophenyl)cyclohexyl]-3-hydroxy-1,4-naphthoquinone.

Атовахон

$C_{22}H_{19}O_3Cl$ = 366.8.

CAS — 95233-18-4.

ATC — P01AX06.



Pharmacopoeias. In *US.*
USP 31 (Atovaquone). A yellow powder. Insoluble in water; slightly soluble in alcohol, in butanediol, in ethyl acetate, in glycerol, in octanol, and in macrogol 200; sparingly soluble in acetone, in di-*n*butyl adipate, in dimethyl sulfoxide, and in macrogol 400; soluble in chloroform; freely soluble in *N*-methyl-2-pyrrolidone and in tetrahydrofuran; very slightly soluble in 0.1N sodium hydroxide. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

Adverse reactions to atovaquone include skin rashes, headache, fever, insomnia, and gastrointestinal effects such as nausea, diarrhoea, and vomiting. Raised liver enzyme values, hyponatraemia, and haematological disturbances such as anaemia and neutropenia may occur occasionally. Atovaquone should be avoided in patients with gastrointestinal disorders that may limit absorption of the drug.

Effects on the skin. Stevens-Johnson syndrome has been reported[1] in a patient taking atovaquone with proguanil.

1. Emberger M, *et al.* Stevens-Johnson syndrome associated with Malarone antimalarial prophylaxis. Abstract: *Clin Infect Dis* 2003; **37:** 158. Full version: http://www.journals.uchicago.edu/doi/pdf/10.1086/375073 (accessed 17/07/08)

Interactions

Use of atovaquone with either metoclopramide, tetracycline, or rifampicin (and possibly also rifabutin) may result in decreases in plasma-atovaquone concentrations. Other drugs which have produced small reductions in plasma-atovaquone concentrations include aciclovir, antidiarrhoeals, benzodiazepines, cephalosporins, laxatives, opioids, and paracetamol.

Atovaquone is reported to decrease the metabolism of zidovudine resulting in moderate increases in zidovudine plasma concentrations. A decrease in trough concentrations of indinavir, and in the area under the indinavir time-concentration curve has been reported when atovaquone was also given. Small decreases in the plasma concentrations of co-trimoxazole have been noted in patients taking atovaquone. There is a theoretical possibility that atovaquone could displace other highly protein-bound drugs from plasma-protein binding sites.

Pharmacokinetics

Atovaquone is poorly absorbed from the gastrointestinal tract after oral doses; bioavailability is especially poor in patients with AIDS. Bioavailability from commercial oral liquid formulations is better than from tablets and can be further improved if taken with food, particularly meals with a high fat content. Atovaquone is more than 99% bound to plasma proteins and has a long plasma half-life of 2 to 3 days, thought to be due to enterohepatic recycling. It is excreted almost exclusively in faeces as unchanged drug.

◊ References.

1. Hughes WT, *et al.* Safety and pharmacokinetics of 566C80, a hydroxynaphthoquinone with anti-Pneumocystis carinii activity: a phase I study in human immunodeficiency virus (HIV)-infected men. *J Infect Dis* 1991; **163:** 843–8.
2. Rolan PE, *et al.* Examination of some factors responsible for a food-induced increase in absorption of atovaquone. *Br J Clin Pharmacol* 1994; **37:** 13–20.
3. Dixon R, *et al.* Single-dose and steady-state pharmacokinetics of a novel microfluidized suspension of atovaquone in human immunodeficiency virus-seropositive patients. *Antimicrob Agents Chemother* 1996; **40:** 556–60.
4. Hussein Z, *et al.* Population pharmacokinetics of atovaquone in patients with acute malaria caused by Plasmodium falciparum. *Clin Pharmacol Ther* 1997; **61:** 518–30.
5. Rolan PE, *et al.* Disposition of atovaquone in humans. *Antimicrob Agents Chemother* 1997; **41:** 1319–21.

Uses and Administration

Atovaquone is a hydroxynaphthoquinone antiprotozoal that is also active against the fungus *Pneumocystis jirovecii*. It is used in the treatment and prophylaxis of pneumocystis pneumonia in patients unable to tolerate co-trimoxazole, and with proguanil in the treatment and prophylaxis of malaria.

In the treatment of mild to moderate **pneumocystis pneumonia**, atovaquone is given orally in a dose of 750 mg with food twice daily as a suspension, for 21 days. For prophylaxis 1500 mg of the suspension is given once daily with food.

Prophylaxis of falciparum **malaria** should start 1 to 2 days before travel to the malarious area, continue daily throughout exposure, and for 7 days after leaving the area. The following doses may be given once daily:

- adults and children over 40 kg: atovaquone 250 mg with proguanil hydrochloride 100 mg
- children 11 to 20 kg: one-quarter the adult dose
- children 21 to 30 kg: one-half the adult dose
- children 31 to 40 kg: three-quarters the adult dose

In the **treatment** of uncomplicated falciparum **malaria**, the following doses are given as a single daily dose for 3 days:

- adults and children over 40 kg: atovaquone 1000 mg with proguanil hydrochloride 400 mg
- children 5 to 8 kg: one-eighth the adult dose
- children 9 to 10 kg: three-sixteenths the adult dose
- children 11 to 20 kg: one-quarter the adult dose
- children 21 to 30 kg: one-half the adult dose
- children 31 to 40 kg: three-quarters the adult dose

Atovaquone with proguanil is one of the antimalarial drugs recommended by some experts to be carried as a **standby** for the emergency treatment of **malaria**. The dose recommended for self-treatment is the same as that for treatment of uncomplicated falciparum malaria.

◊ Reviews.

1. Haile LG, Flaherty JF. Atovaquone: a review. *Ann Pharmacother* 1993; **27:** 1488–94.
2. Artymowicz RJ, James VE. Atovaquone: a new antipneumocystis agent. *Clin Pharm* 1993; **12:** 563–70.
3. Spencer CM, Goa KL. Atovaquone: a review of its pharmacological properties and therapeutic efficacy in opportunistic infections. *Drugs* 1995; **50:** 176–96.
4. Baggish AL, Hill DR. Antiparasitic agent atovaquone. *Antimicrob Agents Chemother* 2002; **46:** 1163–73.
5. McKeage K, Scott LJ. Atovaquone/proguanil: a review of its use for the prophylaxis of Plasmodium falciparum malaria. *Drugs* 2003; **63:** 597–623.
6. Marra F, *et al.* Atovaquone-proguanil for prophylaxis and treatment of malaria. *Ann Pharmacother* 2003; **37:** 1266–75.

Babesiosis. In a prospective, randomised study[1] involving 58 patients with babesiosis (p.823), atovaquone with azithromycin was found to be as effective as, and associated with fewer adverse effects than, standard therapy with quinine and clindamycin. Atovaquone 750 mg twice daily with azithromycin 600 mg once daily, or 500 to 1000 mg on day 1 followed by 250 mg once daily thereafter, both orally for 7 to 10 days, has been recommended by some experts[2,3] in the USA for the treatment of *Babesia microti* infections. Children may be given atovaquone 20 mg/kg twice daily with azithromycin 12 mg/kg once daily, or 10 mg/kg on day 1 followed by 5 mg/kg once daily thereafter, both by mouth for 7 to 10 days.

1. Krause PJ, *et al.* Atovaquone and azithromycin for the treatment of babesiosis. *N Engl J Med* 2000; **343:** 1454–8.
2. Wormser GP, *et al.* The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis* 2006; **43:** 1089–1134. Also available at: http://www.journals.uchicago.edu/doi/pdf/10.1086/375073 (accessed 17/07/08)
3. Abramowicz M, ed. *Drugs for parasitic infections*. 1st ed. New Rochelle NY: The Medical Letter, 2007.

Malaria. Atovaquone with proguanil (*Malarone*) is used in the treatment and prophylaxis of uncomplicated malaria caused by *Plasmodium falciparum* (see p.594).

Atovaquone, a blood schizontocide, is associated with an unacceptably high rate of recrudescence when used alone[1,2] for *treatment* but is more successful in malaria when used with proguanil,[2,3] including that produced by multidrug-resistant strains.[4] Use of the combination to treat *P. ovale* and *P. malariae* malarias has also been studied.[5] Atovaquone with proguanil followed by primaquine may also be effective for the treatment of *P. vivax* malaria.[6]

Atovaquone with proguanil has also been found to be useful for *prophylaxis* of falciparum malaria in both children[7] and adults[8] in endemic areas. It may also be used for prophylaxis in non-immune travellers[9,10] and appears to be well tolerated.[10,11]

1. Chiodini PL, *et al.* Evaluation of atovaquone in the treatment of patients with uncomplicated Plasmodium falciparum malaria. *J Antimicrob Chemother* 1995; **36;** 1073–5.
2. Looareesuwan S, *et al.* Clinical studies of atovaquone, alone or in combination with other antimalarial drugs, for treatment of acute uncomplicated malaria in Thailand. *Am J Trop Med Hyg* 1996; **54:** 62–6.
3. Radloff PD, *et al.* Atovaquone and proguanil for Plasmodium falciparum malaria. *Lancet* 1996; **347:** 1511–14.
4. Sabchareon A, *et al.* Efficacy and pharmacokinetics of atovaquone and proguanil in children with multidrug-resistant Plasmodium falciparum malaria. *Trans R Soc Trop Med Hyg* 1998; **92:** 201–6.
5. Radloff PD, *et al.* Atovaquone plus proguanil is an effective treatment for Plasmodium ovale and P. malariae malaria. *Trans R Soc Trop Med Hyg* 1996; **90:** 682.
6. Looareesuwan S, *et al.* Atovaquone and proguanil hydrochloride followed by primaquine for treatment of plasmodium vivax malaria in Thailand. *Trans R Soc Trop Med Hyg* 1999; **93:** 637–40.
7. Lell B, *et al.* Randomised placebo-controlled study of atovaquone plus proguanil for malaria prophylaxis in children. *Lancet* 1998; **351:** 709–13.
8. Shanks GD, *et al.* Efficacy and safety of atovaquone/proguanil as suppressive prophylaxis for Plasmodium falciparum malaria. *Clin Infect Dis* 1998; **27:** 494–9.
9. Overbosch D, *et al.* Atovaquone-proguanil versus mefloquine for malaria prophylaxis in nonimmune travelers: results from a randomized, double-blind study. *Clin Infect Dis* 2001; **33:** 1015–21.
10. Nakato H, *et al.* A systematic review and meta-analysis of the effectiveness and safety of atovaquone proguanil (Malarone) for chemoprophylaxis against malaria. *J Antimicrob Chemother* 2007; **60:** 929–36.
11. Høgh B, *et al.* Atovaquone-proguanil versus chloroquine-proguanil for malaria prophylaxis in non-immune travellers: a randomised, double-blind study. *Lancet* 2000; **356:** 1888–94.

Microsporidiosis. There is no established effective treatment for microsporidiosis (p.826). Beneficial responses were reported with atovaquone in a preliminary study.[1]

1. Anwar-Bruni DM, *et al.* Atovaquone is effective treatment for the symptoms of gastrointestinal microsporidiosis in HIV-1-infected patients. *AIDS* 1996; **10:** 619–23.

Pneumocystis pneumonia. Atovaquone is one alternative to co-trimoxazole for the treatment of pneumocystis pneumonia (p.521). In open studies, a clinical response to atovaquone was reported in 78% of patients with mild to moderate disease and in 56% of patients with severe disease who were intolerant of, or who failed to respond to, both co-trimoxazole and pentamidine.[1] Comparative studies have shown atovaquone to be less effective than co-trimoxazole[2] and probably less effective than pentamidine,[3,4] but to produce fewer treatment-limiting adverse effects than either.

Atovaquone is also an alternative to co-trimoxazole for both primary or secondary *prophylaxis*, and was as effective as dapsone[5] or inhaled pentamidine[6] in studies in patients intolerant of co-trimoxazole.

1. White A, *et al.* Clinical experience with atovaquone on a treatment investigational new drug protocol for Pneumocystis carinii pneumonia. *J Acquir Immune Defic Syndr Hum Retrovirol* 1995; **9:** 280–5.
2. Hughes W, *et al.* Comparison of atovaquone (566C80) with trimethoprim-sulfamethoxazole to treat Pneumocystis carinii pneumonia in patients with AIDS. *N Engl J Med* 1993; **328:** 1521–7.
3. Dohn MN, *et al.* Oral atovaquone compared with intravenous pentamidine for Pneumocystis carinii pneumonia in patients with AIDS. *Ann Intern Med* 1994; **121:** 174–80.
4. Lederman MM, van der Horst C. Atovaquone for Pneumocystis carinii pneumonia. *Ann Intern Med* 1995; **122:** 314.
5. El-Sadr WM, *et al.* Atovaquone compared with dapsone for the prevention of Pneumocystis carinii pneumonia in patients with HIV infection who cannot tolerate trimethoprim, sulfonamides, or both. *N Engl J Med* 1998; **339:** 1889–95.
6. Chan C, *et al.* Atovaquone suspension compared with aerosolized pentamidine for prevention of Pneumocystis carinii pneumonia in human immunodeficiency virus-infected subjects intolerant of trimethoprim or sulfonamides. *J Infect Dis* 1999; **180:** 369–76.

Toxoplasmosis. Atovaquone, either alone or with pyrimethamine or sulfadiazine, has produced encouraging results for treatment[1-3] or long-term suppression[2-4] of toxoplasmosis (p.826) in patients with AIDS.

1. Kovacs JA, *et al.* Efficacy of atovaquone in treatment of toxoplasmosis in patients with AIDS. *Lancet* 1992; **340:** 637–8.
2. Torres RA, *et al.* Atovaquone for salvage treatment and suppression of toxoplasmic encephalitis in patients with AIDS. *Clin Infect Dis* 1997; **24:** 422–9.
3. Chirgwin K, *et al.* Randomized phase II trial of atovaquone with pyrimethamine or sulfadiazine for treatment of toxoplasmic encephalitis in patients with acquired immunodeficiency syndrome: ACTG 237/ANRS 039 Study. *Clin Infect Dis* 2002; **34:** 1243–50.
4. Katlama C, *et al.* Atovaquone as long-term suppressive therapy for toxoplasmic encephalitis in patients with AIDS and multiple drug intolerance. *AIDS* 1996; **10:** 1107–12.

Preparations

USP 31: Atovaquone Oral Suspension.

Proprietary Preparations (details are given in Part 3)
Austral.: Wellvone; ***Austria:*** Wellvone; ***Belg.:*** Wellvone; ***Canad.:*** Mepron; ***Fr.:*** Wellvone; ***Ger.:*** Wellvone; ***Gr.:*** Wellvone; ***Ital.:*** Wellvone; ***Neth.:*** Wellvone; ***Port.:*** Wellvone; ***S.Afr.:*** Wellvone; ***Spain:*** Wellvone; ***Swed.:*** Wellvone; ***Switz.:*** Wellvone; ***UK:*** Wellvone; ***USA:*** Mepron.

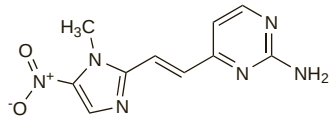
Multi-ingredient: ***Austral.:*** Malarone; ***Austria:*** Malarone; Promal; ***Belg.:*** Malarone; ***Canad.:*** Malarone; ***Cz.:*** Malarone; ***Denm.:*** Malarone; ***Fr.:*** Malarone; ***Ger.:*** Malarone; ***Gr.:*** Malarone; ***Hong Kong:*** Malarone; ***Hung.:*** Malarone; ***Irl.:*** Malarone; ***Israel:*** Malarone; ***Ital.:*** Malarone; ***Malaysia:*** Malarone; ***Neth.:*** Malarone; ***Norw.:*** Malarone; ***NZ:*** Malarone; ***Pol.:*** Malarone; ***S.Afr.:*** Malanil; ***Singapore:*** Malarone; ***Spain:*** Malarone; ***Swed.:*** Malarone; ***Switz.:*** Malarone; ***UK:*** Malarone; ***USA:*** Malarone.

Azanidazole *(BAN, USAN, rINN)*

Azanidazol; Azanidazolum; F-4. 4-[(*E*)-2-(1-Methyl-5-nitroimidazol-2-yl)vinyl]pyrimidin-2-ylamine.

Азанидазол

$C_{10}H_{10}N_6O_2$ = 246.2.
CAS — 62973-76-6.
ATC — G01AF13; P01AB04.
ATC Vet — QG01AF13; QP51AA04.



Profile

Azanidazole is a 5-nitroimidazole derivative similar to metronidazole (p.837) and is used in the treatment of trichomoniasis in usual oral doses of 200 mg twice daily or 250 mg once daily intravaginally.

Preparations

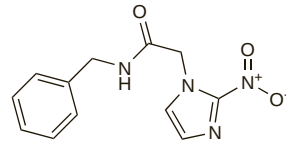
Proprietary Preparations (details are given in Part 3)
Ital.: Triclose.

Benznidazole *(rINN)*

Benznidazol; Benznidazolum; Ro-7-1051. *N*-Benzyl-2-(2-nitroimidazol-1-yl)acetamide.

Бензнидазол

$C_{12}H_{12}N_4O_3$ = 260.2.
CAS — 22994-85-0.
ATC — P01CA02.



Pharmacopoeias. In *Int.*

Adverse Effects

Nausea, vomiting, abdominal pain, peripheral neuropathy, blood dyscrasias, and severe skin reactions have been reported with benznidazole.

◊ A study[1] involving 20 patients with chronic American trypanosomiasis given benznidazole 5 mg/kg daily had to be stopped because of the high incidence of skin rashes and neurological symptoms.

1. Apt W, *et al.* Clinical trial of benznidazole and an immunopotentiator against Chagas disease in Chile. *Trans R Soc Trop Med Hyg* 1986; **80:** 1010.

Pharmacokinetics

Benznidazole is absorbed from the gastrointestinal tract after oral doses.

◊ References.

1. Raaflaub J, Ziegler WH. Single-dose pharmacokinetics of the trypanosomicide benznidazole in man. *Arzneimittelforschung* 1979; **29:** 1611–14.

Uses and Administration

Benznidazole is a 2-nitroimidazole derivative with antiprotozoal activity. It is of value in the treatment of American trypanosomiasis (Chagas' disease) due to infection with *Trypanosoma cruzi*, especially during the early acute stage of the disease.

Benznidazole has been given orally in a dose of 5 to 7 mg/kg daily in two divided doses usually for 60 days (but see below). Children have been given 10 mg/kg daily in two divided doses.