Nifursol *(BAN, USAN, pINN)*

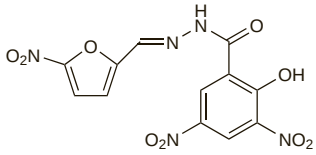
Nifursolum. 3,5-Dinitro-2′-(5-nitrofurfurylidene)salicylohydrazide.

Нифурсол

$C_{12}H_7N_5O_9$ = 365.2.

CAS — 16915-70-1.

ATC Vet — QP51AX05.



Profile

Nifursol is an antiprotozoal used in veterinary practice for the prevention of blackhead (histomoniasis) in poultry.

Nifurtimox *(BAN, rINN)*

Bayer-2502; Nifurtimoxum. Tetrahydro-3-methyl-4-(5-nitrofurfurylideneamino)-1,4-thiazine 1,1-dioxide.

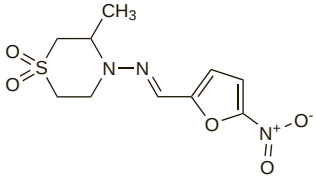
Нифуртимокс

$C_{10}H_{13}N_3O_5S$ = 287.3.

CAS — 23256-30-6.

ATC — P01CC01.

ATC Vet — QP51AC01.



Pharmacopoeias. In *Fr.* and *Int.*

Adverse Effects

Adverse effects are common with nifurtimox and include gastrointestinal effects such as anorexia with loss of weight, abdominal pain, nausea and vomiting, and effects on the nervous system, especially peripheral neuropathy. Psychoses, CNS excitement, insomnia, drowsiness, headache, myalgia, arthralgia, dizziness, and convulsions have also been reported. Skin rashes and other allergic reactions may occur.

Mutagenicity. An increase in chromosomal aberrations has been seen in children given nifurtimox.[1]

1. Gorla NB, *et al.* Thirteenfold increase of chromosomal aberrations non-randomly distributed in chagasic children treated with nifurtimox. *Mutat Res* 1989; **224:** 263–7.

Pharmacokinetics

Nifurtimox is well absorbed and rapidly metabolised after oral doses.

◊ References.

1. Paulas C, *et al.* Pharmacokinetics of a nitrofuran compound, nifurtimox, in healthy volunteers. *Int J Clin Pharmacol Ther Toxicol* 1989; **27:** 454–7.
2. Gonzalez-Martin G, *et al.* The pharmacokinetics of nifurtimox in chronic renal failure. *Eur J Clin Pharmacol* 1992; **42:** 671–3.

Uses and Administration

Nifurtimox is a nitrofuran derivative with antiprotozoal activity. It is of value in the treatment of American trypanosomiasis (Chagas' disease) due to infection by *Trypanosoma cruzi*, especially the early acute stage of the disease. In African trypanosomiasis it has some activity against *T. brucei gambiense*, the organism responsible for West African sleeping sickness.

Nifurtimox is given orally in 3 to 4 divided doses. It is better tolerated by children than by adults. Treatment for American trypanosomiasis is given for 60 to 120 days (but see below). Doses for adults are 8 to 10 mg/kg daily. Doses for children are: aged 1 to 10 years, 15 to 20 mg/kg daily for 90 days; aged 11 to 16 years, 12.5 to 15 mg/kg daily for 90 days.

Leishmaniasis. Mucocutaneous leishmaniasis of the New World (p.824) is usually treated with pentavalent antimony or, in those who do not respond, with amphotericin B or pentamidine. However, nifurtimox 10 mg/kg daily for a minimum of 4 weeks has been shown to be effective in cases of mucocutaneous leishmaniasis in Colombia and Brazil. Despite this, toxic effects with nifurtimox are common and its role as a second-line drug or with pentavalent antimony has not been established.[1]

1. WHO. Control of the leishmaniases. *WHO Tech Rep Ser 793*, 1990.

African trypanosomiasis. Nifurtimox has been tried as an alternative to melarsoprol or eflornithine in the meningoencephalitic stage of *Trypanosoma brucei gambiense* infection (p.827), but higher doses than those used in American trypanosomiasis are necessary. A good initial response was achieved[1] in 25 patients with nifurtimox 15 mg/kg daily for 60 days, but 3 patients relapsed while still receiving nifurtimox and a further 12 of 19 patients who were followed up relapsed subsequently. An attempt[2] to improve the response by increasing the daily dose even higher to 30 mg/kg for 30 days resulted in substantial toxicity and only a modest improvement in results, with 9 of 25 patients relapsing. However, promising results have been reported[3] from use of oral nifurtimox 15 mg/kg daily for 10 days with eflornithine 400 mg/kg daily intravenously for 7 days.

1. Pepin J, *et al.* An open clinical trial of nifurtimox for arseno-resistant Trypanosoma brucei gambiense sleeping sickness in central Zaire. *Trans R Soc Trop Med Hyg* 1989; **83:** 514–17.
2. Pépin J, *et al.* High-dose nifurtimox for arseno-resistant Trypanosoma brucei gambiense sleeping sickness: an open trial in central Zaire. *Trans R Soc Trop Med Hyg* 1992; **86:** 254–6.
3. Priotto G, *et al.* Nifurtimox-eflornithine combination therapy for second-stage Trypanosoma brucei gambiense sleeping sickness: a randomized clinical trial in Congo. *Clin Infect Dis* 2007; **45:** 1435–42.

American trypanosomiasis. The treatment of American trypanosomiasis (p.827) is generally unsatisfactory, but nifurtimox is of value especially in the acute phase. However, there has been controversy over its ability to cure completely, that is to eradicate all parasites, in chronic disease.[1] Doses recommended by WHO[2,3] are 8 to 10 mg/kg daily in three divided doses for adults, and 15 to 20 mg/kg daily in four divided doses for children. WHO recommends that nifurtimox should be given for 60 or 90 days.[2,3] Some in the USA[4] suggest a 90- to 120-day regimen for adults but nifurtimox is not well tolerated and the experience of other workers[1] suggests that few patients may complete the full course.

1. Gutteridge WE. Existing chemotherapy and its limitations. *Br Med Bull* 1985; **41:** 162–8.
2. WHO. Control of Chagas disease: second report of the WHO expert committee. *WHO Tech Rep Ser 905* 2002. Available at: http://libdoc.who.int/trs/WHO_TRS_905.pdf (accessed 17/07/08)
3. WHO. *WHO model formulary.* Geneva: WHO, 2004.
4. Abramowicz M, ed. *Drugs for parasitic infections*. 1st ed. New Rochelle NY: The Medical Letter, 2007.

Nimorazole *(BAN, rINN)*

Nimorazol; Nimorazolum; Nitrimidazine. 4-[2-(5-Nitroimidazol-1-yl)ethyl]morpholine.

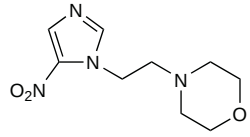
Ниморазол

$C_9H_{14}N_4O_3$ = 226.2.

CAS — 6506-37-2.

ATC — P01AB06.

ATC Vet — QP51AA06.



Pharmacopoeias. In *It.*

Adverse Effects and Precautions

As for Metronidazole, p.837.

Pharmacokinetics

Nimorazole is readily absorbed from the gastrointestinal tract. Peak blood concentrations are achieved within 2 hours, and high concentrations are reported to occur in salivary and vaginal secretions. Trichomonicidal urinary concentrations may persist for up to 48 hours after a dose. It is excreted in the urine together with 2 active metabolites. Unchanged drug and metabolites also appear in breast milk.

Uses and Administration

Nimorazole is a 5-nitroimidazole derivative. It has antimicrobial actions and uses similar to those of metronidazole (p.839).

In the treatment of trichomoniasis, the usual dose of nimorazole is 2 g orally as a single dose with a main meal. It may alternatively be given in a dose of 1 g every 12 hours for three doses, or 250 mg three times daily for 5 to 7 days. In amoebiasis, nimorazole 1 g is given twice daily, usually for 5 to 10 days and in giardiasis a dose of 500 mg is given twice daily, usually for 5 to 7 days.

Nimorazole may also be used in the treatment of acute ulcerative gingivitis in a dose of 500 mg twice daily for 2 days.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Naxogin; Vagarne†; ***Austria:*** Naxogin; ***Belg.:*** Naxogin; ***Braz.:*** Naxogin; ***Chile:*** Naxogin†; ***Ger.:*** Esclama†; ***Rus.:*** Naxogin (Наксоджин).

Multi-ingredient: ***Arg.:*** Vagarne†; ***Braz.:*** Naxogin Composto; ***Chile:*** Naxogin Compositum; Naxogin Dos†; ***Indon.:*** Gynoxa; Naxogin Complex.

Nitazoxanide *(BAN, USAN, rINN)*

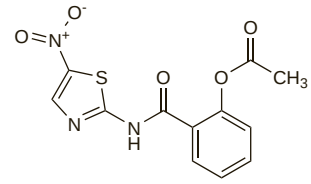
Nitazoxanida; Nitazoxanidum; PH-5776. *N*-(5-Nitro-2-thiazolyl)salicylamide acetate.

Нитазоксанид

$C_{12}H_9N_3O_5S$ = 307.3.

CAS — 55981-09-4.

ATC — P01AX11.



Adverse Effects

The most common adverse effects associated with nitazoxanide are abdominal pain and diarrhoea. Nausea and vomiting, flatulence, and increased appetite have also been reported. Headache may occur. Other reported adverse effects include fever, malaise, pruritus, sweating, dizziness, and rhinitis. Discoloration of urine and of the eyes has been reported rarely. Increased creatinine and liver enzyme values have been noted.

Pharmacokinetics

Nitazoxanide is absorbed from the gastrointestinal tract after oral dosage and is rapidly hydrolysed to an active desacetyl metabolite, tizoxanide. Tizoxanide then partially undergoes conjugation, primarily by glucuronidation. The extent of absorption is enhanced if given with food and peak plasma concentrations of tizoxanide and the glucuronide are seen 1 to 4 hours after an oral dose. The parent drug is not detected in plasma. Tizoxanide is more than 99% bound to plasma proteins. About two-thirds of an oral dose of nitazoxanide is eliminated in the faeces and one-third in the urine; tizoxanide is excreted in the urine, bile, and faeces, while the glucuronide is excreted in only the urine and bile.

Uses and Administration

Nitazoxanide is used for the treatment of cryptosporidiosis and giardiasis in immunocompetent patients. It is given orally and should be taken with food. Doses are 100 mg twice daily for 3 days in those aged 1 to 3 years, 200 mg twice daily for 3 days in those aged 4 to 11 years, and 500 mg twice daily for 3 days in adults. Nitazoxanide has also been tried in a number of other protozoal and helminth infections, particularly in immunocompromised patients, including those with HIV infection. It is also being investigated for the treatment of rotavirus disease and *Clostridium difficile* colitis.

◊ Reviews.

1. Bailey JM, Erramouspe J. Nitazoxanide treatment for giardiasis and cryptosporidiosis in children. *Ann Pharmacother* 2004; **38:** 634–40.
2. Fox LM, Saravolatz LD. Nitazoxanide: a new thiazolide antiparasitic agent. *Clin Infect Dis* 2005; **40:** 1173–80.
3. Musher DM, *et al.* Nitazoxanide for the treatment of Clostridium difficile colitis. *Clin Infect Dis* 2006; **43:** 421–7.
4. Anderson VR, Curran MP. Nitazoxanide: a review of its use in the treatment of gastrointestinal infections. *Drugs* 2007; **67:** 1947–67.

Protozoal infections. As well as its established use in cryptosporidiosis (p.823) and giardiasis (p.824), nitazoxanide has been used in other protozoal infections including intestinal amoebiasis (p.822), blastocytosis (p.823), and microsporidiosis (p.826).