

**Pharmacopoeias.** In *Chin.*, *Eur.* (see p.vii), *Jpn.*, and *US*.

**Ph. Eur. 6.2** (Netilmicin Sulphate). A substance obtained by synthesis from sisomicin. The potency is not less than 650 units/mg, calculated with reference to the dried substance. A white or yellowish-white, very hygroscopic, powder. Very soluble in water; practically insoluble in alcohol and in acetone. A 4% solution in water has a pH of 3.5 to 5.5. Store in airtight containers. Protect from light.

**USP 31** (Netilmicin Sulfate). The potency is equivalent to not less than 595 micrograms of netilmicin per milligram, calculated on the dried basis. A white to pale yellowish-white powder. Freely soluble in water; practically insoluble in dehydrated alcohol and in ether. pH of a solution in water containing the equivalent of netilmicin 4% is between 3.5 and 5.5. Store in airtight containers. Protect from moisture.

**Incompatibility.** For discussion of the incompatibility of aminoglycosides, including netilmicin, with beta lactams, see under Gentamicin Sulfate, p.282. Netilmicin is also reported to be incompatible with furosemide, heparin, and vitamin B complex.

#### Adverse Effects, Treatment, and Precautions

As for Gentamicin Sulfate, p.282. Some studies suggest that netilmicin is less nephrotoxic and ototoxic than gentamicin or tobramycin, although others have not found any significant differences in their toxicity.

It has been suggested that peak plasma concentrations of netilmicin should not exceed 12 micrograms/mL for prolonged therapy, and troughs should be below 2 micrograms/mL.

**Effects on the cardiovascular system.** Severe hypotension was associated with netilmicin in a patient undergoing artificial ventilation.<sup>1</sup> Hypotensive episodes were of short duration and coincided with netilmicin injection. They almost disappeared when sedation was stopped.

1. Ryngsted T. Severe hypotension associated with netilmicin treatment. *BMJ* 1997; **315**: 31.

#### Interactions

As for Gentamicin Sulfate, p.283.

#### Antimicrobial Action

As for Gentamicin Sulfate, p.283. It is active against a similar range of organisms although it is also reported to have some activity against *Nocardia*. It may be somewhat less effective against *Pseudomonas aeruginosa*. It is not degraded by all of the enzymes responsible for aminoglycoside resistance, and may be active against some strains resistant to gentamicin or tobramycin, but this is less marked than with amikacin; for example, gentamicin-resistant *Providencia*, *Pseudomonas*, and *Serratia* are usually also netilmicin-resistant. Between about 5 and 20% of Gram-negative isolates are reported to be resistant to netilmicin.

#### Pharmacokinetics

As for Gentamicin Sulfate, p.284.

After intramuscular injection of netilmicin, peak plasma concentrations are achieved within 0.5 to 1 hour, and concentrations of about 7 micrograms/mL have been reported following doses of 2 mg/kg; similar concentrations are obtained after intravenous infusion of the same dose over 1 hour. Peak concentrations after rapid intravenous injection may transiently be 2 or 3 times higher than those following infusion. Standard, once-daily doses may produce transient peak concentrations of 20 to 30 micrograms/mL. In multiple dosing studies, netilmicin in usual doses every 12 hours produced steady-state concentrations on the second day which were less than 20% higher than those seen after the first dose.

The half-life of netilmicin is usually 2.0 to 2.5 hours. About 80% of a dose is excreted in the urine within 24 hours.

#### Uses and Administration

Netilmicin is a semisynthetic aminoglycoside antibiotic with actions and uses similar to those of gentamicin (p.284). It may be used as an alternative to amikacin (p.201) in the treatment of infections caused by susceptible bacteria that are resistant to gentamicin and tobramycin. As with gentamicin, netilmicin may be used with penicillins and with cephalosporins; the injections should be given separately.

Netilmicin is given as the sulfate but doses are expressed in terms of the equivalent amount of base; 1.5 g of netilmicin sulfate is equivalent to about 1 g of netilmicin. It is usually given intramuscularly in doses of 4 to 6 mg/kg daily as a single dose; alternatively, it may be given in equally divided doses every 8 or 12 hours; for the control of life-threatening infections, up to 7.5 mg/kg may be given daily in divided doses every 8 hours for short periods. In the management of urinary-tract infections, a single daily dose of 150 mg for 5 days may be given; for complicated urinary-tract infections, 3 to 4 mg/kg daily in divided doses every 12 hours has been given. A single dose of 300 mg has been licensed for gonorrhoea (p.191).

The same doses may be given by slow intravenous injection over 3 to 5 minutes or infused intravenously over 0.5 to 2 hours in 50 to 200 mL of infusion fluid; proportionately less fluid should be given to children.

Treatment with netilmicin is usually given for 7 to 14 days. Peak plasma concentrations below 12 micrograms/mL and troughs below 2 micrograms/mL have been recommended for divided daily dose regimens.

Dosage recommendations in infants and children vary somewhat. One regimen is 7.5 to 9 mg/kg daily in infants and neonates older than 1 week, and 6 to 7.5 mg/kg daily in older children, both given in divided doses every 8 hours. Premature infants and neonates less than 1 week old may be given 6 mg/kg daily in divided doses every 12 hours. An alternative regimen is 4 to 6.5 mg/kg daily in neonates less than 6 weeks of age, in divided doses every 12 hours, and 5.5 to 8 mg/kg daily in divided doses every 8 or 12 hours in older infants and children.

Dosage should be adjusted in all patients according to plasma-netilmicin concentrations, and this is particularly important where factors such as age, renal impairment, or prolonged therapy may predispose to toxicity, or where there is a risk of subtherapeutic concentrations. For discussion of the methods of calculating aminoglycoside dosage requirements, see Administration and Dosage, under Gentamicin, p.284.

#### Preparations

**USP 31:** Netilmicin Sulfate Injection.

**Proprietary Preparations** (details are given in Part 3)

**Arg.:** Netira†; **Austral.:** Netromycin†; **Austria:** Certomycin; **Belg.:** Netromycine†; **Braz.:** Netromicina; **Canad.:** Netromycin†; **Cz.:** Netromycine; **Denm.:** Netilyl†; **Fin.:** Netilyl; **Fr.:** Netromicine; **Ger.:** Certomycin; **Gr.:** Netromycin; **Hong Kong.:** Netromycin; **Hung.:** Netromycine; **India:** Netromycin; **Netspan.:** **Indon.:** Netromycin; **Isl.:** Netillin†; **Ital.:** Nettare†; **Malaysia.:** Netromycin; **Mex.:** Neticin†; **Netromicina.:** **Neth.:** Netromycine; **Norw.:** Netilyl; **NZ.:** Netromycine†; **Philipp.:** Keunmixin; **Netromycin.:** **Pol.:** Netromycine; **Port.:** Netromicina; **Tilici.:** **S.Afr.:** Netromycin; **Spain.:** Netrocini†; **Swed.:** Netilyl; **Switz.:** Netromycine; **Thal.:** Bacetrocin; **Nelini.:** Netili; **Netromycin.:** **Turk.:** Netira; **Netromycine.:** **UK.:** Netillin†; **Venez.:** Netromicina.

**Multi-ingredient. Ital.:** Netidex.

#### Nifuroxazide (rINN)

Nifuroksazidi; Nifuroksazid; Nifuroksazidas; Nifuroxazid; Nifuroxazida; Nifuroxazidum. 2'-(5-Nitrofurfurylidene)-4-hydroxybenzohydrazide.

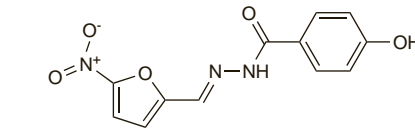
Нифуроксазид

$C_{12}H_9N_3O_5 = 275.2$ .

CAS — 965-52-6.

ATC — A07AX03.

ATC Vet — QA07AX03.



**Pharmacopoeias.** In *Eur.* (see p.vii).

**Ph. Eur. 6.2** (Nifuroxazide). A bright yellow crystalline powder. Practically insoluble in water; slightly soluble in alcohol; practically insoluble in dichloromethane. Protect from light.

#### Profile

Nifuroxazide is an antibacterial that is poorly absorbed from the gastrointestinal tract. It is given orally in a dose of 800 mg daily in divided doses in the treatment of colitis and diarrhoea.

#### Preparations

**Proprietary Preparations** (details are given in Part 3)

**Belg.:** Bacifurane†; **Erceluryl.:** **Braz.:** Passifuril; **Chile:** Diarfin†; **Cz.:** Erceluryl; **Fr.:** Bacterin; **Bifix.:** Diarfuryl; **Ediston.:** Erceluryl; **Erceryl.:** Lumifurex; **Pan-furex.:** Septidiaryl; **Gr.:** Erceluryl; **Hong Kong.:** Erceluryl; **Pan-furex.:** **Indon.:** Fuzide; **Nifudiar.:** Nifural; **Ital.:** Diarret†; **Mex.:** Akabar; **Dianm†.:** Eskapar; **Topron.:** **Philipp.:** Erceluryl; **Rus.:** Enterofuryl (Энтерофурил); **Singapore.:** Nirabenz; **Thal.:** Debby†; **Erceluryl.:** Erfuzide; **Turk.:** Diarfuryl; **Dunsal.:** Endosin; **Erceluryl.:** Erfuryl; **Furil.:** Nifuryl; **Nufuro.**

**Multi-ingredient. Chile:** Diaren; **Diarfin†.:** Enterol Con Nifuroxazida; **Im-ecol.:** Liracol; **Nifurat†.:** **Testisan.:** **Mex.:** Dia-Par Compuesto; **Eskapar Compuesto.**

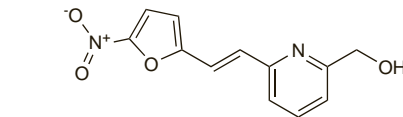
#### Nifurpirinol (USAN, rINN)

Furpirinol; Nifurpirinolium; P-7138.

Нифурпиринол

$C_{12}H_{10}N_2O_4 = 246.2$ .

CAS — 13411-16-0.



#### Profile

Nifurpirinol is a nitrofurantimicrobial used in veterinary medicine for the treatment of bacterial and fungal infections in ornamental fish.

#### Nifurtoinol (rINN)

Hydroxymethylnitrofurantoin; Nifurtoinol; Nifurtoinolium. 3-Hydroxymethyl-1-(5-nitrofurfurylideneamino)hydantoin.

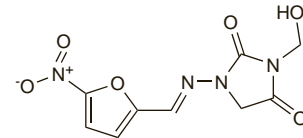
Нифуртоинол

$C_9H_8N_4O_6 = 268.2$ .

CAS — 1088-92-2.

ATC — J01XE02.

ATC Vet — QJ01XE02.



#### Profile

Nifurtoinol is a nitrofurantimicrobial with properties similar to those of nitrofurantoin (below) and is used in the treatment of urinary-tract infections. It is given orally in doses of up to 300 mg daily in divided doses.

#### Preparations

**Proprietary Preparations** (details are given in Part 3)

**Belg.:** Urfadyn PL.

#### Nifurzide (rINN)

Nifurzida; Nifurzidum. 5-Nitro-2-thiophenecarboxylic acid [3-(5-nitro-2-furyl)allylidene]hydrazide.

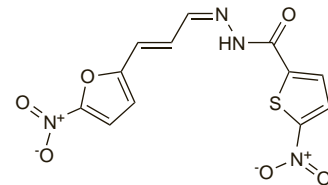
Нифурзид

$C_{12}H_8N_4O_6S = 336.3$ .

CAS — 39978-42-2.

ATC — A07AX04.

ATC Vet — QA07AX04.



#### Profile

Nifurzide is an antibacterial that is poorly absorbed from the gastrointestinal tract. It has been given orally in the treatment of diarrhoea.

#### Preparations

**Proprietary Preparations** (details are given in Part 3)

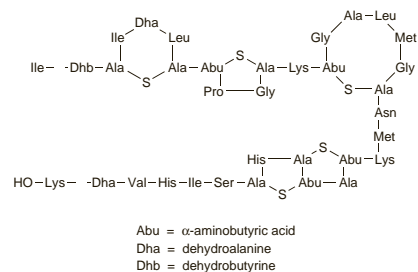
**Fr.:** Ricidenet†.

#### Nisin

E234; Nisina.

Низин

CAS — 1414-45-5.



#### Profile

Nisin is a polypeptide antibacterial produced by *Lactococcus lactis* (*Streptococcus lactis*). It is used as a food preservative.

It has been investigated for the treatment of various infections, including those caused by *Helicobacter pylori* and *Clostridium difficile*.